OCAST Programs Supplemental Information

Reviewer evaluations may be accessed at http://ogx.ok.gov

OCAST 2021 Oklahoma Applied Research Support Applications Approved Below the Funding Line

Rank	Application Number and Title	Organization and PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
20	AR21-042: Development of Reduced-order System Models for Next Generation Comfort Cooling Equipment	Oklahoma State University Craig Bradshaw	$60,000	$60,000	$60,000	$180,000
21	AR21-032: Monolithically Integrated Flat Optics through Additive Manufacturing	Amethyst Research Inc. Weerasinghe Priyantha	$249,959	249,963	$0	$499,922
22	AR21-062: Improving Nutrition and Sustainability: Breakfast Cereal Product Made from Cricket Protein	All Things Bugs LLC Aaron T. Dossey	$210,313	112,313	$0	$322,626
23	AR21-058: Ultrafast Photodetectors for the Mid-infrared Band	Amethyst Research, Inc. Jeff W. Sharp	$149,999	150,000	$0	$299,999
24	AR21-019: Design of Solar-Energy-Combined Desalination Systems	Oklahoma State University Seokjhin Kim	$45,000	$45,000	$0	$90,000
25	AR21-011: Multi-Target Peptide: A Drug to Remember	University of Oklahoma Health Sciences Center Anne Kasus-Jacobi	$50,000	$0	$0	$50,000
	Totals		**$765,271**	**$617,276**	**$60,000**	**$1,442,547**

OCAST 2021 Oklahoma Applied Research Support Applications Not Approved for Funding

Application	Organization	PI	Title
AR21-075	MITO Material Solutions, Inc.	Bhishma Raj Sedai	MANUFACTURING OF HYBRID GRAPHENE FILLERS (A-GO) FOR COMPOSITES REINFORCEMENT AND ANTI-CORROSION COATINGS
AR21-004	Veroplane Inc	Chuck Boyer	Adaptive & Resilient Unmanned Flight Control System
AR21-033	Amethyst Research, Inc	Keith Jamison	Development of high speed, high sensitivity NDIR trace gas sensors
AR21-039	Ghost Display Technologies, LLC	Gijun Seo	High-resolution SWIR sensors using optical ROIC integration
AR21-046	Oklahoma State University	Do Young Kim	Flexible infrared-stimulated self-emitting projection screen
AR21-056	Tulsa Community Foundation	Kastle Jones	Advanced Aerial Mobility Living Laboratory
AR21-059	Sustainment Technologies Inc	Michael Morford	Developing AI-Based Solution for Segmentation of CAD Model's Geometric Entities from Part Designs for Maintenance Repair and Overhaul (MRO) & Military Depot-Level Sustainment for the Aerospace & Defense Industry
AR21-061	Skydweller US, Inc.	Joel David Martin	Multi-Mode Airborne Radar and All-Weather Detect and Avoid Demonstration with Long-Endurance Unmanned Aerial Vehicle Platform
AR21-066	BERRY AVIATION, Inc.	Rick Gaeta	Accelerated-OARS-Plan-for-Multirole-Unmanned-Aerial-System
AR21-003	Excitant Therapeutics LLC	Yuhong Anna Wang	A Drug Candidate Targeting PPARa for DME
AR21-010	University of Oklahoma	Christian El Amm	Surgical Enhanced Visualization Systme
AR21-041	Extraction Alternatives Biotech	Patricia Klee	A Toll Processing Facility: Effects of pre-processing and turbulent flow of liquefied, light hydro-carbon gasses on oil extraction from oil bearing agricultural commodity products
AR21-045	Optecks, LLC	Hakki Refai	WEARABLE LUNG FLUID SENSOR FOR REMOTE HEALTH MONITORING
AR21-063	Viribus VR Labs	Robert A. Eskew	Evaluation of a Novel Virtual Reality System for the Treatment of Children with Cerebral Palsy
AR21-079	General Genomics	Warren Gieck	Individualized Treatment and Illness Symptoms Risk Assessment (ITAI-SRA)
AR21-002	Bedrock Gas Solutions	Michael Mercer	H24OK - Oklahoma's First Hydrogen/CNG Fueling Station
AR21-009	Oklahoma State University	Javier Vilcaez	A new methanogenic biodegradation method to remove oil from petroleum produced water
AR21-027	Pinnacle Partners West LLC	Mark Nash	Process 1st Software Development
AR21-028	Oklahoma State University	Yongwei Shan	Intelligent Quality Assurance and Integration Tool for Sewer Inspection Data
AR21-036	Oklahoma State University	Christian K. Bach	Development of a validated heat exchanger charge model for next generation low GWP refrigerants
AR21-053	Amethyst Research, Inc	Khalid Hossain	Failure Analysis Toolset for Semiconductor Devices using Ion Beam Induced Current Microscopy

Application	Organization	PI	Title
AR21-054	Nitro-Chem Solutions, LLC	Jim Williams	Field Tests of nanoActiv® Nanoparticle Fluids.
AR21-060	University of Tulsa	Mahdi Khodayar	Interpretable Artificial Intelligence Framework for Smart Grid Fault and Cyberattack Detection, Localization, and Recovery

PI: Jeff Potts	**Project Title: Meta and Multimodal Learning for Smart Visual Borescope Inspection**
AR21-070	**Organization:** Baker Hughes
Rank: 1	**Project Type: Accelerated**
Approved Funding	**Year 1:** $152,485 **Year 2:** $173,551 **Year 3:** $170,495 **Total:** $496,531
Research	Borescope visual inspection is a non-destructive testing method that can detect the internal structure and surface features of various equipment parts and assemblies. Developments in computer vision and image processing have significantly improved the capability of visual techniques for defects identification. Although the video borescope solutions from Baker Hughes provide high definition image quality with 3D measurement details, recognition of defects still requires domain expertise, which is challenging, time-consuming, and subject to human error. To address this issue, a prospective solution is to introduce a next-generation borescope by interweaving vision with the AI technology for automatic defect recognition. However, successful implementation of the deep learning algorithms heavily depends on the training dataset size and quality, and such large datasets are usually unavailable, especially for visual inspection tasks. Further, the implementation of machine learning models in portable devices, such as a borescope, is challenging due to the limitations with computational capabilities. The overall objective of this collaborative research proposal is to develop an AI-driven borescope for visual inspection of safety-critical equipment by introducing a graph network-enabled meta-learning framework. We will accomplish the objective by 1) developing a few-shot meta-learning scheme for the visual borescope classification task and 2) introducing graph network-enabled structure for few-shot learning. Our focus is to investigate capability of Model-Agnostic and Reptile Meta-Learning algorithms with the developed new multimodal FewShot-BorescopeNet dataset for adapting to new environments with a few training examples and draw a baseline for visual inspection. We will then introduce new deep-learning architectures, referred to as Optimized-Meta Graph Neural Network, to make use of both the labeled and unlabeled data for training by correlating the images via a relationship graph. We expect this new machine-learning framework will significantly improve the generalization capability of the models for new images not encountered during training. We will evaluate these machine learning algorithms numerically and experimentally using field data. The trained model will be deployed onboard the existing borescope hardware for the field test. Success of the project will lead to a next-generation borescope with improved autonomy.
Economic Benefit	Baker Hughes has operated a research and development center in Oklahoma City, OK, since 2016. More than $100 million has been invested in this state-of-the-art facility, with more than 50 full-time employees working in advanced technology innovation, creating a significant economic impact on the State of Oklahoma. This accelerated applied research project aims to design, develop, test and validate algorithms with the potential to significantly improve the performance and shorten the development time of automated defect recognition algorithms, which have become a key differentiating feature of visual inspection technology solutions offered by Baker Hughes. This will, in turn, create significant benefits for customers of Baker Hughes who utilize these technologies for critical inspections of, e.g, aircraft engines and power generation equipment, who rely upon these algorithms to capture critical defects that could compromise asset performance.

	Baker Hughes technical staff will collaborate with the OSU's research team in both theoretical and experimental work in this project. The developed system will maximize the probability of detection of defects in order to ensure measurement accuracy. The research activities will also improve the scientific and technical capabilities of both OSU and Baker Hughes personnel, therefore enhancing the R&D capabilities of Baker Hughes. As a result, the research outcome will contribute to the next-generation video borescopes product for Baker Hughes, offering benefits to aerospace companies with a presence in the state, both of which may increase highly skilled job creation in Oklahoma. In the long-term, the developed system will be expanded to other Baker Hughes products and business units, such as Pan-Tilt-Zoom Cameras, Waygate Technologies Robotics inspection services, and Avitas aerial inspection services. Furthermore, the visual detection efficiency is expected to increase significantly due to the advanced artificial intelligence (AI) algorithm implementation. The borescopes are commonly used in the visual inspection of aircraft engines, aero-derivative industrial gas turbines, steam turbines, diesel engines, and automotive and truck engines. Considering that aerospace, autonomous vehicles, and petroleum manufacturing are Oklahoma's strongest industry ecosystems, a powerful borescope will significantly improve the visual inspection efficiency in those industries and thus benefit the entire state's economy.
Match Source	Matching funds will be contributed by Baker Hughes Company, located in Oklahoma City, OK. This match support is estimated in the amount of $530,898 for the work provided by Baker Hughes and includes personnel support, supplies, and field validation test. Personnel: Matching funds will be provided by Baker Hughes Company to support Baker Hughes researchers. Each member will be paid for between 100 and 200 hours of work, depending on role, at a burdened labor rate of $161 per hour for each year of the project. Fringe benefits will be provided as a direct labor cost. Supplies: Funds in the amount of $210,000 will be provided by Baker Hughes for the purchases of a Mentor Visual iQ borescope for algorithm deployment and testing, along with specialized cloud-based deep learning computer services required to carry out the algorithm development, testing and deployment activities for this project.
Research Area	Aircraft Manufacturing

PI: Jay Martin, CP, FAAOP	**Project Title: Modular Exoskeleton Interface for Greater Comfort and Mobility**
AR21-015	**Organization:** Martin Bionics
Rank: 2	**Project Type: Accelerated**
Approved Funding	**Year 1:** $300,000 **Year 2:** $150,000 **Year 3:** $0 **Total:** $450,000
Research	The goal of this project is to develop a modular, lightweight, and volume accommodating orthotic exoskeleton using dynamic and fabric-based materials to enhance user's comfort and functional outcomes. Instead of sculpting conventional orthotic devices using rigid or semi-rigid custom composites or plastics, Martin Bionics created counter-intuitive methods for making exoskeletons and orthotics using modular assemblies of lightweight fabrics and dynamic materials. The physical interface with the human body and skin is by far the most important component of a successful orthotic device. Conventional orthotic designs have seen very little change in how they are fit to the user, with the only primary changes in the past 50 years being the materials used. Many orthotics users have not had their needs met by traditional orthotic devices and end up with limited quality of life due to discomfort from their antiquated orthotic interface. Conventional fitting methods are expensive, time consuming and impractical to meet the needs of orthotics users around the world. Especially in areas of the world without access to expensive equipment and labs for forming resins and thermoplastics, there is a need for modular components that can be fit to a user without expensive tools or extensive training. The modularity and simplicity of the Martin Bionics designs enables for wide-spread use around the world and truly meets the needs of those even in developing nations. The modularity of this design will enable a clinical practitioner to fit the socket in just one appointment using only simple hand tools, and its dynamic nature will provide greater stability and fit than with conventional methods. It is anticipated to serve as the initial step towards replacing crutches, conventional orthotics, and eventually wheelchairs, as Martin Bionics is simultaneously creating computer controlled powered joints to work in conjunction with this exoskeleton interface design.
Economic Benefit	Martin Bionics Innovations is developing a revolutionary method of fitting orthotic users and those who need additional muscular support and stability through complaint, adjustable materials. The development efforts will result in a product that will serve as a replacement for many outdated, uncomfortable orthotic devices as well as create a platform for high-tech exoskeleton interfaces, which Martin Bionics is developing. It will generate significant economic impact to the Oklahoma economy through company revenue and job creation. Through the success of this project we anticipate the creation of over 40 new jobs and annual revenue of over $30,000,000 within 5 years. This success will position Martin Bionics Innovations as a world-class leader in orthotic interface designs, which it already is for prosthetics interface designs. Most importantly, the daily quality of life of persons who rely on orthotics and assistive devices will be significantly enhanced.
Match Source	Martin Bionics Innovations, LLC will provide 100% of the matching funds for this project in the form of a cash match. This project will ultimately allow Martin Bionics Innovations to launch their patent pending technology to the commercial market, and see direct benefit to the orthotics user populations. The successful

	development of this technology will allow for a quick product launch and commercial success, generating significant and long-term economic impact.
Research Area	Biotechnology

PI: Brent Stockton	**Project Title: Next Generation Defrosting Sequence for AAON's Variable Speed Air-Source Heat Pump RTUs**
AR21-071	**Organization:** AAON Inc.
Rank: 3	**Project Type: Accelerated**
Approved Funding	**Year 1:** $138,960 **Year 2:** $115,000 **Year 3:** $127,890 **Total:** $381,850
Research	Timed defrost initiation and termination (TDI/T) is still commonly used in heat pump equipment, including for AAON's rooftop unit heat pumps. However, smarter defrost initiation strategies, especially if combined with a controlled defrost process, can substantially reduce energy consumption. Current defrost algorithms are not properly accounting for actual outdoor coil frosting conditions under various ambient conditions. This generally leads to defrosting processes being initiated more often than necessary, reducing occupant comfort, and increasing equipment energy consumption. More problematically, under rare and severe weather conditions, current algorithms may lead to incomplete defrosting, risking heat pump's reputation and occupant comfort. In addition, they do not take advantage of modern variable speed components that promise the ability for further adjustments and defrosting delay. The project will develop a next generation smart control strategy to delay defrost initiation and control the defrosting process itself, specifically for AAON's variable speed heat pump RTUs. This will allow a reduction in energy consumption while simultaneously reducing comfort complaints due to temperature fluctuations and ensuring robustness of the equipment's controls under a wide range of weather conditions. The project includes development of the algorithms, simulation of their impact on seasonal heating energy efficiency, and rigorous testing of their robustness. Simulation and algorithm development will be conducted primarily at OSU with AAON's controls engineers implementing the algorithms into the equipment's embedded control system. Testing will be conducted both, at Oklahoma State University's psychrometric chambers as well as at the AAON NAIC's climatic chamber. At Oklahoma state, the algorithms will first be tested and parametrized using steady state operating conditions and then later with diurnal temperature profiles. In the third year of the project, additional testing and hardening of the control algorithms will occur at the AAON NAIC climatic chamber utilizing its wind, snow, and low temperature rain capabilities. This will result in a algorithm ready for field implementation testing by 2025.
Economic Benefit	The current defrosting algorithms hinder future growth of AAON's variable speed heat pump equipment sales into areas traditionally served by gas and inefficient resistive electric heating. We anticipate that this project will provide a key technology to continue to grow our heat pump equipment sales beyond the 2025 target of $75M/year. Our growth in the variable speed heat pump market has been a huge success in recent years; it is likely that this project will contribute to an increase in sales of $20M annually by 2028. Since AAON manufactures these units as a semi-custom series this also will likely contribute to growing our Oklahoma based workforce by 2 research and development engineers, 1 technician, and 10 manufacturing staff by 2028.
Match Source	We anticipate a combined AAON cost-sharing contribution in the amount of $385,000 which includes the student internships, staff engineer and technician time and travel expenses for visits to OSU, facility usage expenditures, several variable speed heat pump units, as well as instrumentation, materials and

	supplies for the student training and equipment testing to be conducted at AAONs NAIC.
Research Area	Energy Conversion

PI: Aravind Seshadri	**Project Title: Data Driver Controller Development for Web Guiding Systems**
AR21-034	**Organization:** Roll-2-Roll Technologies LLC
Rank: 4	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $54,033 **Year 2:** $ **Year 3:** $0 **Total:** $54,033
Research	Advances in automation over the last 10 years have significantly improved the productivity of Roll-to-roll machines. The automation advances rely on sensors, transducers and actuators that measure and control physical quantities such as web position. Significant increases in productivity seen in the last few decades have been possible by making them faster, precise and more accurate. However, the next generation of automation in the R2R industry demands control systems to not only react to disturbances but to proactively identify deterrents to its performance and subsequently mitigate their effect to achieve higher performance. Roll-2-Roll Technologies' first generation of web guiding products are reactive control systems. This project will explore the proof-of-concept data driven approach for the development of a proactive disturbance identification system that could eventually lead to proactive control. The first step towards the goal is to understand if the data collected, with existing sensors within the web guiding systems, would show correlation to some common disturbances experienced by the web guiding system. The goal of this project is to answer that question. Experiments will be conducted on a small scale R2R machine, wherein common disturbances related to machines (misaligned rollers, eccentric rollers), materials (non-uniform density, thickness, splices), transport conditions (loss of traction, wrinkles, speed and tension issues), and operator errors will be introduced. Data will be collected from existing sensors, actuators and controllers from the web guiding system to see the correlation between the disturbances and the data collected. Analysis of the data will be carried out using both statistical and dynamic system identification methods. Based on the analysis, models (statistical/heuristics/dynamics/machine learning) for robust identification and classification would be created. If the models are able to accurately (>75% accuracy) predict the disturbances based on gathered data then this project is a success. Successful completion of this proof-of-concept would enable Roll-2-Roll Technologies to eventually develop a web guiding system that can proactively control the deterrents in real-time. The proactive control could involve automatic gain changes of the web guiding system, coordination with the overall R2R machine to change certain process and transport parameters, or an alert to the operator to proactively remove deterrents.
Economic Benefit	Roll-to-Roll (R2R) manufacturing, one of the few manufacturing industries still active within the U.S. It is employed to produce a wide variety of products such as baby diapers, sanitary products, flexible packaging, labels, tapes, plastics bags, and even electronics printed on a flexible substrate; there are over 20,000 R2R manufacturers in the US creating revenues in excess of $100 bn. Many are forced to produce different products, with a variety of sizes and physical properties, within the same R2R machine, to meet the rapidly changing market demand. Roll-2-Roll Technologies is one of three US based web guide manufacturers that produces automatic devices (called web guiding systems) that help manufacturers increase the productivity of their R2R machines by reducing waste and increasing processing speed. The data driven research proposed in this project will enable the next generation of automation for web guiding systems; such a system not only reacts to disturbances within the machines but will proactively identify

	deterrents to its performance for subsequent mitigate of the deterrents to achieve higher performance. Emerging R2R processes and existing R2R processes with frequent product changeover would benefit from products commercialized based on this proposed research. Specifically, Roll-2-Roll Technologies would be able to expand its market share by providing a solution with significantly higher value proposition than the current state-of-art solutions in the market. Successful commercialization of the research in this project could have a direct impact on the revenue for Roll-2-Roll Technologies LLC. This will allow the company to expand its market share with its higher value proposition and allow it to compete with large multinational competitors. Successful commercialization of this project is anticipated to generate over $2 million in additional revenues for our company within five years from the completion of this project. The commercialization efforts will create jobs in Stillwater and bring additional revenue into Oklahoma since almost all of our potential customers are outside of Oklahoma. This project is anticipated to add about 4 full-time employees with an overall annual payroll of over $250,000 within five years from the completion of this project.
Match Source	The matching funds for this project will be provided by Roll-2-Roll Technologies from the cash reserves.
Research Area	Intelligent Controls

PI: Eldon Jupe	**Project Title: Development of a serum biomarker test for predicting disease relapse in multiple sclerosis**
AR21-012	**Organization:** Progentec Diagnostics, Inc.
Rank: 5	**Project Type: Accelerated**
Approved Funding	**Year 1:** $252,772 **Year 2:** $ **Year 3:** $0 **Total:** $252,772
Research	Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) afflicting over 2.5 million people worldwide. MS is thought to be initiated by an autoimmune response to CNS antigens leading to the destruction of neurons. MS has a relapsing and remitting course. Relapses are disease flare ups or exacerbations followed by periods of remission where patients partially or fully recover. Neurological damage accumulates with repeated relapses resulting in accrued loss of function and ultimately disability. Currently, gadolinium (Gd) MRI contrast scans are used to determine relapse. However, MRIs are expensive and there are emerging concerns about Gd toxicity with repeated exposures. Often MRIs are used reactively after clinical relapse is already evident and significant inflammatory damage has occurred. Therefore, there is an urgent need for an inexpensive, safer, non-invasive test for early proactive identification of MS relapse. The goal of this project partnering Progentec and the Oklahoma Medical Research Foundation (OMRF) is to complete the development and refinement of the first clinically actionable biomarker-based blood test to proactively distinguish MS patients at risk of relapse from those in remission. Progentec has significant experience in development, commercialization, marketing, and reimbursement of clinical tests. Our team completed the development of a lupus flare risk index and released the test last year. OMRF and Progentec investigators bring over 50 years' experience in neurology, autoimmunity, and clinical disease research. Our preliminary data on an MS patient cohort indicate that serum blood protein profiles have strong potential to differentiate relapse from remission. The proposed research will focus on confirming the candidate serum protein biomarkers from our preliminary data in two additional independent MS cohorts (Aim 1). The top biomarker candidates confirmed in Aim 1 will be validated using an independent, innovative, highly robust, microfluidic analysis platform used for commercial testing in our CAP-CLIA clinical laboratory (Aim 2). A successful outcome of this proposal will be a Relapse Risk Index (RRI) test refined and optimized using advanced machine/deep learning analytical methods. This non-invasive biomarker test to assess MS disease activity will be a powerful tool with applications to clinical care, patient selection for clinical trials and identification of targets for new therapies.
Economic Benefit	Progentec Diagnostics, Inc. is focused on providing state of the art diagnostics for MS patients. Progentec has established a strong partnership with the Oklahoma Medical Research Foundation (OMRF), which is an Autoimmunity Centers of Excellence (ACE) in the USA. Progentec has developed a strong presence in the social media and patient support areas through their mobile app and patient portal through which Progentec has access to about 90,000 users in the US on a quarterly basis and with new features and platforms being added, we expect this to grow significantly. The goal of the proposed project is to develop a serum biomarker test for predicting disease relapse in multiple sclerosis Progentec is confident that this OARS project will have a tremendously positive impact on Oklahoma's economy. Progentec has a fully set-up and accredited CLIA lab located in Oklahoma City. The project will result in a significant amount of activity

	generation within Oklahoma City, ranging from additional infrastructure development and capital investment in operating a lab to deployment of scientific and lab personnel thereby leading to creation of high paying jobs and boosting the economy. We expect a strong interest in the market for the tests and therefore a strong uptake and expect the tests to generate significant revenues. With this we expect to have a positive impact on the overall commercial activity levels within the area as other ancillary and supporting services are developed to support this business.
Match Source	Progentec Diagnostics, Inc. will provide the matching funds required for the project through private funds using the company's own resources as well as money raised from investors. Progentec has proposed a budget of $527,337 ($256,972 OCAST + $270,365 Matching Funds) for the successful completion of the research project. Progentec will be providing for this match of $270,365 through the company's own resources and capital raised from investors. The company is committed to making sure that adequate funds will be earmarked towards meeting the matching requirements of this project. The funds raised through investors are linked to commercial performance metrics and will be used only towards commercialization related activities
Research Area	Diagnostic and Therapeutic Biotechnology

PI: Craig Bradshaw	**Project Title: Development of Semi-Empirical Compressor Model to Reduce Time to Market for Next Generation Vapor Compression Systems**
AR21-040	**Organization:** Oklahoma State University
Rank: 6	**Project Type: Accelerated**
Approved Funding	**Year 1:** $60,000 **Year 2:** $60,000 **Year 3:** $60,000 **Total:** $180,000
Research	Regulatory changes, aimed at mitigating climate change, are rapidly forcing Air-Conditioning (AC) and Heat Pump (HP) manufacturers to include more diverse product lines and add additional features such as compressor modulation. Traditional development of modulating compressor systems requires large experimental datasets and heuristic design iterations that are slow and expensive. With the critical addition of fast, accurate, compressor models that can extrapolate beyond trained bounds, Oklahoma-based AC and HP manufacturers have an opportunity to create a competitive advantage during the development of their next generation products. This project will accomplish this by developing a predictive modeling platform developed by Oklahoma State University (OSU) specifically for expediting compressor selection. The development will focus on enhancing the speed and flexibility to expedite the addition of new features and modulation in future products. The development will leverage machine learning techniques and data collected on in-house compressor testing infrastructure to generate the model. The final model will be a semi-physical model, validated with high-fidelity data, that is more extensible, flexible, and fast enough to solicit a strong economic impact. These results will be disseminated to the industry through the Center for Integrated Building Systems (CIBS) at OSU with the strong support of an Oklahoma-based AC and HP manufacturer, AAON Inc. CIBS includes a plurality of Oklahoma-based companies, which creates the potential for a multiplicative effect on the economic impact that traditional relationships are unable to match.
Economic Benefit	This project has the potential to leverage the OCAST funding by a factor of 100:1, add up to 215 jobs and generate $21.3M in economic impact. This is accomplished by spreading the economic impact across all the companies (including four Oklahoma-based) that are members of the Center for Integrated Building Systems.
Match Source	CIBS will match 1:1 with in-kind project funds that originated 100% from industry sponsors of CIBS.
Research Area	Energy Conversion

PI: Rui Q Yang	**Project Title: Tunable interband cascade lasers for detection of hydrocarbons**
AR21-024	**Organization:** University of Oklahoma
Rank: 7	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	In this project, we propose to develop efficient and widely tunable single-mode interband cascade (IC) lasers (ICLs) in the 3 to 4 microns wavelength region for detection of hydrocarbons such as methane (CH4), ethane (C2H6), propane (C3H8), butane (C4H10), and pentane (C5H12). These ICLs will be combined with a newly emerged half-wave V-coupled cavity approach to widely tuning the lasing wavelength. This innovative approach will enable a tuning range of more than 30 nm, which is wide enough to scan across the fundamental rotational-vibration absorption lines of several hydrocarbons. As such, specific hydrocarbons can be correctly identified, and their concentrations can be accurately determined. ICL structures are based on quantum-engineered type-II quantum wells (QWs) made from III-V semiconductors. Building on our extensive experience and previous accomplishments in ICL research, we will design ICLs for continuous wave (cw) operation at room temperature and use molecular beam epitaxy (MBE) to grow the ICL structures. We will also do material characterization, laser device fabrication, and device testing. The goal is to achieve single-mode lasing with a side-mode suppression ratio (SMSR) exceeding 30 dB and a tuning range wider than 30 nm in a wavelength region from 3-4 microns. Also, these ICLs will be packaged into sensor prototypes in collaboration with our industrial partners to examine and validate their functionality of detecting hydrocarbons.
Economic Benefit	The market for gas sensors based on tunable diode lasers is projected to reach $736 million by 2025 at an annual growth rate of 7.6%. The proposed interband cascade laser will have better tunability and be more energy efficient than competing technologies in the wavelength range where hydrocarbon molecules can be detected. This innovation will have a significant impact on the performance and price of gas sensors used by the oil and gas industry. After the proof-of-principle demonstration, the technology can be extended to wavelength ranges that are useful for healthcare applications, such as metabolic monitoring and disease diagnosis, detection, and analysis of the volatile compounds in the exhaled breaths of patients. This project will initially create job opportunities to conduct the research at the University of Oklahoma. More jobs will be created as the technology is transferred to our industrial partners, whose portfolios are already well positioned to take advantage of the new tunable laser technology. The new technology will benefit customers in the oil and gas industry, the healthcare industry, and other areas of the Oklahoma economy.
Match Source	The matching funds are federal monies from an award entitled “Widely Tunable Single-Mode Interband Cascade Lasers,” which was granted by the National Science Foundation (NSF) to the University of Oklahoma (Grant No. ECCS-1931193 and total amount of $447,979). The NSF project is led by Rui Yang and Michael Santos, the same leadership as for the proposed OCAST project, which will ensure smooth coordination and mutual support. OU will provide $90,000 in matching funds ($45,000 for Year 1 and $45,000 for Year 2) from this NSF grant. The dates for the NSF grant were originally set at September 1, 2019 to August 31, 2022. However, the end date will be extended to August 31, 2023 (due to the interruption caused by the pandemic). The NSF project, which focuses on the development of the half-wave V-coupled cavity for wavelength tuning, is

	complementary to the proposed OCAST project, which will advance this device concept to commercial application as a chemical sensor of hydrocarbon molecules.
Research Area	Optics and Photonics

PI: Rick Pendergraft	**Project Title: Archimedes™ home automated peritoneal dialysis (APD) system**
AR21-076	**Organization:** Simergent
Rank: 8	**Project Type: Accelerated**
Approved Funding	**Year 1:** $500,000 **Year 2:** $0 **Year 3:** $0 **Total:** $500,000
Research	The Problem: Dialysis patients consume $36B in Medicare expenses each year, or 7% of the entire Medicare budget! Globally, there are 2.3 million patients who die each year in emerging markets because they either can't afford or can't access dialysis therapy. There is a tremendous need for an affordable, easy to use home dialysis system for the US and emerging markets. Automated peritoneal dialysis can address the accessibility problem and allow patients to perform dialysis in their homes while they sleep, but those dialysis machines cost up to $20,000 plus recurring disposables costs, which is out of reach for most families' budgets. Our Solution: Simergent is developing the Archimedes home dialysis system which delivers therapy to a sleeping patient each night. Our automated peritoneal dialysis (APD) device focuses on specific needs for the US and emerging markets, including Mexico, India, China, and other Latin American and Asian countries. It supports faster training with fewer nursing staff using a color touch screen. Our proprietary fluid measurement technology incorporates proprietary software and patent-pending hardware to enable our dialysis device cost to be up to 80% less expensive than traditional home devices using low cost sensors, allowing the home nocturnal dialysis market to save millions in healthcare costs, while delivering safe and effective therapy more quickly than currently available devices. Our novel patent-pending disposable tubing set is expected to reduce peritonitis risk, which currently is the largest cause of preventable peritoneal dialysis patient deaths.
Economic Benefit	Oklahoma currently has only 415 medical device jobs across the state, lagging many of the surrounding states and those with similar population according to Harvard research. Simergent's Archimedes automated peritoneal dialysis system will create 699 jobs in Oklahoma within five years after project completion, of which, 84 will be high paying scientist and engineering positions, with the remainder in high technology manufacturing and supporting business-related positions. Seven engineering positions will be supported or created during the project, with 84 engineers and scientists hired within five years after project completion to support on-market devices, manufacturing operations, and develop next generation dialysis devices and ancillary products. Engineering compensation will range from $60,000 to $150,000. Simergent has the potential to generate $114 million in revenue within 5 years after project completion. A company with a comparable home dialysis device, NxStage Medical, was recently sold for $2.0 billion. By manufacturing our Archimedes affordable dialysis devices in Oklahoma and selling to all 50 states in the US and emerging market countries including Mexico, India, and China, 99% of Simergent's income will come from outside of Oklahoma. This will bring much-needed 21st century, recession-proof jobs in the high technology medical device sector which will more than double the number of medical device jobs in our state.
Match Source	Simergent will provide the matching funds for the project from funds that have been raised from VC and angel investors. One hundred (100)% of the funds are held at Midfirst Bank.
Research Area	Diagnostic and Therapeutic Biotechnology

PI: Paige Johnson	**Project Title: Surface Active Nanomaterials for Cobalt-free EV Battery Cathodes**
AR21-067	**Organization:** Ten-Nine Technologies
Rank: 9	**Project Type: Accelerated**
Approved Funding	**Year 1:** $235,855 **Year 2:** $187,855 **Year 3:** $0 **Total:** $423,710
Research	Ten-Nine Technologies develops new materials for new economies. It has become the first company in the world to demonstrate fossil fuel parity in a battery active material and is gearing up to produce this unique nanomaterial at tonnage scale with market entry anticipated in 2021-22. Ten-Nine's proprietary surface-functionalized nano-oxides are the subject of six issued patents, with sixty-one national and international filings pending and are currently undergoing evaluation testing with a major US manufacturer. Ten-Nine's patented nanomaterials are designed to improve the energy storage capacity of other battery materials when used as a blend with traditional active materials. Having demonstrated transformative improvements in primary (single-use) batteries, Ten-Nine is now focusing on secondary (rechargeable) batteries, and specifically EV batteries, for the next generation of its product line. Ten-Nine's nanomaterials will meet a critical need in the EV industry for cathode materials that have long lifetimes but do not contain cobalt. This project is designed to enable the production of a domestically produced alternative to cobalt-containing cathodes by blending Ten-Nine's high-energy nano-oxide with lower-energy LMO (lithium manganese oxide) and lithium nickel manganese oxide (LNMO) battery active materials, thereby increasing the capacity and cyclability of the blend to the levels of the NMC and NCA (nickel manganese cobalt and nickel cobalt aluminum respectively) that are the current preferred cathode materials for EV batteries.
Economic Benefit	Ten-Nine Technologies has outlined a growth plan based on the implementation and success of the proposed project that will add 50 full-time scientific and technical positions by five years post-project completion. These positions are high paying and have an excellent benefits package. We anticipate hiring numerous additional workforce team members over this time period as well. The proposed project is expected to contribute 1M to Ten-Nine's gross profit in 2024, scaling to nearly 20M as market penetration increases. Ten-nine has anticipated the need for larger facilities, and is in the process of renovating a warehouse for pilot scale production. After the conclusion of this project, a larger production facility is planned, with structure, equipment and design totals in the 30M range.
Match Source	In this proposal, Ten-Nine is asking for $423,710.00 Ten Nine is contributing $445,671 as match. Ten Nine is using employee salary, contract employee salary, travel, supplies, equipment, and external laboratory expenses as matching funds.
Research Area	Energy Storage / Fuel Cell, Battery

PI: Binbin Weng	**Project Title: A Novel Photonic Sensing Technology for Sour Gas Detection in the Oil and Gas Industry**
AR21-052	**Organization:** University of Oklahoma
Rank: 10	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $41,206 **Year 2:** $43,151 **Year 3:** $0 **Total:** $84,357
Research	The objective of this project is to develop a novel chip-scale photonic gas sensing technology that offers in-situ and real-time remote detection of sour gas for oil and gas applications. The key technical innovation is to create a unique photonic sensing membrane that could greatly boost light-and-gas interactions within a micron-scale range. This photonic sensing membrane is a two-dimensional photonic crystal microchip constructed upon lead-chalcogenide mid-infrared semiconductor materials. The development of absorption-based photonic crystal gas sensors has recently drawn increasing attention from gas sensing research communities, mainly because of their extraordinary ability to address size, power, stability, selectivity and cost issues simultaneously. Unfortunately, by far, none of the reported works can further improve the performance of photonic crystal sensors to a desirable level (i.e. <10 ppm) which would enable them in a wide variety of important real-world applications. The technical challenges in developing such powerful photonic crystal gas sensors include the following three main aspects:1) lack of suitable materials; 2) lack of low-cost light sources; 3) requires a complicated light coupling setup.The proposed idea of developing a mid-infrared active photonic crystal enabled sensing technology will be able to well address all these technical challenges, and lead to a compact, low-cost and highly sensitive (<1ppm) and real-time remote sensing device with a long operation lifetime and zero recalibration/maintenance requirement. If success, the novel in-situ and real-time gas sensors will help the oil and gas industry: 1) reduce the health risks of the employees in the oilfields; 2) protect expensive infrastructure (pipeline, equipment, and facilities); 3) assist decision-makers assess the effectiveness of the expensive remediation strategies and optimize their investment accordingly.
Economic Benefit	Exposure to sour gas can cause severe health issues including immediate death when only taking two breaths of H2S over 1000 ppm. In addition to being toxic, sour gas is highly corrosive and can damage piping and other related equipment in the oil and gas production, transportation, and storage processes, involving over $1.372 billion annual cost globally. And because of the increase in demand for natural gas and depletion of many sweet gas fields, use of sour fields are now a more economically viable undertaking, with the use of sour fields rising from 16% in 1971 to 21% in 2004, with a prediction that 26% of all gas will be from sour reserves in 2030. The safe production and transportation of sour gas is a big challenge faced by the oil and gas industry, which will only increase with the rapid growth in demand as aforementioned. By far, there is no reliable sour gas sensing solution that can help stakeholders to track the pipeline corrosion situations in different infrastructure components, therefore, the mitigation procedure has to be applied blindly for every segment in the whole production, transmission, and storage components. Thus, it will involve a lot of unnecessary and blind investments over 10s of million dollars annually. This is an existing extreme-costly issue that the oil and gas companies want to address urgently. Therefore, the successful technology development through this proof-of-concept phase will attract a broad range of private funds to help the oil and gas industry navigate the

	problems with reliable and sensitive “eyes and ears”. That said, it is very clear that a significant return on the investments (ROI) can be made after the success of the research and development stages. Further, it is noted that the technology can be tailored for detecting other fugitive gases including both the natural gases (C1-C5) as well as the volatile organic compounds. According to the new market research report on the "Gas Sensors Market by Gas Type (Oxygen, Carbon Monoxide, Carbon Dioxide, Ammonia, Chlorine, Hydrogen Sulfide, Nitrogen Oxide, Volatile Organic Compounds, Hydrocarbons), Technology, End-Use Application, Geography - Global Forecast 2023", this market is expected to be valued at USD 1,297.6 Million by 2023, at a CAGR of 6.83% between 2017 and 2023. Therefore, the success of this project has a huge potential to transfer the technology and licensing to high-tech startups in the State of Oklahoma.
Match Source	The total matching funds are provided from the collaboration company Flogistix, headquartered in the Oklahoma City. The total contribution from the company values $86,760. To breakdown, a Technical Principal (TP), a Field Engineer (FE) and a Design Engineer (DE) from Flogistix will be engaged in this research project. The TP will be responsible for directing and coordinating the meetings and labor activities over Flogistix. The FE will assist the PI’s research team on their facility visits, oil and gas field survey and sensor device testing and proving efforts. The DE will assist the PI’s team on the refinement of the sensing system design for enabling the practical deployment of sensor to the field for the remote use. Besides, the engagement will involve the use of their fugitive gas monitoring equipment for supporting the Field Engineer and the PI’s team on the field research activities over the course of the project.
Research Area	Optics and Photonics

PI: Brek Wilkins	**Project Title: Reliability, Validity, Normative Data, and Accuracy of SWAY Mobile Application Assessments in Healthy Adults and Adults with Mild Cognitive Impairment and Dementia**
AR21-014	**Organization:** Sway Medical
Rank: 11	**Project Type: Accelerated**
Approved Funding	**Year 1:** $135,240 **Year 2:** $104,323 **Year 3:** $0 **Total:** $239,563
Research	Sway Medical, Inc. (SWAY) has developed an innovative, scientifically validated, reliable, and FDA approved mobile-based application for cognitive, functional, and balance assessment. SWAY is currently purchased for commercial use by clinicians screening for mild traumatic brain injury following sports related injury. Clinical reliability, validity, and normative data have been studied extensively in individuals aged 5 to 21. The accuracy of the SWAY Mobile Application to assess balance instability and cognitive dysfunction has been well established. Recently, SWAY has onboarded several early-stage clinical customers interested in using SWAY for Cognitive Wellness screening of individuals 65+ during Medicare Annual Wellness visits. However, before scaling clinical sales in this market, SWAY must produce more robust test reliability, validity, and normative data, for SWAY cognitive, balance, and functional assessments in healthy adults aged 21 and older, particularly those 50+. The objective of this study is to examine the reliability and validity, and to establish normative data, for SWAY balance, functional, and cognitive assessments in healthy adults aged 21 or older. An additional objective includes examining the accuracy of SWAY balance, functional, and cognitive assessments to identify MCI and dementia in participants 50 and older. Aim 1, Hypothesis: SWAY balance, functional, and cognitive test scores collected at baseline and 30 days will show acceptable test-retest reliabilities. Aim 2, Hypothesis: SWAY balance, functional, and cognitive test scores will have medium to high correlations with psychometrically supported neuropsychological tests of similar constructs (convergent validity) and small correlations with psychometrically supported neuropsychological tests of disparate constructs (discriminant validity). Aim 3, Hypothesis: Age, education, gender, and race-based normative data will be collected for SWAY balance, functional, and cognitive tests. Aim 4, Hypothesis: SWAY balance, functional, and cognitive test scores will show acceptable sensitivity and specificity in the detection of MCI and dementia, which will be diagnosed with accepted research criteria based on neuropsychological test performance. The overarching objective of this project is to develop the necessary product validation for clinical market acceptance and to meet the requirements set forth in 21CFR882.1470 as an improvement over current cognitive testing modalities.
Economic Benefit	Economic Impact Analysis – During OARS Project (Years 1 & 2 in Pro Forma) SWAY Medical's total economic impact on the Oklahoma economy during this study is projected to be approximately $5,277,565. Please see the notes below as well as the table for specific details. Important notes: ?OARS/Matching funds will support three 'Scientific Personnel and Technical Staffing.' ?Increased 'Workforce Staffing' will be needed during this time. ?Zero profits are anticipated during the study period. ?$ 728,373 in gross sales are anticipated during the study period. ?There is no anticipated technology transfer.

	?The initial effort to raise a significant second round of financing to accelerate commercialization is anticipated at this time. Additionally, it is possible that SWAY will raise a small amount of private financing during this period. Economic Impact Analysis – 2 Years Following OARS Project (Two years post-study completion in the pro forma) SWAY Medical's total economic impact on the Oklahoma economy during the two years following the completion of the OARS project is projected to be approximately $ 45,290,954. Please see the notes below as well as the table for specific details. Important notes: ?SWAY Medical will continue to support three 'Scientific Personnel and Technical Staffing' during this period. ?Increased 'Workforce Staffing' will be needed during this time. ?Zero profits are anticipated during this period. ?$ 3,287,691 in gross sales are anticipated during the study period. ?There is no anticipated technology transfer. ?A significant second round of financing to accelerate commercialization is anticipated to close during this time. Economic Impact Analysis – 5 Years Following OARS Project (2 to 5 years post-study completion in the pro forma) SWAY Medical's total economic impact on the Oklahoma economy five years following the completion of the OARS project is projected to be approximately $ 50,080,390. Please see the notes below as well as the table for specific details. Important notes: ?SWAY Medical will continue to support three 'Scientific Personnel and Technical Staffing' during this period. ?Increased 'Workforce staffing' will be needed during this time. ?$ 3,287,691 in profits are anticipated during the study period. ?$ 17,792,076 in gross sales are anticipated during the study period. ?There is no anticipated technology transfer. ?No additional sources of funding are anticipated during this period.
Match Source	Sway Medical will pay upfront costs for budgeted items qualifying for OCAST matching costs. Sway will keep a detailed report of what items have been paid each month, with supporting documentation including financial reports, bank statements, and check stubs, and provide those to OCAST as needed for reimbursement as outlined in the grant guidelines.
Research Area	Other: Mobile Health Technology

PI: Christian Bach	**Project Title: Enabling Thermal Energy Storage to Accommodate Oklahoma Wind Energy – TriCoil as Cost Effective Means for Residential System Integration.**
AR21-037	**Organization:** Oklahoma State University
Rank: 12	**Project Type: Accelerated**
Approved Funding	**Year 1:** $65,000 **Year 2:** $65,000 **Year 3:** $60,000 **Total:** $190,000
Research	This project will evaluate a novel water-refrigerant-air heat exchanger, the TriCoil, that is anticipated to allow cost effective integration of diurnal timespan thermal energy storage (TES) with conventional air conditioning (AC) or heat pump (HP) systems. Such TES is required to ensure reliable electricity grid operation as the fraction of renewable energy in Oklahoma and in the Southwest Power Pool (SPP) increases. A unique aspect of the TriCoil based AC/HP system, compared to fully hydronic AC/HP systems, is the elimination of heat transfer-based losses during direct, non-storing, cooling mode. The project will evaluate the TriCoil as a cost-effective way to integrate TES with conventional AC/HP systems at a lower cost with fewer energy penalties and other problems compared to alternative systems. This project is planned to be accompanied by a series of parallel projects at the Center of Integrated Building Systems (CIBS) at Oklahoma State University. These projects will allow synergistic expansion of the project outcomes and allow Oklahoma companies to swiftly develop commercial versions of TES-enabled systems. These will become necessary to support the utilization and stabilization of the Oklahoma electricity grid as the fraction of renewable energy continues to increase.
Economic Benefit	This project is anticipated to economically benefit CIBS and a unitary equipment manufacturer (Johnson Controls International). It has the potential to also benefit other Oklahoma unitary equipment manufacturers such as AAON and ClimateMaster. In addition, it will lead to additional business for system installers. CIBS, as sponsoring company, benefits from additional capabilities that can be utilized for further member recruitment, including for recruiting additional Oklahoma companies that would benefit from this project (e.g. ClimateMaster, RAE, and others). However, this impact is difficult to quantify since new members may join for a combination of reasons and therefore this is not included as a OCAST benefit. Johnson Controls International is anticipated to benefit through increased competitiveness, leading to additional product sales and requiring additional workforce. This will bring both tax income to Oklahoma and additional purchasing power to the Norman community. Furthermore, equipment installers will have additional business. It is estimated that a total of 0.5 manufacturing and installment jobs within two years of completion are needed, in addition to 4 new technical staff. Within five years of completion, this increases to 6 staff and 60 manufacturing jobs, and 8 years after completion the estimated impact for manufacturing and installment jobs increases to a total of 300.The total combined impact within 8 years of completion is estimated at $166 million, leveraging the invested OCAST funds by over 875:1. From the perspective of tax income to Oklahoma, if both companies pay a ~5% corporate tax rate similar to AAON's 2020 numbers, OCAST funds are leveraged by over 43:1 from a corporate taxation perspective alone.
Match Source	CIBS's will provide in-kind matching funds from CIBS. The matching cash costs will leverage hiring an additional graduate student to work on the same project family and supplement with an undergraduate research assistant. This will effectively

	double the effort provided to this project track, leveraging OCAST's funding by a 2:1 ratio. The proposed project is allowing to utilize AC and HP equipment to reduce the effects of renewable electricity generation fluctuations and enable the CIBS membership to continue with near-series pre-production prototype development and testing after project completion.JCI will contribute a variable speed HP, a speed adjustable indoor unit, and two custom circuited heat exchangers. JCI will also provide administrative support to interact with the PIs and the research associates to ensure manufacturability of the heat exchangers. JCI's match will contribute $5,000 during year 1 of the project and $5,000 during year 2 of the project.
Research Area	Energy Storage / Fuel Cell, Battery

PI: Dr Rick Gaeta	**Project Title: Proof-of-Concept-OARS-Plan-for-Expendable-Tube-Launched-UAS**
AR21-068	**Organization:** Berry Aviation. Inc
Rank: 13	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $90,000 **Year 2:** $ **Year 3:** $0 **Total:** $90,000
Research	The proposed proof of concept project will take place over a one (1) year period. The project will be split into a rapid prototyping effort and capability demonstrator development effort. The capability demonstrator development effort will be informed by lessons learned from testing of the rapid prototype UAS. The Key Performance Parameters (KPP) will include (but not limited to) a $7,000 cost per launch, tube-launch capable from both ground and air, autonomous C2, and a 1U Modpayload capacity. Different types of manufacturing techniques will be researched to determine the most efficient way to manufacture the airframe. Stability and control analysis, CFD, and performance estimates will be completed to assist and inform the aerodynamic design of the aircraft. Both FEA analysis and structural testing of the material will be completed to determine the minimum required structure. Bench testing and an iron bird will be utilized to conduct ground testing of the electronic components of the capability demonstrator. Task 1 – Design of Rapid Prototype: BAI engineers will design a prototype that will enable further investigation of the 3D printed rocket motors, the wing deployment mechanism, and the low cost fabrication methods for use in a tube launched UAS. Task 2 – Ordering of Materials and Equipment for Rapid Prototype: BAI will obtain materials and equipment for the rapid prototype, while considering future availability and quantity with respect to mass production. Task 3 – Fabrication of Rapid Prototype: BAI will fabricate 2 prototypes of per the design resulting from Task 1, with the materials and equipment procured during Task 2. Task 4 – Testing of Rapid Prototype: BAI will conduct ground and flight testing. The results of testing will inform design of the capability demonstrator. Task 5 – UAS Design of Capability Demonstrator: BAI will design a capability demonstrator UAS informed by the prototype testing. This design process with include aerodynamic, propulsion, structural, and avionics design optimization. Tools used during this design process will include CFD, FEA, a dynamometer, and others. BAI engineers will leverage their experience gained from similar sized UAS design efforts. Task 6 - Fabrication of Capability Demonstrator: BAI will fabricate 3 capability demonstrator of per the design resulting from Task 5, with the materials and equipment procured during Task 2, Task 5, and Task 6. Task 7 – Flight Testing of Capability Demonstrato
Economic Benefit	In the next 5 years Berry Aviation, Inc. (BAI) has plans to increase its unmanned aircraft systems (UAS) branch by 150%. The UAS branch is located in Stillwater, Oklahoma and utilizes relationships with local companies and Oklahoma State University. The projected growth of the BAI's UAS branch corresponds to an increase in local employment opportunity in the state of Oklahoma. Berry Aviation's unmanned aircraft branch has knowledge based in the practical approach and development of unmanned systems. The UAS branch has experience in designing, integration, operations, and logistics. With this

	experience the UAS division has capably provided support to the United States Department of Defense (DoD), proudly serving in multiple UAS support roles and missions. Several of our customers include USSOCOM, US Air Force, US Army, US Navy, and other DoD organizations. The tube-launched system being proposed for development will lead to an 80% decrease in per unit cost of each system. This cost reduction is projected to increase the operational deployment of tube-launched systems with an aircraft that is a more affordable expendable system. To support the projected production numbers, BAI will source local labor and partner with local businesses to meet product demands.
Match Source	Berry is providing matching funds in the form of labor and facilities. Berry has state of the art facilities that allow for manufacture and design of the UAS. Berry is providing a seasoned Research Engineer and a Principle Engineer to support the development.
Research Area	Other: UAS design, prototype fabrication, integration, ground testing, and flight testing

PI: Ranjith Ramanathan	**Project Title: Novel biodegradable active packaging film to improve color of dark-cutting beef**
AR21-051	**Organization:** Oklahoma State University
Rank: 14	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	Beef color plays an important role in purchasing decisions. Any deviation from a characteristic bright-red color leads to economic losses and/or carcass is discounted in price during grading. Dark-cutting beef is a condition in which meat fails to have a consumer-preferred bright red color when exposed to air. Due to dark-red color, dark-cutting beef is discounted during grading, and the meat is not sold at retail. Dark-cutting beef has worldwide occurrence and results in economic losses to producers and beef processors. Depending on the severity of the dark cutter, the US beef industry lost $128 to $320 million in 2019. More specifically, this loss results from the discounted price of beef carcasses, and the beef is not sold in retail. Previous OCAST-OARS has allowed us to standardize a nitrite-embedded packaging technology to improve the color of dark-cutting beef to appear like a normal beef with a bright red color (final patent application under-review). However, improved fresh beef color was compromised by light pink color after cooking to USDA recommended temperature. More specifically, greater muscle pH and heat stable nitric oxide myoglobin predispose to pink cooked color. Research from our laboratory has shown a synergistic effect of nitrite and antioxidants to form bright-red color, which can decrease the amount of nitrite to form the same bright red beef color. In the present proposal, we are developing a biodegradable nitrite and antioxidant-containing active packaging to improve the color of dark-cutting steaks. The specific objectives are a) to optimize the levels of nitrite and biodegradable packaging ingredients to develop meat packaging film and b) to determine the effects of developed biodegradable film on raw and cooked dark-cutting beef color. Chitosan-polylactic-based and potato starch-protein-based packaging films will be tested with different levels of nitrite and antioxidants such as rosemary, vitamin C, and vitamin E. In the current research, we are addressing two critical needs of the meat industry 1) improve color and value of dark-cutting beef so that meat can be sold at retail stores and 2) developing biodegradable packaging material. We anticipate that developing environmentally friendly active packaging to improve color of dark-cutting will improve value and profitability.
Economic Benefit	Visual appearance plays an important role in purchasing decisions of beef. Any deviation from a characteristic bright-red color leads to economic losses and/or carcass is discounted in price during grading. Dark-cutting beef is a condition in which meat fails to have a consumer-preferred bright red color when exposed to air. Due to dark-red color, dark-cutting beef is discounted during grading, and the meat is not sold at retail. Dark-cutting beef has worldwide occurrence and results in economic losses to producers and beef processors. Depending on the severity of the dark cutter (severity based on pH and dark color), the US beef industry lost $128 to $320 million in 2019 due to a discounted price. More specifically, this loss results from the discounted price of beef carcasses, and the beef is not sold in retail. Previous OCAST-OARS has allowed PI's laboratory to standardize a nitrite-embedded packaging technology to improve the color of dark-cutting beef to appear like a normal beef with a bright red color (final patent application under-review). However, improved fresh beef color was compromised by light pink color

	after cooking to USDA recommended temperature. In the current research, we are developing a biodegradable nitrite and antioxidant-containing active packaging to improve the color of dark-cutting steaks. The specific objectives are a) to optimize the levels of nitrite, antioxidants, and biodegradable packaging ingredients to develop meat packaging film and b) to determine the effects of developed biodegradable film on raw and cooked dark-cutting beef color. We anticipate that developing environmentally friendly active packaging to improve color of dark-cutting will improve value and profitability. In the current research, we are addressing two critical needs of the meat industry 1) improve color and value of dark-cutting beef so that meat can be sold at retail stores and 2) developing biodegradable packaging material. The product will be a prototype of packaging film, and the newly developed technology will be licensed through the Technology Development Center at Oklahoma State University. The benefiting firms include the beef industry (packers and retail) in the US and worldwide. We have included letters of support from two companies (Empirical and Tyson Foods) that may benefit from this technology. We anticipate developing a prototype packaging film helps to license the technology and generate economic benefits to Oklahoma.
Match Source	In the current research, a 1:1 match will be provided from PI and Co-PI's salaries.
Research Area	Other: Food Processing/Meat Science

PI: Parvaneh Rouhani	**Project Title: Metal-organic Framework based Solid Polymer Electrolytes for Structural Supercapacitors**
AR21-078	**Organization:** Structured Ions, LLC
Rank: 15	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $89,925 **Year 2:** $ **Year 3:** $0 **Total:** $89,925
Research	The proposed research focuses on the development of the multifunctional composite structures by modifying and optimizing all relevant constituents of a composite system and by employing multi-scale measurements to obtain a fundamental understanding of how the constituents influence the overall macro-level behavior of the materials. Past research have shown that functionality of thin film batteries embedded within a composite laminate is limited due to lowered load-bearing capacity and tendency towards delamination. Multifunctional materials offer an alternative to the drawbacks of sandwich structures. These systems are expected to simultaneously perform two or more functions while accommodating operational cell malfunction and impact damage. Nonetheless, the development of multifunctional structures has been largely Edisonian in which different material combinations and energy cell architectures are fabricated, and then tested to evaluate the electrical and mechanical properties. Also, there are several challenges in the development of multifunctional materials including the ionic conductivity of solid polymer electrolyte (SPE) being inversely correlated with its mechanical properties and softening of electrolyte interface due to improving the access of ions from the electrolytes to the carbon fiber electrodes. The uniqueness of our approach lies in synthesizing a solid polymer electrolyte with high ionic conductivity, simultaneously enabling the electrical and mechanical properties of the supercapacitor structure, and by enhancing the surface area of electrolyte to facilitate electrode-electrolyte connectivity.
Economic Benefit	Oklahoma is positioning itself as a major hub for the future of the country's unmanned aerial systems industry. UAS is the fastest growing area in the aviation industry with billions of dollars generated over the last decade. The economic impact of UAV in Oklahoma is approximated to be \$657 million and importantly it is expected to generate over 800 jobs by 2025. Additionally, over $5.6 million will be collected as taxes from these industries, adding to the revenue of the state. The presence of Tinker Air Force Base and major aeronautic centers such as Mike Monroney Aeronautical Center in Oklahoma has attracted many companies to open facilities in the state. Recently, Kratos Defense & Security Solutions, which received \$93 million dollar contract to supply drones to the army announced plans for moving their facility to Oklahoma City. It is estimated that the new facility will create over 350 jobs in Oklahoma. This showcases the economic boost that will be provided by the growth of the UAV industries in Oklahoma. Nonetheless, Oklahoma will need to focus on significant research and development (R\&D) in this sector to remain competitive in attracting new investments. Development of new technologies in fabrication of UAV is expected to benefit other vital applications in the state that rely heavily on drones such as monitoring of volatile storms, observing crop growth/harvesting and exploration of oil fields. Currently, these applications are restricted by the technical limitations of existing drones specifically the time of flight and weight of the drones. All these factors indicate the need for creation of technologies that will help to expand the functionalities of the future UAV. The proposed technology

	will be instrumental to improve the time of flight and eliminate the need for external devices to power the drones.
Match Source	Matching funds for the OCAST OARS award will be provided through a currently awarded NASA Phase I SBIR contract and through pending Phase II funds. This source of federal funding provides a cash match that is directly aligned with the proposed research and development activities. Additional funding is expected through equity participation and fund-raising activities.
Research Area	Energy Storage / Fuel Cell, Battery

PI: scott crain	**Project Title: Design, Fabrication and Placement of a Downdraft Gasifier for Use in Processing Yard Waste for the City of Stillwater**
AR21-030	**Organization:** Texoma Mfg LLC
Rank: 16	**Project Type: Accelerated**
Approved Funding	**Year 1:** $189,627 **Year 2:** $189,627 **Year 3:** $0 **Total:** $379,254
Research	Gasification uses a partial oxidation process to convert carbonaceous feedstocks into a useful syngas energy source. The current prototype for the patented OSU downdraft gasifier is capable of converting 2.5 tons of carbonaceous waste daily producing sufficient syngas to generate 60 kilowatts of electricity using a common commercial internal combustion generator. Tar scrubbers used to clean the syngas output result in a total system exhaust from the internal combustion engine that meets California emission standards. Our goal for this project is to complete the design, fabrication and placement into operation for a downdraft gasifier specifically target to process the yard waste stream for the City of Stillwater, Oklahoma. The development program will complete a design for manufacturing process on the gasifier, design a 2.5 ton per day feedstock drying system, design a feedstock handling system and program a programmable logic controller to allow continuous unattended operation of the system. All system components will be fabricated, integrated into a continuous waste handling system and placed into operation at the Stillwater waste handing facility. Our objective is to eliminate disposal fees for the yard waste stream while generating electricity from the waste disposal process. The successful completion of the program will provide the technical data necessary to allow Texoma Manufacturing to offer gasification based waste processing systems to any entity that is generating in excess of 2.5 tons of carbonaceous waste daily.
Economic Benefit	This proposal supports the development and placement of a downdraft gasification system to be used as a yard waste processing system for the City of Stillwater. Use of the system to process the yard waste stream eliminates the tipping fees on 900 tons of yard waste annually while generating 500MWH of electricity to be feed into the grid on behalf of the City of Stillwater. The cost savings realized will allow the City of Stillwater to recapture their investment in approximately 3 years time. Completing the design, fabrication and initial operation of the gasifier system provides Texoma Manufacturing with all technical information required to launch the gasifier system sales business. Sales will be targeted at municipalities and companies that currently generate a carbonaceous waste stream in excess of 2.5 tons per day. The gasification system will eliminate the cost of waste stream disposal while generating energy in the process. Upon completion of this research and development program our projections highlight in excess of 4 million in annual sales within 5 years of launching the product. This level of sales will provide for an additional 21 jobs in Durant, Oklahoma.
Match Source	The match for this proposal is provided in cash from Cowboy Technologies and the City of Stillwater and Texoma Manufacturing. City of Stillwater - $200000.00 Cowboy Technologies - $100000.00 Texoma Manufacturing - $65179.00
Research Area	Energy Generation/Distribution

PI: Soroor Karimi	**Project Title: Improving Service Lift of Coal Pneumatic Transport Hardware**
AR21-025	**Organization:** The University of Tulsa
Rank: 17	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $44,630 **Year 2:** $45,370 **Year 3:** $0 **Total:** $90,000
Research	Erosion of materials due to the impingement of solid particles is one form of wear degradation that jeopardizes the functionality of the system in particle-contained flows by damaging pieces of equipment. The application includes but is not limited to production, process, and transportation facilities in petroleum, power plants, and aerospace industries. The accurate prediction of erosive damage is of great importance from both economic and safety aspects, since estimating the life of the equipment and scheduling maintenance are beneficial for companies and the environment. This project aims to increase the life span of Pulverized Coal (PC) pneumatic transport equipment. The proposed research will accomplish this goal by taking an existing sand erosion model in pipelines and extending the applicability of the model to pulverized coal pneumatic transport. The updated model will be utilized to optimize both materials and designs of existing equipment. Both the analytic evaluation and improved hardware will be offered to the world-wide clientele.
Economic Benefit	RJM-International has serviced Pulverized Coal generation facilities in the EU continuously for 15 years. Their experience includes 100's of nozzles over a dozen PC boilers and multiple fuels. The facilities they have serviced kept 100% replacement nozzle on hand at all times and scheduled replacement (without inspection) at least every (4) years. If there were unplanned down times, the nozzles were inspected and replaced, if needed. Often, condition of nozzles at replacement is "barely serviceable". RJM Corporation (USA) has started contact with local PC generators. They have similar experiences to RJM-International observations in Europe. With success in the proposed project, we expect to gain significant advantages in the US market. By being able to use computer modeling, we can analyze OEM designs and correct flow patterns, embed high hardness materials in critical locations and determine the effect of changing particle size distributions and coal types. Even though coal use is in decline the United States, for the next 10-20 years there is significant opportunity projected for replacement hardware on the fleet of PC Fired Power Stations. From review of the information available, there are at least 340 active power PC boilers in the US. Active being defined as a capacity factor in excess of 20% and not scheduled for closure during the next ten years. RJM, as a company with worldwide connections, sees a significant opportunity to improve PC wear on high-cost injectors. This will provide competitive advantages to the US after market and supply to the world-wide construction. For the estimated 340 power boilers in the US, we estimate 85 boilers replace nozzles each year. Using an average nozzle count of 20 nozzles per boiler, we estimate about 1700 nozzles are replaced each year in the US. Using costs and sales prices for the exemplar nozzle in the proposal and an average life span of four years, we calculate $39,500,000 per year are spent by generators on coal nozzles. In addition, the providers of the nozzles spend an average of $14,300,000 with casting companies (either an internal resource or external shop) to fabricate the nozzles. Based on the pro forma (provided in the proposal), yearly gross economic activity in the state of Oklahoma is estimated to be over $3,200,000 by year 5. This represents a market penetration only 4.7%. Year over year increases are anticipated beyond year 5.

Match Source	Matching funds for the proposed project are provided by RJM Corporation (USA), Inc. a for-profit corporation located in Tulsa, Oklahoma and The University of Tulsa. Together they will provide matching fund of $44,630 and $45,370 for year one and two, respectively (total of $90,000). RJM Corporation will provide matching funds of $31,590 and $29,590 for year one and two, respectively. This matching will be in from of salary for the Vice President of RJM and the RJM engineer in addition to travel funds for data acquisition and initial supply fund. The University of Tulsa will provide matching funds of $13,063 and $15,780 for year one and two, respectively. Dr. Karimi will contribute approximately 5% AY time in Year 1 and 6% in Year 2; Dr. Shirazi will contribute 5% academic year time in Year 1 and 6% in Year 2 as cost share on this proposal. Associated fringe benefits and indirect costs will be provided by TU as cost share.
Research Area	Other: Wear of Materials and Modeling

PI: weng kheong (Ben) loh	**Project Title: Modular Advanced Aerial Mobility Systems (MAAMS)**
AR21-029	**Organization:** Unmanned System Research Institute
Rank: 18	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $90,000 **Year 2:** $0 **Year 3:** $0 **Total:** $90,000
Research	The need for an Advanced Aerial Mobility (AAM) platform that can perform missions requiring a combination of hover and efficient/rapid forward flight has sparked an interest in developing hybrid vehicle concepts and systems that can operate in both flight modes at a level of performance approaching that of optimally designed single-mode operating systems. The electric Vertical Take-off and landing (eVTOL) aircraft is the lead technology enabler for implementing AAM. The current eVTOLs in development can be categorized into three types based on the various advantages and market needs based on their configuration: Multirotor, Tilt-Prop, and Vectored Thrust. Like conventional aircraft, eVTOL vehicle designs are also weight-sensitive, with weight impacting flight range, endurance, energy required, and payload capability. From the endurance and range view, the Multirotor (e.g., Ehang) has lower cruise efficiency than tilt-wing models due to the lack of a lifting area. Still, they demonstrate a higher efficiency for VTOL and hovering due to the low disc-loading. In contrast, the Tilt-Prop eVTOL (e.g., Cora) has a wing for an efficient cruise operation with separate propulsions for cruise and VTOL operation while the Vectored Thrust eVTOL concepts (e.g., Lilium) uses distributed electric propulsion systems for both hover and cruise flight using a series of tilting mechanisms on its wing design. The necessary tilting mechanisms mean additional weight and increased system complexity. In terms of storage, the Multi-rotor design has the smallest form-factor, which optimizes parking space on top of an elevated building or vertiports in an urban environment. The eVTOLs with wings have large, fixed wingspans that require more space for storage. According to Roland Berger's eVTOL market studies, companies with multi-rotor designs may be converging in the direction of efficient, wing-borne Tilt-Prop concepts. For extended range, a conventional winged design is still needed to dominate the market. The potential advantage of a multi-rotor with fewer moving parts is the lower manufacturing cost and smaller footprint for urban operation, which would outweigh associated drawbacks. In multi-rotors, the battery pack accounts for more than half of the vehicle payload. Until breakthroughs are made to improve battery energy density, long-range multi-rotor UAMs will remain elusive.
Economic Benefit	The goal of this research after 1-year of completion is to establish an Oklahoma's Advanced Aerial Mobility (AAM) company that manufacture an electrical Vertical-Take-Off-and-Landing(eVTOL) vehicle as transformative airborne technology to transport people and goods in new, community-friendly, and cost-effective aircraft in both rural and urban environments. In order to usher in this era of historic change in aviation, public & private institutions will have to work together in close partnership to facilitate the safe construction, deployment, and acceptance of new advanced aerial mobility technologies, along with supporting infrastructure and regulatory processes. The partnership between USRI and Choctaw Nation can bring in revenue, high-skilled labors, and investment into Oklahoma. Within 5 years, will continue to invest in developmental research and test facilities as part of the Tier 1 program, of which USRI is a lead thrust. USRI will

	expand its technical and admins staffing between 10 to 15 people to support both the Stillwater's Excelsior Building and Oklahoma City's Discovery Building to support various research for academia, military, and industries on unmanned aerial systems. The Choctaw Nation of Oklahoma expects a total of $30 million of non-State funding injection for facilities and staff expansion to support the BEYOND program with the goal of to safely test and validate advanced operations of manned and unmanned aerial vehicle. Within the next 2 years, Choctaw Nation will begin the construction of a new three-story Operation center with 7,900 sqft of space and a $1 million Maker Space Hanger as part of the BEYOND program. The BEYOND program at CNO is a follow-on effort to the Federal Aviation Administration's (FAA) Unmanned Aircraft Systems (UAS) Integration Pilot Program (IPP). In this new program, CNO will continue its partnership with the FAA and other industry partners to safely test and validate advanced operations for drones. This expansion will attract aerospace companies around the United States and the world and spend millions into the Oklahoma economy in the aviation sector. By the next 5 years, following the research project period, the AAM company started by the PI may have raised a significant investment round of several million dollars. The company continues to build relationships with investment groups through the research and commercialization phases of developing its AAM vehicle in the state of Oklahoma.
Match Source	Choctaw Nation was one of 10 selectees in the initial Unmanned Aircraft Systems, or drone, Integration Pilot Program, also known as UAS IPP. Choctaw Nation focused on agriculture, public safety, infrastructure inspections, and planned Extended Visual Line of Sight, or EVLOS, operations over people and nighttime operations. The Choctaw Nation of Oklahoma will provide matching funds of $90,000 that include providing testing facilities, equipment, salary for a pilot, materials, and supplies for the development and testing of the Modular Advanced Aerial Mobility platform. Choctaw Nation of Oklahoma will provide accommodation at their 44,000 acres of ranch land as a flight-testing site.
Research Area	Other: Advanced Aerial Mobility (AAM)

PI: Srinivas Swaroop Kolla	**Project Title: Performance Enhancement of Cyclonic separators and Control Valves by Investigating Bubble Breakup and Coalescence**
AR21-038	**Organization:** Oklahoma State University
Rank: 19	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $46,000 **Year 2:** $44,000 **Year 3:** $0 **Total:** $90,000
Research	Over the last few decades, separation technology has improved in leaps and bounds owing to the technological advancements in measurements and process fields. Compact separators have advanced considerably leading to better and faster separation of mixtures as compared to the conventional separators that are heavy, expensive, with higher maintenance costs. These compact separators rely on centrifugal forces to separate the phases with a lower footprint, smaller size and easy to maintain, and less expensive. One such separator is the Gas-Liquid Cylindrical Cyclone (GLCC) compact separator that relies on swirling flow to separate the incoming gas from the gas-liquid mixture by the petroleum and other industries. The quantification and distribution of gas bubbles in the liquid of the incoming gas-liquid mixture as well as the secondary entrainment generated as it exits the inlet section are the key design parameters linked to the performance of the separator. These separators work on control strategies utilizing valves and the design of downstream equipment such as valves, chokes, and flow meters are affected by the performance of these separators. For decades, industries relied on using empirical models for bubble breakup/coalescence to size downstream equipment such as valves, flow meters, chokes, etc. This experimental study is to understand and analyze the bubble breakup/coalescence in these cyclone separators to validate the existing mechanistic models and also investigate the gas void fractions exiting the GLCC on the performance of valves which in turn does affect the performance of the GLCC. The aim of the project is two-fold: one is to investigate the bubble breakup/coalescence in the cyclone separator operating under different swirl intensities. The second objective of the project is to investigate the gas void fraction ratios downstream of a control valve installed downstream of the GLCC. The first year of the project focuses on using single-phase water/air or mineral oil/air as fluid medium and the second year will target acquiring the data utilizing various watercuts of water and mineral oil (Tulco Tech 80) and air. This will be carried out by designing and building/adding to the current experimental setup of GLCC utilizing the existing facilities at Tulsa University Separation Technology Projects (TUSTP) at the University of Tulsa and control valve to be provided by Valve System International LLC and services from Lobo Engineering PLC.
Economic Benefit	The objective of the project is to investigate the fundamental mechanism involving centrifugal gas-liquid separators and their effect on downstream equipment such as valves. These compact separators are not only used in the oil and gas industry but also in the chemical, refinery, and environmental sectors. Oklahoma's natural gas reserves are fifth largest in the nation and the state has 7% of the nation's total reserves and contains all or part of 14 of the 100 largest U.S. natural gas fields as measured by reserves (www.eia.gov). Oklahoma's annual natural gas production was about 2.8 trillion cubic feet in 2020 and it produces three to four times more natural gas than it consumes, it needs to transport this natural gas to other states. These gas-liquid separators in conjunction with other compact separators can form small compact multiphase separation units to separate natural gas, produced water and also used for wastewater treatment.

	Apart from natural gas, Oklahoma has substantial shale gas and coalbed methane resources and in 2019, the state accounted for 6% of the nation's proved shale gas reserves and was the 6th largest shale gas producer that year. Oklahoma's shale well produced more than 9 trillion cubic feet of natural gas between 2010 and 2019. With Oklahoma being in the top 5 states in the production of crude and natural gas, for many years, the average wages in the oil & gas sector in Oklahoma ($104,000) are more than twice that of the state average wages ($44,178). The state is the largest oil and gas hub in the USA and ranks 3rd most attractive oil and gas market among 126 markets worldwide, and $20.3 billion investment accounts towards just oil and gas activity alone. The oil and gas firms and their employees paid $2.55 billion in state and local taxes in FY2015, and each new direct oil and gas job supports slightly more than two additional jobs statewide. Meeting the proof-of-concept objectives will result in the development of improved design codes for these compact separators and control valves that are used in various industries in multiphase flow scenarios. Successful completion of this proposed project will permit the development of fluid discharge manifold designs, prototype testing, and later field testing to validate the performance of Atlas valves developed by VSI and will lead to increase the Atlas sales with the assurance that the fluid process system gains the advantage of the valve.
Match Source	The proof-of-concept proposal matching funds are provided by Valve System International LLC, Lobo Engineering PLC, annual membership of Tulsa University Separation Technology Projects member companies and The University of Tulsa. Valve System International LLC is providing matching monies through the control valves, Lobo Engineering PLC is providing matching funds in the form of services to fine tune the control valves.
Research Area	Separation Technology

PI: Craig Bradshaw	**Project Title: Development of Reduced-order System Models for Next Generation Comfort Cooling Equipment**
AR21-042	**Organization:** Oklahoma State University
Rank: 20	**Project Type: Accelerated**
Approved Funding	**Year 1:** $60,000 **Year 2:** $60,000 **Year 3:** $60,000 **Total:** $180,000
Research	To enable maximum energy utilization and grid flexibility, building energy use needs to be well understood. Comfort and ventilation systems and equipment represent 50% of building energy use (roughly 20% of total US energy use) and are therefore the most critical to target. Most critically, transient equipment behavior is not well understood which reduces grid integration and increases building energy use. Additionally, transient unit behavior is necessary to understand for future equipment energy rating (e.g. load-based testing). These challenges can be addressed through improvements such as model-predictive control, building energy modeling, and equipment mapping, but each require transient models. In this project, scope summarized in Figure 1, the uniquely qualified team, will address this by first generating the needed dynamic datasets of unitary equipment utilizing Hardware-In-the-Loop (HIL) techniques in OSU's state-of-the-art facilities. These datasets will then be used to create high-fidelity dynamic models. Using the high-fidelity model, in parallel, a reduced order model will be developed and the experimental data generated in this project will be used to validate the reduced-order model developed and quantify the effect of model order reduction. These outcomes will be disseminated to Oklahoma-based, comfort system manufacturers, through the Center for Integrated Building Systems (CIBS). These outcomes present an opportunity for the Oklahoma-based members of CIBS to generate increased market share through the multiplicative economic impact afforded by CIBS.
Economic Benefit	This project has the potential to leverage the OCAST funding by a factor of 100:1, add up to 215 jobs and generate $21.3M in economic impact. This is accomplished by spreading the economic impact across all the companies (including four Oklahoma-based) that are members of the Center for Integrated Building Systems.
Match Source	CIBS will match 1:1 with in-kind project funds that originated 100% from industry sponsors of CIBS.
Research Area	Energy Conversion

PI: Weerasinghe Priyantha	**Project Title: Monolithically Integrated Flat Optics through Additive Manufacturing**
AR21-032	**Organization:** Amethyst Research Inc
Rank: 21	**Project Type: Accelerated**
Approved Funding	**Year 1:** $249,959 **Year 2:** $249,963 **Year 3:** $0 **Total:** $499,922
Research	Optical packaging technology for infrared electro-optical devices is decades behind that of comparable visible light. Unfortunately, materials used in the visible are too absorptive or even opaque at infrared wavelengths. The objective of this proposal is to develop monolithically integrated low-loss metasurface optics utilizing two-dimensional (2D), and three-dimensional (3D) advanced additive manufacturing techniques via two-photon polymerization (TPP) combined with reactive ion etching (RIE). These optical surfaces will be able to: i) efficiently focus ingoing and outgoing light, ii) filter specific wavelength bandpass with low-losses, iii) select specific directionality of light and iv) control its polarization. These metaoptics will enhance performance and functionality of almost all infrared electro-optical devices including infrared light emitting diodes (LED), interband cascade lasers (ICLs), quantum cascade lasers (QCLs), photodetectors (PDs) and focal plane-arrays (FPAs). Metalenses rely on high-aspect-ratio waveguide pillars with lengths comparable to the wavelength of light. This reduced length naturally mitigate the losses of the host material and ensure a design of reduced size and weight. Added potential advantages of such optics is the direct integration to electronic devices and temperature invariance. We propose to explore and produce flat optics based on 2.5D and 3D unlocking the true potential of this disruptive technology. These Metasurfaces will be printed directly on infrared photodetectors and light emitting diodes. We foresee that this technology will also be suitable for other infrared technologies such as focal plane arrays, quantum cascade lasers, interband cascade lasers, etc. This program is possible by leveraging Amethyst Research's expertise in infrared devices and Dr. Tischler's Laboratory at the University of Oklahoma expertise on flat optics. Amethyst Research will support this effort with their state-of-the-art semiconductor growth and electro-optical characterization facility in Ardmore, Oklahoma while Dr. Tischler will support the program with the only sub-micron 3D printer in the state of Oklahoma.
Economic Benefit	This program will provide a significant impact to the Oklahoma economy by leveraging both the business plan of Amethyst - the manufacture of ultra-high performance infrared sensors in Norman, Oklahoma, and the new aspirations of a high-technology ecosystem on quantum devices and materials at the University of Oklahoma. The program will directly impact Aerospace and Autonomous systems including advanced manufacturing and materials in the field of cybersecurity and sensors/electronic systems.
Match Source	Matching funds are coming from a NASA STTR Phase II Contract No: 80NSSC20C0590 entitled "Ultra-efficient integrated photonic quantum transceiver for high-speed quantum communications". Amethyst has a number of Phase I SBIRs in this area including the one listed above and another DOE SBIR entitled "Resonant Cavity Enhanced Photodetector for Quantum Information Science Systems" Contract No: DE-SC0021690. The matching funds from this OARS program will greatly improve the chances of these

	programs going to Phase I in the first year of the OARS program. The Phase II funds will be used as Year 2 matching for this OARS proposal.
Research Area	Electronic Instrumentation / Sensors and Control Systems

PI: Dr. Aaron T. Dossey	**Project Title: Improving Nutrition and Sustainability: Breakfast Cereal Product Made from Cricket Protein**
AR21-062	**Organization:** All Things Bugs LLC
Rank: 22	**Project Type: Accelerated**
Approved Funding	**Year 1:** $210,313 **Year 2:** $112,313 **Year 3:** $0 **Total:** $322,626
Research	The goal of this OCAST effort is to contribute a nutritious, novel, high protein and more sustainable product to the food industry: a cricket protein based breakfast and snack cereal. To become competitive in the market, the insect based food industry must innovate and diversify. A very large portion of the population consumes cereal as a complete meal for breakfast. However, most cereals either include very little protein or unsustainable forms of protein. Experts believe adding protein is a way to improve not only the healthy impact of cereal, but also its appeal to consumers. We feel strongly that a breakfast cereal helps address not only sustainability and the market for novel protein, but also nutrition, particularly childhood nutrition. Further, it provides a robust major staple food product market to help scale and grow the insect farming and insect based food industries. As the human population grows, it is ever more important to sustain rather than increase levels of consumption from earth and it's ecosphere. Already 70% of agricultural land, 30% of the land on earth, is used for livestock. The good news is farming crickets holds promise as a sustainable solution. They utilize less energy, feed, land and water than other livestock, contributing less to climate change and pollution. The overall objective of this research is to develop, evaluate and demonstrate the feasibility of a high protein breakfast cereal utilizing cricket protein as a major ingredient. With these funds we will develop, produce, and evaluate a novel high protein breakfast/snack cereal product utilizing our finely milled Griopro® brand whole cricket powder product already commercialized. This product will be a puffed extruded breakfast and snack cereal which is at least 30% protein by dry weight. The formulations will evaluate levels of cricket powder incorporation at 0, 10, 20 and 30%. Various gluten-free and wheat containing formulations will be evaluated based on food quality parameters such as sensory analysis, shelf-life, consumer acceptance, flavor, texture, crunchiness, bowl life, shelf-life, ease in manufacturing, and quality of puffing. Different flavor coatings will also be evaluated to improve product acceptance by consumers in sensory studies. If successful, this project will be a step toward revolutionizing the food industry by adding value to and diversifying an industry based on an entire Class of animals largely ignored to date – Insecta.
Economic Benefit	This project and our company's overall work can provide substantial economic development in Oklahoma. For example, our insect based food ingredient innovations have the potential to increase profitability and improve our competitiveness against competing products such as whey and more expensive, less effective protein sources. The global cereal market is currently over $30 billion, but is challenged to expand its use and utility. Experts believe adding protein is a way to improve not only the healthy impact of cereal, but also its appeal to consumers. The market for protein is exploding. The global market for protein ingredient was $38 billion in 2019. Over the five years starting at the end of the project, as our company commercializes the proposed product, we will engage in the following stages of commercialization and company development. The following outlines those stages and anticipated jobs created. 1) Finish product development (OCAST project); 2) Manufacture and sell product.

	Manufacturing will take place outside of Oklahoma initially as facilities to manufacture this product do not exist in this state. However, all other operations such as warehousing, distribution and order fulfillment will take place at our new facility in Oklahoma. 5-10 new employees to run the sales, warehouse and order fulfillment as well as 1 dedicated to marketing; 3) Once we have sufficient capital we plan to build our own cereal manufacturing facility in Oklahoma (10 additional employees to operate and maintain the cricket based cereal manufacturing facility); 4) Once we have sufficient capital to build our own cricket powder facility, we plan to invest in building a new cricket farm and cricket powder spray drying plant to do all cricket protein related aspects of the business – from farm to table – in Oklahoma. At that stage, it is possible even non-cricket ingredients will be able to be sourced from within the state (20-50 new employees to operate the cricket farm and cricket powder spray drying manufacturing plant owned by ATB). In addition to economic development overall, this project has the potential to provide employment, educational and career opportunities to Oklahomans directly at our firm and indirectly through our collaborators, strategic partners, customers and other firms attracted to this area. Longer term, we hope to catalyze a new insect based food industry in Oklahoma, producing low cost, high quality food products in Central Oklahoma.
Match Source	All Things Bugs LLC has applied for a Phase II SBIR from the USDA of $650K with a project start date of November 1, 2021 (recommended for funding as of 6/30/21). We will utilize this $650,000 award as matching funds for the proposed OCAST project, as these 2 projects will run nearly exactly concurrently (both are 2 year projects with starting dates a few months apart. The USDA funds are being used to enhance insect farming through automation and mechanization. Improving insect farming cost will have a huge positive impact on the overall cost and ability of insect protein ingredient to compete with other protein ingredients. This project could result in significant manufacturing capabilities in Oklahoma, as All Things Bugs LLC works to create and deliver the solutions developed under these grant projects. In addition, our subcontractors are also generously offering matching funds as part of their efforts. OSU will provide $29,540 in in-kind matching funds.
Research Area	Food Processing and Preservation

PI: Jeff W. Sharp	**Project Title: Ultrafast Photodetectors for the Mid-infrared Band**
AR21-058	**Organization:** Amethyst Research, Inc.
Rank: 23	**Project Type: Accelerated**
Approved Funding	**Year 1:** $149,999 **Year 2:** $150,000 **Year 3:** $0 **Total:** $299,999
Research	This research project is based on a type of infrared detector known commonly as a "barrier detector". Barrier detectors are heteroepitaxial structures that contain a unipolar barrier capable of blocking one type of charge carrier (electrons or holes) while allowing the other type to traverse the structure. Barrier detectors were conceived to decrease intrinsic current ("dark" current) relative to photocurrent, and they have proven capable of doing so, becoming a viable alternative to mercury-cadmium-telluride detectors. For mid-wave infrared detectors, barrier detector structures are grown on GaSb substrates using molecular beam epitaxy. At a minimum, they consist of one or more contact layers and an nBn or pBp structure, wherein one of the n or p layers is the absorber and is significantly thicker than the barrier (B) and the other n or p layer. The unipolar barrier has a large band offset relative to the doped layers for the majority carrier band, but little offset for the minority carrier band, thus allowing only minority carrier transport in that region. nBn structures are more developed than pBp structures, partly due to the ease of making barriers with large conduction band offset and minimal valence band offset. In Amethyst's designs, there is a p-n junction that allows zero bias operation. Amethyst has made high-performing pnBn structures and detectors, using InAs1-xSbx absorbers, either in a single layer or as Type II strained-layer superlattices, depending on the desired cutoff wavelength. For GHz speeds (response time < 100 picoseconds), though, the greater mobility of electrons compared to holes (40,000 cm2/V-s vs. 400 cm2/V-s) motivates study of npBp designs. This research program will focus on the growth of good quality p-type layers and on the development of barriers with minimal conduction band offset, which requires compositional grading. The MBE work will be supported by in-house high-resolution x-ray diffraction, photoluminescence, and surface analysis tools. This OARS project seeks to develop npBp structures for high-speed MWIR detectors that can be used with pulsed MWIR lasers to accomplish, for example, remote chemical detection or free space communications. Experimental detectors (single pixel) will have dimensions in the range of (0.1 mm)^2 to (1.0 mm)^2; developing or accessing ultrafast infrared characterization for these detectors will be one beneficial project outcome.
Economic Benefit	Amethyst's contributions to the Oklahoma economy--as salaries to Oklahoma residents, subcontracts to OU, and payments to in-state suppliers--have been nominally $750K per year (recent five-year average). These contributions are possible due to the strong efforts by Amethyst personnel to obtain external funding for infrared detector R&D and by the company's past investments in its capabilities, including those in its Analytical Branch, which does both R&D and fee-based analyses for private sector customers.
Match Source	Amethyst will match the OCAST funding from federal sources. There are three selected programs that are active or soon will be active: a DARPA Phase II program, a DOE Phase I program, and a NASA Phase I program. All three programs include a requirement for high-speed infrared detectors. The DARPA Phase II has $400K remaining and is expected to run to June of 2022; the DOE Phase I is for $199K and runs to June of 2022; the NASA Phase I is for $125K and

	runs to November of 2021 (without any extensions). Program titles and program manager information are supplied in a separate document.
Research Area	Electronic Instrumentation / Sensor and Control Systems

PI: Seokjhin Kim	**Project Title: Design of Solar-Energy-Combined Desalination Systems**
AR21-019	**Organization:** Oklahoma State University
Rank: 24	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	The treatment of brackish and produced water presents a complex engineering problem because its composition is dependent upon local geology and requires removal of many classes of contaminants, including suspended solids, dissolved solids, and hydrocarbons. The team proposes to combine a thermal desalination system with a solar energy collector as an energy efficient solution. The overall goal of the proposed research is to develop novel, energy-efficient solar-energy-combined desalination systems for treating BPW to levels suitable for reuse. The primary research objectives of the proposed investigation are to (1) Design a chemical pretreatment process, (2) Synthesize ceramic membranes for organics rejection, (3) Develop solar evaporation and condensation system for oil and salt removal, and (4) Incorporate 1-3 into a flow-through desalination system. The successful completion of this project will increase water supplies and reduce operational costs, energy consumption, and environmental impacts of brackish and produced water management. The OCAST grant will be used for the development and application of ceramic membranes in tandem with solar evaporators, which provide an opportunity to separate oils, greases, salts, and other pollutants from brackish and produced water in a highly energy efficient manner.
Economic Benefit	Brackish and produced waters vary widely in quality but often exhibit high concentrations of salts, oils and greases, heavy metals, and other organic compounds depending on both the characteristics of the formation and the technologies used in extraction. The costs of treating produced water typically outweigh the costs of injection, and as a result, 91% of produced water in the United States in 2012 was disposed of via reinjection. The successful completion of this project will increase water supplies and reduce operational costs, energy consumption, and environmental impacts of brackish and produced water management.
Match Source	Chappell Supply and Equipment will provide $90,000 of match over the two year project in the form of contributed time. The company agrees to allow the OSU research team to perform testing at their facilities, and they will help with this testing.
Research Area	Separation Technology

PI: Anne Kasus-Jacobi	**Project Title: Multi-Target Peptide: A Drug to Remember**
AR21-011	**Organization:** University of Oklahoma Health Sciences Center
Rank: 25	**Project Type: Proof of Concept**
Approved Funding	**Year 1:** $50,000 **Year 2:** $0 **Year 3:** $0 **Total:** $50,000
Research	Alzheimer's disease is a type of neurodegenerative disease in which brain neurons progressively become damaged and die. As the disease progresses, symptoms of cognitive decline arise first and progress to full dementia, followed by a decline in motor functions, and eventually death. AD is the 6th leading cause of death in the US. In 2020, 5.8 millions of Americans were suffering from AD and this number is projected to increase by 40% every decade until 2040. Current treatments can marginally improve behavioral and cognitive symptoms for a time, but these drugs do not modify the root cause for the symptoms, which is the progressive neurodegeneration. Developing disease-modifying drugs for AD has proven extremely difficult. For 20 years, none of the tested drug candidates obtained FDA approval, because of limited effects on cognitive decline and risks of adverse effects outweighing the benefits. The first disease-modifying drug for AD has received a controversial approval by the FDA in June of 2021. This drug has modest efficacy on cognitive decline in patients with early stage of the disease. Limited benefits of disease-modifying drugs on cognitive decline is thought to be due to the complex pathogenesis of AD, involving multiple interconnected pathways, and making this disease extremely difficult to control by targeting only one pathway. Our long-term goal is to develop a multi-target peptide drug that targets amyloid beta (Aß) to inhibit its neurotoxic and pro-inflammatory effects, and simultaneously target pro-inflammatory mediators to inhibit neuroinflammation and neurodegeneration. This combination of targets is unique to our drug candidate, and is expected to synergistically inhibit the cognitive decline in AD. The specific objectives of this project are: 1-To perform lead optimization in vitro: Milestone 1 (M1): Select a peptide sequence optimized for target engagement in vitro (lead peptide) M2: Generate a peptide with optimized chemical modifications to increase stability in plasma and brain (prototype) 2-To perform proof-of-concept in vivo: M3: Proof-of-concept for brain penetration of the prototype M4: Proof-of-concept for engagement of targets in mouse brain At the end of this project, we will have developed a prototype with proof-of-concept for engagement of targets in the mouse brain, protected by new IP.
Economic Benefit	Our proposed product is a first-in-class peptide-based biologic drug that synergistically inhibits neuroinflammation and neurodegeneration to slow, stop or reverse the cognitive decline due to Alzheimer's disease. It is a game-changing solution for Alzheimer's disease, for which there is no efficient drug yet. During the OARS, the impact will be retention of personnel, 2 years following the OARS we will have formed a startup and obtained funding for pre-clinical and pre-IND studies. At this stage and up to 5 years post-OARS we expect to increase the personnel involved in the development of this new biologic drug. At 10-years post-OARS, this technology will have been licensed. Given the size of the market, gross sales projections for the licensee start at more than $2 Billions/year. Startup royalties are projected to start at more than $100 Millions/year, based on a 5% royalties rate.

Match Source	The OU Growth Fund will provide $50,000 in matching funds for this OARS project, which is 100% of the matching funds. OU Office of Technology Commercialization Five Partners Place 201 Stephenson Pkwy., Ste. 4400 Norman, OK 73019 Phone: 405-325-4488 Fax: 405-325-7162
Research Area	Diagnostic and Therapeutic Biotechnology

OCAST 2021 Intern Partnership Applications Not Approved For Funding

Application Number	Title	Organization	PI
IP21.2-017	Venture capital internship w/ high growth technology companies	Cortado Ventures	Susan Moring
IP21.2-010	Formulation and Analysis of Antimicrobial Sealants at Red Devil Inc.	The University of Tulsa	Syed Raziullah Hussaini
IP21.2-019	Faculty and Student Intern Partnership	Berry Aviation. Inc	Rick Gaeta
IP21.2-009	Development of Low-Cost Quality Control Methods for use at Marshall Brewing Company	The University of Tulsa	GABRIEL LEBLANC
IP21.2-011	The Oklahoma Venture Project	Victorum Capital	James Roller

IP21.2-003	**Project Title: Design and Development of Composite Pressure Vessels**	**Rank: 1**
PI: Surendra Singh	**Organization:** The University of Tulsa **Industry Partner:** Infinite Composites, Inc.	
Funding:	**Year 1:** $30,000 **Year 2:** $30,000	**Total**: $60,000
Research	The student interns will participate in the design and development of a system for continuous in-situ inspection in order to characterize and optimize different variables in the manufacture of type V composite over wrapped pressure vessels (COPVs). Two undergraduate students from The University of Tulsa (TU) will work full time during summer and part time during the school year at Infinite Composites, Inc (ICI) in Tulsa, OK. The interns will work under the guidance of two research mentors. The interns will be involved in the engineering design, specifications, development, testing, and manufacturing phases. The interns will learn to utilize 3-D mechanical modeling tools. They will also be introduced to the business aspects of engineering, such as the benefit-cost analysis. The interns will learn workplace ethics and expectations. The report writing and presentations are one of the key components of this internship program. The interns will write monthly progress reports and make presentations before their peers and in regional technical conferences. The interns will be provided format for the reports as well as regular feedback on their written reports. The interns will have opportunity to attend local trade shows and technical conferences to broaden their view of the industry. This will provide them with valuable experience in sales and marketing aspects of the business. The experience gained will provide the interns with job opportunities in the aerospace and transportation industries in Oklahoma and across the nation. The internship program will serve as a recruiting tool to attract students to the engineering programs at The University of Tulsa. The internship provides a unique opportunity for the students to complement their educational experience with industrial experience. Lectures by the mentors in the classroom and at student meetings will help other students to see practical applications in the real world. This will enhance the undergraduate engineering curriculum and also help in developing a unique partnership with the local aerospace company. This program will help ICI in recruiting local engineering talent. The experience gained by the interns as part of this project will enhance their engineering skills and make them potential employees for the company. The innovations in ICI's product line will help in increasing the company's revenue base and hence create job opportunities for engineers and technicians in Oklahoma.	
Match Source	100% Match provided by Intern Host Company (Infinite Composites Inc., Tulsa, OK)	
Research Area	**Aerospace**	

IP21.2-016	**Project Title: Engineering Internships to Develop Regional-Scale Gas Modeling Added Value Product for Flogistix' Vapor Recovery Services**	**Rank: 2**
PI: Xiao-Ming Hu	**Organization:** University of Oklahoma **Industry Partner:** Flogistix	
Funding:	**Year 1:** $10,000 **Year 2:** $10,000	**Total**: $20,000
Research	To enhance the relative sensitivity of any sensing scheme, the background noise must be subtracted. In the case of Flogistix, an Oklahoma-based oil and gas vapor recovery specialist, the background levels of petroleum-derived gases must be subtracted from sensor reports so they can accurately assess their customer's site needs when addressing potential leaks. To achieve this, Flogistix will partner with the University of Oklahoma to hire an undergraduate intern from the highly renowned School of Meteorology to develop a novel tool to estimate background levels of relevant gases based on advanced atmospheric modeling tools developed by the university. By this partnership, Flogistix and OU will establish a research transfer framework which allows the best academic ideas to transition to real-world applications, enhancing the competitive edge which can only be found in Oklahoma.	
Match Source	1 to 1 across the board	
Research Area	**Energy**	

IP21.2-020	**Project Title: Enhancing the Workforce for the Fastest Growing Industry in Oklahoma**	**Rank: 3**
PI: Rio Lirag	**Organization:** Cameron University **Industry Partner:** Bud's Testing Analytical Laboratory	
Funding:	**Year 1:** $10,034 **Year 2:** $10,551	**Total**: $20,585
Research	One of the fastest growing industries in Oklahoma is the sale of medical marijuana. The global cannabis testing services market size was valued at USD 1.1 billion in 2019 and is expected to grow at a compound annual growth rate (CAGR) of 15.4% from 2020 to 2027. The leading factor attributing to market growth is the growing need for cannabis testing services due to a rise in contamination cases. As medicinal and recreational cannabis markets continue to grow, analytical testing will ensure that consumers are receiving accurately labeled products that are free from contamination. In this project, Cameron University will be partnering with Bud's Testing Analytical Laboratory located in Duncan, Oklahoma. Bud's Testing is Oklahoma's premium analytical testing laboratory, an OMMA licensed and fully ISO 17025:2017 accredited laboratory, for accurately measuring and classifying the cannabis content in a samples and screening for harmful toxins. Bud's Testing is less than two years old and is actively acquiring instrumentation to perform all the analysis required to support their customers. They offer services to the Oklahoma State Department of Health, the Medical Marijuana Authority, Agriculture, Oil/Gas, Remediation and Hazmat analysis. Bud's Testing provides full panel compliance testing for growers, processors, dispensers, and individuals with a quick and accurate analyses of flowers. This internship program will enable 3 undergraduate student interns at Cameron University to participate in an intern projects at Bud's in the spring and summer of 2022. In this project students will learn to prepare samples for analysis and to perform standard analyses which are approved by certified authorities. As new methods of analysis are developed, the students will perform the analysis and compare them with current certified methods. In addition to the research, the interns will learn workplace ethics and expectations. The report writing and presentations are one of the key components of this internship program. The experience gained will provide the interns with job opportunities in analytical service industries in Oklahoma. This project will also help in developing unique partnerships with local industries and will open up further avenues for research and practical experience for the interns. The state of Oklahoma will benefit by producing better-trained chemists who will be able to transition more effectively into industry or to graduate school.	
Match Source	Year One: $10,034 Year Two: $10,551	
Research Area	**Other: Analytical Procedures**	

IP21.2-018	**Project Title: Mitigation of Swelling Soil-Induced Problems in Oklahoma Using AI-Based Models and Chemical Injection**	**Rank: 4**
PI: Musharraf Zaman	**Organization:** University of Oklahoma **Industry Partner:** Standard Testing and Engineering, Inc	
Funding:	**Year 1:** $23,824 **Year 2:** $24,756	**Total**: $48,580
Research	Expansive soils in Oklahoma cause major damages to foundations, pavements, and other structures if not properly accounted for in designs and construction. Expansive soils undergo significant changes in volume due to changes in moisture. They swell with increased moisture and shrinks with reduced moisture. Swell potential of such soils is influenced by many factors including liquid limit, plastic limit, clay content, clay mineralogy, and in-situ moisture, in-situ density, and state of stress. The current methods used by geotechnical engineers for estimating swell potential and potential vertical rise (PVR) or heave are highly empirical and do not account for the influencing factors together. Recent developments in artificial intelligence (AI)-based models and availability of laboratory and field data at Standard Testing -- our industry partner providing matching support for this project -- create a unique opportunity for developing AI-based models. The developed models will include the influencing factors together and rank order their level of influence on swelling. As a leading geotechnical company in Oklahoma, Standard Testing is involved in drilling hundreds of boreholes, collecting soil samples (both undisturbed and disturbed) and conducting pertinent laboratory tests each year. Over the years, the company has conducted hundreds of swell tests on expansive soils involving different clay mineralogy and properties (soil classification, moisture-density, unconfined compressive strength, consolidation, etc.). The AI-based models along with the evaluation of chemical injection technique, which is gaining popularity in treating sites with expansive soil, will be a great resource for geotechnical and construction companies in combating expansive soil-induced problems in foundations, pavements, and other structures. Nationally, homeowners spend billions of dollars annually in tackling such problems. Data-driven estimates of swell pressure and PVR will reduce uncertainty and empower designers with new tools. Equally important, the training received by the intern will motivate her/him to pursue graduate studies and industry career. Also, this project enhances collaboration between a local firm and a major university. Finally, this project enhances collaboration between two different disciplines (Civil Engineering and Industrial Engineering). Multidisciplinary approaches are essential to solving complex problems and ensuring success.	
Match Source	The matching support from Standard Testing and Engineering is provided both as cash and in-kind. Specifically, the cash match will partial support the student intern ($5,000 in Yr 1 and $5,150 in Yr 2). In addition, $1,000 ($500/year) will support travel costs directly related to this study such as field trips for drilling, soil sample collection, and attending meetings and conferences. $1,300 ($800 in Yr 1 and $500 in Yr 2) will be used for expendable supplies for laboratory testing. The in-kind match ($23,250; $11,250 in Yr 1 and $12,000 in Yr 2) will support the time spent by the mentor on this project. The collaborative nature of this project requires significant	

	commitment of time from the mentor (150 hrs in Yr 1 and 160 hours in Yr 2) to train the intern in laboratory and field work, compilation of existing data, and development of AI-based models. Finally, the in-kind match ($3K/year) will support drilling and sample collection for testing.
Research Area	**Other: Artificial Intelligence Models, Chemical Injection, Foundation**

IP21.2-006	**Project Title: Ten-Nine Technologies Intern Project 21**	**Rank: 5**
PI: Paige Johnson	**Organization:** Ten-Nine Technologies	
Funding:	**Year 1:** $30,000 **Year 2:** $30,000	**Total**: $60,000
Research	The proposed intern program will allow two students from chemistry, chemical engineering, material sciences, or related backgrounds the opportunity to participate in cutting edge research in the field of energy storage nanotechnology at Ten-Nine Technologies. Interns will have the opportunity to synthesize new, enhanced energy capacity nanomaterials. They will test the materials, design additional tests for the materials during the production process, and investigate the doping properties of various metal salts on the new materials. The results will be added to Ten-nine's collective body of knowledge and testing for their patented family of nanomaterials. Intern research will potentially result in the development of a new electroactive material that can be added to Ten-Nine's list of products manufactured for sale and pre-sale. Additionally both interns will collaborate in the assembly a battery half-cell for testing using the intern developed materials. Each intern will work with their mentor on a daily basis, they will participate in the weekly all hands meeting, as well as taking part in meetings with our clients (frequently industry peers). Dr. Iski will coordinate with the interns to plan and organize a scientific outreach event. Interns will write two project progress reports per year in addition to the slide presentations typically shown at the weekly all hands meeting. Ten-nine staff (in addition to their mentors) will be available for any additional assistance needed to ensure their success in every aspect of the intern project.	
Match Source	It should be noted that Ten-Nine Technologies' proposed match does not include everything that Ten-Nine is funding in regard to the intern program. We have included "official match" to exceed the required 50%, but the actual monetary amount that Ten-Nine Technology will contribute toward the intern program is approximately double what the budget shows. First, the time spent in consultation with CEO Paige Johnson is not included in the budget, secondly, we are only using 20% of Dr. Iski's time with the interns as match. The remaining 80% of Dr. Iski's intern related time is funded by Ten-Nine with the understanding that she is vital to this program. The intern program is in addition to, not part of her contractual duties at Ten Nine Technologies. Ten-Nine Technologies is asking for $60,000 of OCAST funds over two years to support 2 interns for that time. Ten Nine is matching with intern related salaries of the mentors, Dr. Iski, and the remainder of the intern salaries.	
Research Area	**Energy**	

IP21.2-012	**Project Title: Aerospace Development Internship**	**Rank: 6**
PI: Jamey Jacob	**Organization:** Oklahoma State University **Industry Partner:** N/A	
Funding:	**Year 1:** $29,109 **Year 2:** $29,982	**Total**: $59,091
Research	Aerospace Development Internship The advanced air mobility (AAM) market, encompassing both unmanned aircraft systems (UAS) and urban air mobility (UAM) air taxis, is rapidly growing and Oklahoma is uniquely poised to be a key participant in this space. This effort will support workforce development and key research to support and enable this market, allowing Oklahoma to be at the forefront. These aircraft require a high level of automation to fly without pilot input, avoiding obstacles, other aircraft, integrating into unmanned air traffic (UAM) management networks, and adapting to changing weather conditions, particularly winds as Oklahoma is well known for. Winds in an urban environment are especially a concern with their strength, turbulence, and rapid changes as they wrap around buildings. For this technology to be safely used anywhere around a city, enabling services such as air taxis and package delivery, these weather conditions must be better understood and predicted. This effort will support undergraduate interns from multiple disciplines to perform research in conjunction with currently ongoing research at OSU to develop ways to sense and better understand winds at the micro-scale level that will directly impact the operation of AAM aircraft. In addition to advancing knowledge in this area and enabling the market, students performing research at this level will poise them to be strong contributors to the Oklahoma workforce when they graduate. Undergraduates who perform research are much more likely stay for a graduate degree, further educating our workforce to allow Oklahoma to continue to lead in this industry.	
Match Source	The support provided by the State of Oklahoma for this research and development project will be matched by a one-for-one dollar match by utilizing federal funds as provided through a NASA grant through the NASA University Leadership Initiative.	
Research Area	**Aerospace**	

IP21.2-005	**Project Title: Internships for hybrid nano-additives**	**Rank: 7**
PI: Ranji Vaidyanathan	**Organization:** Oklahoma State University-Tulsa **Industry Partner:** MITO Material Solutions	
Funding:	**Year 1:** $14,012 **Year 2:** $16,057	**Total**: $30,069
Research	Under this Intern Partnership project, a senior graduate intern with an interdisciplinary background in materials science and engineering or chemistry will be trained to understand how product development in the area of nano-additives is conducted in MITO Material Solutions Inc., a high-technology company in Stillwater, Oklahoma. Additional activities such as manufacturing scale-up, customer interactions, product testing specific to customers etc. will also be undertaken at MITO by the intern, with any needed testing for customers conducted at the OSU labs. The technology is based on current efforts by MITO and OSU to produce hybrid nano-additives, where MITO manufactures low-cost, environmentally friendly nano-additives that can be added to different resin systems to benefit the aerospace, automotive and the marine industries. The technology to be developed is also based on nano-additives currently jointly being developed by the PI and the mentors from MITO as well as those that are being manufactured under a current NSF SBIR Phase II project [1-3]. We will leverage the efforts that are currently on-going under an OCAST accelerated OARS project that was initiated in 2019 [4], matched by the NSF Phase II SBIR. The graduate intern will be trained in customer discovery of the product based on the Lean Startup method (the PI is an NSF I-Corps instructor for the OSU I-Corps site program), allowing the intern to understand how commercialization plays a role in the product development and contribute to economic development. In order to meet the needs of an effective graduate thesis, the PI and co-PI have identified additional research activities that are different from the Intern project. The intern will assist in product development for MITO. Supporting a graduate student would be beneficial for conducting the necessary testing and characterizing the composite materials. But most importantly, the graduate student can evaluate customer feedback to help to evaluate the improvement in reliability of composite systems used for the aerospace, automotive and marine industries. A successful product development and intern project is projected to result in 6 jobs in the first 5 years and 14 jobs by year 2029. Through this project, MITO expects to increase the sales of products from approximately $2.3 million in 2022 to $6.2 million in 2025 and $30.9 million by 2029.	
Match Source	TOTAL DIRECT COSTS are $14,012 in year 1 and $16,057 in year 2. The total direct costs for the project are estimated to be $30,069. The matching grants will be provided by MITO Material Solutions and are estimated to be $23,015 for year 1 and $23,460 for year 2 for a total of $46,475.	
Research Area	**Other: Nano-additives**	

OCAST 2021 Plant Science Applications Not Approved for Funding

Application Number	Title	Organization	PI
PS21-007	Elucidate the role of amino acid metabolic pathways in the regulation of plant immunity	Oklahoma State University	Heejin Yoo
PS21-021	Drought impacts on net carbon balances in an Oklahoma mixed-grass prairie	University of Oklahoma Norman	Gregory Newman
PS21-016	Understanding the impacts of low light and nitrogen fertilization on photosynthetic acclimation	Northeastern State University	Elizabeth Waring
PS21-009	Determine the effect of lignin down-regulation in alfalfa on microbiota	Oklahoma State University	Kirankumar Mysore
PS21-010	Optimization of plant lignin degradation by microbial consortia for butanol production	Oklahoma State University	Babu Fathepure
PS21-014	Virus-Host Interactions in Plant Stress Responses	University of Oklahoma	Susan J. Schroeder
PS21-024	Controlling Productivity of a Major Crop Plant	University of Oklahoma	Scott Russell
PS21-022	Identification of Plants as Indicators of Exposure to Toxic Industrial Chemicals	Cameron University	Alimamy Fornah

PI: Feng Feng	**Project Title: Deciphering the mechanism of ß-glucan-induced plant immunity and symbiosis**
PS21-008	**Organization:** Oklahoma State University
Rank: 1	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	Plants roots in soils naturally harbor an extraordinarily diverse array of microorganisms including both pathogenic and symbiotic ones. The pathogenic microbes, which threaten food security, can restrict plant growth and induce plant immunity. In contrast, the symbiotic microbes promote plant growth through establishment of beneficial relationships with plant roots for increasing nutrient availability. This raises the question of how plants distinguish between beneficial and harmful microbes so that they can respond appropriately leading to symbiosis or immunity. The activation of plant immunity and symbiosis is governed by the perception of microbe-associated molecular patterns (MAMPs) and symbiotic signals, respectively. However, MAMPs are not specific to pathogens but are also present in symbionts, suggesting that MAMPs might have an additional role beyond their function in activation of plant immunity. The ß-glucans are one of the MAMPs predominant in fungal cell walls that trigger plant immunity. Although it has been well-understood for ß-glucans-induced innate immunity in mammals, there is little known about how plants recognize ß-glucans to activate plant immunity and if ß-glucans also regulate plant symbiosis. This project aims at dissecting the molecular mechanisms underlying ß-glucans-induced plant immunity and symbiosis in roots of the legume Medicago truncatula by combining genetic and biochemical approaches to identify the receptor complex involved in plant perception of ß-glucans. The research will contribute a better understanding of MAMPs-triggered immune and symbiotic signaling in plant roots, which should provide a critical foundational for fully elucidating the molecular basis governing plant discrimination and engagement with pathogenic and symbiotic microbes in nature. In addition, identifying the receptor complex required for ß-glucans perception will provide us new insights and potential strategies to engineer the plant immune system against pathogen infection and increase plants ability for nutrient acquisition through enhancement of symbiotic microbial associations, which addresses a significant agricultural challenge.
Research Area 1	**Other Plant Science Research**

PI: Bruce Dunn	**Project Title: Potential of Eastern Red Cedar Biochar as Potting Media for Greenhouse**
PS21-012	**Organization:** Oklahoma State University
Rank: 2	**Year 1:** $49,827 **Year 2:** $49,959 **Total:** $99,786
Research	The overall goal of this project is to evaluate the potential for turning an abundant yet under-utilized native Oklahoma plant species, eastern red cedar (Juniperus virginiana L.), which is displacing preferred native grass species into a local, economically viable alternative product for peat moss in the greenhouse industry. The objectives are to provide basic information on 1) cedar biochar chemical and physical characteristics at different pyrolysis temperatures, 2) determine rates of biochar incorporation, 3) chemical and physical properties of new media blends, and 4) develop an economic analysis of biochar in terms of media costs and potential carbon credits. In face of grower demands for potting media and dwindling supply of available peat moss, there is a new opportunity for eastern red cedar to be processed into biochar and used in the greenhouse industry. This project is focused on establishing eastern red cedar biochar as a new Oklahoma product. The suppression of fire and increase of intensive grazing, combined with the rapid growth rate, high reproductive output, and dispersal ability of the eastern red cedar have allowed it to dramatically expand beyond its original range. Mechanical and chemical control measures are quite common and widely available, but it is uneconomical due to high removal cost and lack of the material utilization that would offset costs. Therefore, utilizing biochar prepared using eastern red cedar biomass, would also offset the cost associated with mechanical removal of trees and increase the willingness of landowners' for removal of eastern red cedar trees.
Research Area 1	**Environmental Issues**

PI: Junran Li	**Project Title: Deterioration, Die-off, and Removal of Shelterbelts: Effects on microclimate and wheat productivity in Oklahoma**
PS21-023	**Organization:** Department of Geosciences, The University of Tulsa
Rank: 3	**Year 1:** $50,000 **Year 2:** $46,696 **Total:** $96,696
Research	Born place of the "Number One Shelterbelt", Oklahoma planted more than 20 million trees, termed shelterbelts or windbreaks, in response to the devastating droughts and the Dust Bowl of the 1930s. Wheat is the top cash crop of Oklahoma and represents an average annual value of more than $600 million. In southwestern Oklahoma, many wheat farms benefit from favorable microclimatic conditions created by shelterbelts. However, the growth and vigor of many of the trees has declined in recent years and are no longer providing the benefits that they used to, causing broad concerns on agricultural economy and food supply in Oklahoma and the nation. While numerous studies have focused on the beneficial effects of shelterbelts, the consequences of deterioration, die-off, and removal of functioning shelterbelts have largely been overlooked. The significance of shelterbelts to the agroecosystems in the southern Great Plains may be amplified by climate change and the most recent multi-year drought. The proposed study will use an integrated approach of field monitoring, unmanned aerial vehicles, and model simulations to address this critical knowledge gap in the contexts of projected climate change and increasing demand in food, feed, and fiber. The proposed study directly contributes to the objectives of "plant productivity" and "environmental applications" of the OCAST Basic Plant Science program. This project will provide research and training opportunities for undergraduate and graduate students in hydrology, geographic information systems (GIS), and other environmental disciplines. Results from this project will facilitate the environmental assessment and valuation of the economic impact and potential policy ramifications for wheat production in the state. Data obtained from this project will build a strong foundation for Oklahoma researchers to compete for federal funding and support, including the Sustainable Agricultural Systems program supported by the US Department of Agriculture, programs of Ecosystem Science Cluster and Dynamics of Integrated Socio-Environmental Systems of NSF, and to advance the research and application of plant science in Oklahoma and beyond.
Research Area 1	**Ecology**

PI: Million Tadege	**Project Title: Understanding the mechanism of STF and MtWOX9 antagonistic interaction in regulating leaf blade development in Medicago truncatula.**
PS21-006	**Organization:** Oklahoma State University
Rank: 4	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	The leaf blade is a highly organized photosynthetic apparatus in which solar energy and carbon dioxide from the atmosphere are assimilated into sugar to sustain life on earth. Following its recruitment from pluripotent stem cells of the shoot apical meristem, the leaf primordium organizes itself into defined cell layers through highly regimented cell division and cell expansion patterns forming a flattened blade with distinct adaxial (upper) and abaxial (lower) surfaces. Because the leaf blade functions as a solar panel, its size and design are of fundamental interest to basic biology and crop productivity. However, despite extensive research and tremendous progress, we still know relatively little about how blade expansion is controlled. STENOFOLIA (STF), a WOX family transcription factor in Medicago truncatula, also called LAM1 in Nicotiana sylvestris is critically required for blade outgrowth and promotes cell proliferation at the adaxial-abaxial juxtaposition through a transcriptional repression mechanism that involves the transcriptional co-repressor TOPLESS (MtTPL). We identified that another WOX gene, MtWOX9, regulates blade outgrowth antagonistically to STF. MtWOX9 acts as a transcriptional activator and enhances the stf and lam1 mutant phenotypes. The molecular mechanism of MtWOX9 function in leaf blade development and the basis of its antagonistic activity to STF are unknown. The overarching goal of this proposal is to understand the molecular mechanism of MtWOX9 function in leaf blade development and uncover the molecular basis of its antagonistic relationship to STF in blade outgrowth. Our hypothesis is that STF and WOX9 antagonistically regulate the same target(s) to balance cell proliferation and cell differentiation during leaf blade development. This hypothesis will be tested using a combination of genomics, transgenic, and biochemical approaches. MtWOX9 targets will be identified using RNA-seq technology and compared with that of STF to identify common targets. The mechanism by which STF and WOX9 orchestrate their functions will uncover a transformative new concept in plant biology; how directional growth in plant lateral organs is antagonistically modulated by transcriptional repressor and activator functions of WOX genes. The project aims to engineer alfalfa to improve biomass yield and forage quality by increasing leaf surface area for more efficient photosynthesis, and will contribute to sustainable livestock production in Oklahoma and the nation.
Research Area 1	**Molecular Biology**

PI: Naichong Chen	**Project Title: Genetic regulation of AGL15, a critical regulator of seed development**
PS21-015	**Organization:** Oklahoma State University
Rank: 5	**Year 1:** $49,716 **Year 2:** $49,716 **Total:** $99,432
Research	Seed maturation is a critical developmental phase during which seed nutrient reservoirs such as storage proteins and seed oils accumulate. Mature seeds become desiccation tolerant and dormant, which allows them to survive harsh conditions and disperse to new habitats. AGAMOUS-LIKE15 (AGL15) is a MADS domain transcription factor that plays a critical role in regulating seed development in Arabidopsis. Expression of AGL15 remains high during embryogenesis to maintain seed maturation. Our previous findings showed that, during seed germination and subsequent seedling growth, AGL15 expression is directly repressed by a transcriptional silencing complex that alters epigenetic marks to inhibit the seed maturation program. The makeup of this silencing complex and the molecular mechanisms that control AGL15 expression remain unclear. We propose to use an unbiased genetic approach to address this shortfall. Seeds of a transgenic Arabidopsis line that express a luciferase reporter gene under control of the AGL15 promoter (AGL15p:LUC) were treated with the potent chemical mutagen ethyl methanesulfonate (EMS). Three putative mutants that exhibit strongly increased luciferase activity were selected from initial screens of M2 seedlings. Phenotypic characterization of these mutant plants will be carried out, including the identification of epigenetic histone marks associated with the AGL15p:LUC reporter and native AGL15 genes. Following genetic analysis, the causative lesions of these mutants will be identified using next a generation sequencing approach. This research will allow us to identify potentially novel genes involved in the developmental silencing of AGL15. Functional characterization of these genes will provide critical information about their roles in seed development and plant reproduction and could provide new strategies for the genetic improvement of crop productivity.
Research Area 1	**Molecular Biology**

PI: Lu Zhai	**Project Title: Tree-size effects on forest mortality and related economic loss in Oklahoma during the drought from late-2010 through mid-2015**
PS21-019	**Organization:** Oklahoma State University
Rank: 6	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	Drought is becoming more frequent and intense due to the changing climate, causing accelerated rates of tree mortality, particularly during Oklahoma's recent drought from late-2010 through mid-2015. The mortality-caused economic loss was substantial given the important role of forestry in Oklahoma's rural economy. Notably, drought-related tree mortality tends to vary with tree size. Both larger and smaller trees are reported to suffer more mortality in previous studies, resulting in considerable heterogeneity in the tree-size effect. However, mechanisms driving the heterogeneity remain unknown. More importantly, the heterogeneity causes uncertainty about projecting economic impacts of the tree mortality, given that large trees are more valuable due to their greater biomass and product class than small ones. Moreover, the different timber values by tree sizes tend to be neglected by previous analyses, leading to significant bias in economic assessments of drought impacts. Therefore, there are apparent knowledge gaps in the tree-size effects on mortality and related economic loss under drought. To address the gap and improve projection of the mortality impacts on Oklahoma's economy, we propose two inter-related studies: (1) Determine how the tree-size effects on mortality are affected by drought magnitude and stand attributes, e.g., stand density, species diversity; (2) Assess economic impacts of tree mortality during drought, e.g., impacts on output, employment, and income of forest and other related industries, given the tree size effect. At the completion of this project, we expect to identify the mechanisms of heterogenous tree-size effects on mortality and assess the economic impacts of drought on Oklahoma's forestry. These outcomes will improve both understandings of forest drought responses and economic assessments of climate change impacts, ultimately advancing forest management and increasing forestry profitability.
Research Area 1	**Ecology**

PI: Lu Zhang	**Project Title: The Role of Pruning and Irrigation Management in Pecan Tree Rejuvenation**
PS21-020	**Organization:** Oklahoma State University
Rank: 7	**Year 1:** $49,602 **Year 2:** $49,946 **Total:** $99,548
Research	Pecan tree rejuvenation is when epicormic shoots, which only have vegetative growth and do not set flowers or fruits, also known as 'suckers' or 'water sprouts', grow at the broken and cut limbs. This process is required after severe canopy damage caused by ice storms, tornadoes, or thunderstorms. Pecan trees usually take anywhere from 3 to 10 years of rejuvenation for epicormic shoots to develop fruiting shoots and recover sufficient productivity. Improper orchard management, such as improper epicormic shoot pruning or irrigation management, will delay nut reproduction and can result in devastating economic losses. There is a lack of research-based information regarding these management strategies after severe canopy loss. Previous research and our preliminary trials have proven that, during summer, pecan trees require a large amount of water when nuts are at the water stage (liquid endosperm). Drought stress could exacerbate fruit drop and poor kernel fill. However, for canopy-damaged trees with a lower transpiration requirement, excessive irrigation encourages massive vegetative growth that may or may not be suitable for optimal recovery. This project will study epicormic shoot removal strategies including removal level and application timing, and irrigation adjustment at different epicormic shoot removal levels of damaged pecan trees to better recover from rejuvenation. Soil moisture, stem water potential, photo-assimilation, return bloom, epicormic shoot growth, and nut quality will be evaluated and analyzed to discover the optimum epicormic shoot removal strategy and irrigation schedule for pecan trees with broken canopies.
Research Area 1	**Environmental Issues**

PI: Ming Yang	**Project Title: Toward a Systems-Level Understanding of Seed Dormancy Regulation**
PS21-005	**Organization:** Oklahoma State University
Rank: 8	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	Maintaining or breaking seed dormancy in appropriate environmental conditions is crucial to survival of plants. Many genes of diverse functions and multiple hormones including auxin have been reported to affect seed dormancy, but a systems-level understanding of seed dormancy regulation is lacking. Our experimental investigation has uncovered that AUXIN SIGNALING F-BOX PROTEIN 1 (AFB1) and 5 maternally promoted seed dormancy and our in silico analysis enabled the prediction of genetic networks consisting of 30 auxin-up- or downregulated genes in maternal seed dormancy regulation in Arabidopsis. Two-thirds of these genes encode either positive or negative factors for seed germination according to previously published reports. The remaining one-third genes are uncharacterized with respect to seed germination. In this proposal, I hypothesize that these uncharacterized genes also encode both positive and negative factors for germination, respectively, and their expression levels and positions in the networks determine their effect sizes on seed germination kinetics. To test the hypothesis, I propose to determine in Arabidopsis 1) if mutants of the uncharacterized genes in the predicted networks have an abnormal seed germination phenotype, 2) how the levels of expression of selected genes affect germination kinetics, and 3) the epistatic relationships between selected loci in seed germination. While 1) and 2) are apparently relevant to the hypothesis, 3) is essentially double mutant analysis for gaining information about the relative positions of selected genes in the networks and their effects on seed germination. The experimental approaches include primarily studies of mutant seed germination kinetics, gene transcript quantification coupled with germination kinetics studies in appropriate mutant alleles or wild type plants treated with different levels of auxin (IAA), and detection of tissue localization and levels of one or more selected proteins using transgenic plants harboring a protein-reporter transgene. Findings from this investigation should significantly deepen and broaden the current knowledge in the field of seed biology, and laying a foundation for future systems understanding of seed dormancy regulation. The known or predicted functions of the identified components already suggest that the auxin signaling networks involve both dormancy-promoting and germination-promoting factors, which is conceivably relevant to the plant's need of either remaining dormant or going into germination in response to the dynamics of environmental conditions. This work is expected to yield clues to the structures of auxin signaling networks in seed dormancy regulation and possibly in other processes in plants. In the applied aspect, knowledge gained from this investigation may help manipulate seed dormancy for better control of the timing of seed germination and prolonging seed lifespan (maintaining dormancy) in agricultural and other industrial practices.
Research Area 1	**Genomics and Genetics**

PI: Elijah Schnitzler	**Project Title: Biomass Burning Aerosol Emissions from Prescribed Wildland Fire Leading to Diffuse Radiation Fertilization**
PS21-004	**Organization:** Oklahoma State University
Rank: 9	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	Prescribed fire is used in wildlands in Oklahoma and across the southern Great Plains to promote native plant species, manage wildlife habitat, and enhance forage quality for livestock. Prescribed fire also releases into the atmosphere significant amounts of smoke, which includes nano-scale particles composed mainly of elemental and organic carbon. These biomass burning aerosol particles absorb and scatter radiation from the sun. Conducting many burns within a short period of time, traditionally spring, leads to concentrated smoke plumes that can travel downwind from wildlands into cities, where they negatively impact public health as well as the perception of prescribed fire as a land management practice, in general. One strategy to lessen smoke incursions into cities is to distribute burns more widely throughout the year. Recently, burns have been increasingly conducted during the growing season, when smoke could offer a critical advantage in the southern Great Plains. Sunlight scattered by biomass burning aerosol can reach more of the plant canopy than direct sunlight alone. In turn, this diffuse radiation fertilization can result in greater plant productivity. Consequently, there is a critical need to evaluate the potential of biomass burning aerosol from prescribed wildland fire to facilitate diffuse radiation fertilization during the growing season. We will bridge key knowledge gaps towards this first evaluation. Specifically, we will measure the physical and optical properties that govern light scattering by biomass burning aerosol from a wide range of regionally relevant grass species, determine aerosol emission factors from grasses transplanted from the field to a large combustion facility, and monitor smoke emission and dispersal from real prescribed wildland fires in the field during the growing season. The results will be combined and implemented in a simple model of aerosol interactions with sunlight to evaluate the potential for diffuse radiation fertilization. We expect this work to have practical implications for land managers, policy makers, and the people of Oklahoma, as it will impart an overlooked advantage of distributing burns from the traditional burning period in spring to the growing season and a new public perspective on smoke from prescribed fires. In the absence of this investigation, smoke will continue to play solely a negative role in the implementation and perception of prescribed wildland fire in the southern Great Plains.
Research Area 1	**Ecology**

PI: Eric LoPresti	**Project Title: Identification and Development of Mucilage Crops With Economic Potential for Utilization in the South-Central U.S.**
PS21-002	**Organization:** Oklahoma State University
Rank: 10	**Year 1:** $50,000 **Year 2:** $50,000 **Total:** $100,000
Research	A rapidly increasing, billion-plus dollar, market for plant seed mucilage (PSM) used in fiber supplements and food science applications as a binder and stabilizer relies totally on Chinese and Indian production of psyllium, Plantago ovata. Many other plants, including many native and naturalized species of the south-central US, produce PSM, though comprehensive screening of PSM chemistry, quantity, and mucilage properties has been done for very few of these species. My lab at Oklahoma State University has developed, and is currently set-up for, rapid assaying of seeds to quantify important PSM and seed traits (with six multi-part assays) across species to identify desirable characteristics. We have found in preliminary screenings that some of these species produce PSM in quantities which rival or even exceed P. ovata. In this proposal, I propose two specific aims: (1) to screen 100+ diverse species with PSM and crop potential from OK/TX in these six specific assays, and (2) to screen many 50+ OK/TX populations of a native psyllium, P. patagonica, a species for which our preliminary screenings have found has high potential for PSM utility, for desirable PSM and breeding characteristics using the same assays. While this proposed project would be by far the largest PSM investigation done to date, my lab's optimization of these assays means the project can be completed within the two years with the funding requested. The proposal funds a graduate student research assistant and undergraduate assistants to perform the assays; the results will be well-suited to publication in applied botanical journals. This project would both greatly expand our knowledge of PSM and the economic potential of OK/TX plants; it would more than double the number of species with quantified PSM traits and serve as a springboard for further development of a potentially lucrative crop for the South-Central United States. The results of this will be used to develop larger future grants for USDA for breeding and field testing of these PSM crops.
Research Area 1	**Seeds**

PI: Benedicte Bachelot	**Project Title: The Roles of Mutualism and Antagonism in Controlling Prairie Communities Following Disturbances**
PS21-003	**Organization:** Oklahoma State University
Rank: 11	**Year 1:** $49,674 **Year 2:** $49,573 **Total:** $99,247
Research	Grasslands, including tallgrass prairie, are one of the most productive and diverse ecosystems in the world and provide multiple ecosystem services. In particular, managed grasslands hold special economic importance in Oklahoma, which relies on a USD $3.7 billion annual cattle industry and is the nation's fifth-leading producer of cattle and calves (USDA-NASS). Despite their importance, these ecosystems are threatened by invasive species in Oklahoma and throughout the world. This is problematic, not only from an ecological point of view, but also from an economic perspective because some of these invasive plant species, such as Hypericum perforatum and Sorghum halepense, are toxic to livestock and Bison that graze in managed grasslands. In order to protect these ecosystems, it is crucial to understand the mechanisms that shape these plant communities. The long-term objectives of this study are to uncover how the biological controls (such as insects, and fungi) interact and shape plant communities in managed grasslands. In this proposal, I aim to 1) elucidate the roles played by natural enemies and fungi in plant dynamics, 2) assess how these roles are altered by land management, and 3) characterize how the biotic controls differ for native and invasive plant species. In addition to addressing these specific aims, this project will contribute to the overarching goals of the Bachelot research group: understanding the biotic controls of plant communities and the human impacts on these controls. This research will provide the preliminary data required to identify the biotic controls shaping tallgrass prairie communities. Knowledge acquired from the tallgrass prairie can be extrapolated to grasslands throughout Oklahoma, which are also managed by fire and grazing. Therefore, the proposed research will also contribute to the development of cost-efficient strategies to limit the spread of invasive grasses in Oklahoma using biotic controls.
Research Area 1	**Ecology**

OCAST 2021 Health Research Applications Approved Below the Funding Line

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
32	HR21-007: Identifying inhibitors of siderophore, heme and ferrous iron acquisition pathways of Pseudomonas aeruginosa	Oklahoma State University Avishek Mitra	$45,000	$45,000	$45,000	$135,000
33	HR21-017: Composition and functions of the human class B GPCR-RAMP interactome	University of Oklahoma Health Sciences Center Augen A. Pioszak	$45,000	$45,000	$45,000	$135,000
34	HR21-003: Improving health literacy and preventive care use among rural populations in Oklahoma	Oklahoma State University Xuewei Chen	$45,000	$45,000	$45,000	$135,000
35	HR21-069: Functional Network Alterations in Medically Intractable Epilepsy	University of Oklahoma John P. Masly	$44,940	$44,969	$44,928	$134,837
36	HR21-143: Multi-Target Peptide: A Drug to Remember	OUHSC Anne Kasus-Jacobi	$45,000	$45,000	$45,000	$135,000
37	HR21-083: Functional Characterization of a Novel Regulator of Tissue Growth in Drosophila	University of Oklahoma John P. Masly	$44,940	$44,969	$44,928	$134,837
38	HR21-012: Mechanisms of Action of Novel Antifungal Macrocycle Derivatives	Oklahoma State University Karen Wozniak	$45,000	$45,000	$45,000	$135,000
39	HR21-146: Safer Sugar-based Sepsis Therapeutics	University of Oklahoma Health Sciences Center Paul DeAngelis	$45,000	$45,000	$45,000	$135,000

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
40	HR21-082: DM505, A positive allosteric modulator of alpha7 nicotinic acetylcholine receptors for novel non-opioid anti-pain therapy	Oklahoma State University - Center for Health Sciences Hugo R. Arias				
			$44,948	$44,709	$44,662	$134,319
41	HR21-180: The past is prologue: Assessing whether glucocorticoid and immune epigenetic biomarkers link childhood adversity to adult psychosocial stress	Oklahoma State University Center for Health Sciences William Kyle Simmons				
			$44,978	$44,540	$44,624	$134,142
42	HR21-091: The Helmet-like Armor of Snapping Shrimp may Mitigate Blast-Induced Neurotrauma	The University of Tulsa Alexandra C N Kingston				
			$45,000	$45,000	$45,000	$135,000
43	HR21-150: Ribosome Biogenesis as a Therapeutic Target in Cancer	Board of Regents of the University of Oklahoma Health Sciences Center Lawrence Rothblum				
			$45,000	$45,000	$45,000	$135,000
44	HR21-040: Breast milk-derived exosomes for delivery of radiosensitizers for breast cancer	University of Oklahoma Health Sciences Center Anupama Munshi				
			$45,000	$45,000	$45,000	$135,000
45	HR21-112: Towards Monitoring Month Breath During Sleep Leveraging Off-the-shelf Sensors	University of Oklahoma Song Fang				
			$45,000	$45,000	$45,000	$135,000
46	HR21-098: Effects of Microplastics and Nanoplastics Contamination on Mammalian Cell Function	Oklahoma Medical Research Foundation Gary J Gorbsky				
			$45,000	$45,000	$45,000	$135,000

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
47	HR21-087: TREATMENT EFFECT OF 9-VALENT HPV VACCINE IN HPV POSITIVE WOMEN	Board of Regents of the Univ. of OK Health Sci. Center Caroline Markey	$45,000	$45,000	$45,000	$135,000
48	HR21-066: Allostery in Flavivirus NS3: A Target for Selective Antivirals	Oklahoma State University Martin McCullagh	$45,000	$45,000	$45,000	$135,000
49	HR21-072: Exploring the complex interplay between device-measured daily movement behavior and health: a prospective cohort study.	The University of Tulsa Eric Wickel	$44,712	$38,166	$19,517	$102,395
50	HR21-141: Interoceptive Processing in Adolescents Exposed to Early Life Stress	Laureate Institute for Brain Research Namik Kirlic	$44,962	$44,863	$44,784	$134,609
51	HR21-148: The Therapeutic Potential and Molecular Mechanism of a Novel Decoy Peptide Inhibitor in Polycystic Ovary Syndrome	University Of Oklahoma Health Sciences Center Hongliang Li	$45,000	$45,000	$45,000	$135,000
52	HR21-124: Early Detection of Oral Cancer Through Deep Neural Network and Edge Computing	Oklahoma State University Gary Yen	$45,000	$45,000	$45,000	$135,000
53	HR21-099: Mps1-interacting proteins that promote tumor cell survival	Oklahoma Medical Research Foundation Dean Dawson	$45,000	$45,000	$45,000	$135,000
54	HR21-126: Role for Acetylation in DNA Replication Origin Site Selection	Oklahoma Medical Research Foundation Christopher L. Sansam				

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
			$45,000	$45,000	$45,000	$135,000
55	HR21-172: The role of very long chain polyunsaturated fatty acids in male fertility	Board of Regents of the University of Oklahoma Health Sciences Center Karl Hansen				
			$45,000	$45,000	$0	$90,000
56	HR21-131: Earth-Abundant Iron- and Copper-Based Photocatalysts for Continuous Syntheses of Pharmaceuticals through C-N, C-S and C-O Coupling Reactions	Oklahoma State University Marimuthu Andiappan				
			$44,571	$44,543	$44,548	$133,662
57	HR21-169: Unravelling the complex functions of B Cell Maturation Antigen in neuro-autoimmunity	Oklahoma Medical Research Foundation Gaurav Kumar				
			$45,000	$45,000	$45,000	$135,000
58	HR21-004: Nonsuicidal Self-Injury: Development of a Personalized Mobile Intervention	Oklahoma State University Stephanie Sweatt				
			$44,987	$43,390	$44,745	$133,122
59	HR21-025: PFKFB3-dependent regulation of adipocyte mRNA and protein expression	Board of Regents of the University of Oklahoma Health Sciences Center Ann Louise Olson				
			$42,575	$44,215	$44,215	$131,005
60	HR21-117: Designing a User-Friendly Diabetic Retinopathy Screening App Using Routine Lab Results for Rural Primary Care Providers	Oklahoma State University Tieming Liu				
			$45,000	$45,000	$45,000	$135,000
61	HR21-153: Peptide-based tool for controlling immunogenic cell death	University of Oklahoma Handan Acar				
			$34,679	$34,679	$34,679	$104,037
62	HR21-067: H2S Regulation of Airway Epithelial Programming and Injury during Neonatal Development	University of Oklahoma Health Sciences Center				

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
		Abhrajit Ganguly				
			$45,000	$45,000	$45,000	$135,000
63	HR21-162: Prevention of cognitive decline in older adults with peripheral artery disease	University of Oklahoma Health Sciences Center Andriy Yabluchanskiy				
			$45,000	$45,000	$45,000	$135,000
64	HR21-079: Computer Simulation Enabled Machine Learning for Early Detection of Heart Disease	Oklahoma State University Bing Yao				
			$45,000	$45,000	$45,000	$135,000
65	HR21-042: Hepatitis C virus Associated Inflammation and Cancer Development	Oklahoma State University Center for Health Sciences Rashmi Kaul				
			$45,000	$45,000	$45,000	$135,000
66	HR21-077: Better Health for Oklahomans by Reducing Technostress through Active Computer Workstations and Digital Wearables	University of Oklahoma Radhika Santhanam				
			$45,000	$45,000	$44,993	$134,993
67	HR21-039: The mechanisms by which acetylation regulates stu2 and microtubule function	Oklahoma State University Rita K. Miller				
			$45,000	$45,000	$45,000	$135,000
68	HR21-060: AI-enabled real-time imaging and diagnosis technique for effective drug delivery in solid tumor treatment	Oklahoma State University Chenang Liu				
			$44,836	$44,971	$44,953	$134,760
69	HR21-057: Blocking myostatin to improve vascular cell function and enhance blood flow in diabetic skeletal muscle	Oklahoma State University Pamela Lovern				
			$45,000	$45,000	$45,000	$135,000
70	HR21-061: Alzheimer's disease associated pathology is accelerated by herpes simplex virus 1 infections	Oklahoma State University Clinton Jones				
			$45,000	$45,000	$45,000	$135,000
71	HR21-055: Physical, Emotional, and Cognitive Effects of Brain Training Programs in Sjogren’s Patients	University of Oklahoma Health Science Center Robert Hal Scofield				

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
			$45,000	$45,000	$45,000	$135,000
72	HR21-108: Addressing psychiatric hospitalizations among autistic adolescents and emerging adults: The role of social inclusion and community mental healthcare resources	Oklahoma State Univeristy DJ McMaughan				
			$40,620	$39,088	$37,109	$116,817
73	HR21-010: Developing a Fourier Ptychography based Microscopic Scanning System to Facilitate the Diagnosis of Thyroid Carcinoma	The University of Oklahoma Yuchen Qiu				
			$45,000	$45,000	$45,000	$135,000
74	HR21-102: Thermosensory Processing	Univ. of Oklahoma Christian Lemon				
			$45,000	$45,000	$45,000	$135,000
75	HR21-176: Dissecting the molecular basis of bacterial plasmid addiction systems	University of Oklahoma Christina R. Bourne				
			$44,242	$0	$0	$44,242
76	HR21-118: Threshold Strength Ceramic Dental Crowns by Direct Ink Writing 3D Printing	Oklahoma State University Jim Smay				
			$40,387	$39,471	$40,593	$120,451
77	HR21-037: Cardiac glycolysis affects systemic glucose homeostasis	Oklahoma Medical Research Foundation Kenneth Humphries				
			$45,000	$45,000	$45,000	$135,000
78	HR21-073: Focusing the immune response to enhance efficacy, safety, and cross-protection of a single-cycle live RSV vaccine	Oklahoma State University Antonius Oomens				
			$45,000	$45,000	$45,000	$135,000
79	HR21-085: Novel Role for Neuritin in Adipogenesis	Oklahoma State University Myron Hinsdale				
			$45,000	$45,000	$45,000	$135,000
80	HR21-111: Post-Mechanical Trauma, Autoimmune Reactions to Red Blood Cells as Markers	University of Oklahoma Edgar A. O'Rear				
			$44,960	$44,441	$44,792	$134,193

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
81	HR21-011: Targeting carbonic anhydrases in calcification and virulence of P. aeruginosa	Oklahoma State University Marianna Patrauchan	$45,000	$45,000	$45,000	$135,000
82	HR21-138: Chemical Free Advanced Local Pesticide Validation System	Oklahoma State University Jay Hanan	$45,000	$45,000	$0	$90,000
83	HR21-089: Targeting CTRP for macrophage-based therapy in diabetes	Oklahoma State University Xia Lei	$45,000	$45,000	$45,000	$135,000
84	HR21-104: Correlating BPEI PEGylation with PAMP Neutralization	University of Oklahoma Charles Rice	$45,000	$45,000	$45,000	$135,000
85	HR21-048: Smart Linkage for Optimized Specific Upper-Limb Muscle Rehabilitation	Oklahoma State University Yujiang Xiang	$45,000	$45,000	$45,000	$135,000
86	HR21-128: Regulation of OATP1B1 and OATP1B3 by lysine acetylation and lysine deacetylase inhibitors	University of Oklahoma Health Sciences Center Wei Yue	$45,000	$45,000	$45,000	$135,000
87	HR21-160: Effects of SARS-CoV-2 Spike Protein on Hematopoietic and Cardiovascular Systems	OUHSC Joe zhao	$32,959	$33,089	$32,139	$98,187
88	HR21-056: Developing a Decision Support System Prototype for Predicting the Effect of Medicinal Addictive Drugs on Individuals	Oklahoma State University Rittika Shamsuddin	$44,804	$41,036	$42,311	$128,151
89	HR21-140: The role of mitochondrial redox signaling in iNKT cells	Oklahoma Medical Research Foundation Meng Zhao	$45,000	$45,000	$45,000	$135,000

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
90	HR21-096: Motion Capture on-the-fly for Cognitive Load Assessment	Oklahoma State University Guoliang Fan	$45,000	$45,000	$45,000	$135,000
91	HR21-094: Endogenous Retroviral RNA Expression in Influenza and COVID-19	University of Oklahoma Susan Schroeder	$45,000	$45,000	$45,000	$135,000
92	HR21-084: 3D Printed Drug Release on Cell-Based Tissue Model	Oklahoma State University Sundararajan Madihally	$45,000	$45,000	$45,000	$135,000
93	HR21-059: The intersection of cell shape, size and metabolism	Oklahoma State University Randy Morgenstein	$45,000	$45,000	$45,000	$135,000
94	HR21-029: Assistive Technology Interventions for Dementia Homecare Environments	Oklahoma State University Emily Roberts	$45,000	$45,000	$45,000	$135,000
95	HR21-157: Deciphering metabolic pathways utilized by Streptococcus sanguinis during blood dissemination and endocardial growth: Roles of SSA_2154 (carbonic anhydrase), SSA_0809 (enamine deaminase) and SSA_0908 (substrate binding protein).	Southwestern Oklahoma State University Vijay Somalinga	$42,249	$44,346	$42,673	$129,268
96	HR21-159: Characterization of lactic acid bacterial isolates showing antimicrobial activity against food pathogens.	Oklahoma State University-Center for Health Sciences Ratnakar Deole	$45,000	$45,000	$45,000	$135,000
97	HR21-116: A Novel Urine Biomarker to Identify Bladder Infections in Pregnant and Non-Pregnant Women	Board of Regents of the Univ. of OK Health Sci. Center Jameca Price	$45,000	$45,000	$45,000	$135,000

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Year 3 Request	Total Request
98	HR21-070: Mechanical transmission of Trypanosoma cruzi by brown dog ticks	Oklahoma State University Kelly E. Allen				
			$45,000	$45,000	$45,000	$135,000
99	HR21-154: Role of mTOR/IGF-I and gut microbiome in isoleucine and valine induced growth in piglet model of small for gestational age infants	Oklahoma State University Adel Pezeshki				
			$45,000	$45,000	$45,000	$135,000
100	HR21-133: Characterization of Genes Associated with Resistance to Hydrophobic Antibacterial Agents and Biofilm Formation in Nosocomial Species of the Genus Serratia	Oklahoma State University Center for Health Sciences Franklin R. Champlin				
			$45,000	$45,000	$0	$90,000
101	HR21-014: Novel Gram-negative antibiotic resistance mechanism	Department of Biochemistry and Molecular Biology, Oklahoma State University John E. Gustafson				
			$43,938	$44,938	$0	$88,876
102	HR21-181: Genome Epidemiology of COVID-19 in Oklahoma	Souther Nazarene University Caio Martinelle Barbalho de França				
			$45,000	$45,000	$45,000	$135,000
	Totals		**$3,155,347**	**$3,100,454**	**$2,856,265**	**$9,112,066**

OCAST 2021 Health Research Applications Not Approved for Funding

Application No.	Organization	PI	Title
HR21-008	OSU-Center for Health Sciences	Subhas Das	Epigenetic Regulation of Glutaminase in Neuro-inflammatory pain.
HR21-018	Oklahoma State University	Jill Joyce	Spouses First Challenge: Impact on an Online Theory-Based Nutrition and Physical Activity Program on Chronic Disease Risk Factors Among First Responder Spouses
HR21-019	Oklahoma State University	McKale Montgomery	The Influence of Iron Regulatory Proteins on Ferroptosis and Neurodegeneration
HR21-020	Oklahoma State University	Sumit Mandal	Can Wearing Contaminated Workwear Affect Oilfield-workers' Physiology? - An Empirical Investigation
HR21-023	Oklahoma State University	John Tetnowski	Effacious Stuttering Intervention: Taking it to the Rural Population
HR21-024	Oklahoma State University	Ziad El Rassi	Siliceous precursor sorbent for various columns and ProteoMiner for in-depth proteomics
HR21-027	Oklahoma State University	Jeanne Bolliger	New synthetic strategies to access biologically active sulfur containing heterocycles
HR21-028	The University of Tulsa Syed Hussaini	Syed Hussaini	Targeting Mitochondria for the Prevention and Treatment of COVID-19
HR21-033	Oklahoma State University	Arunkumar Bagavathi	Networks Based Deep Learning Methods for Point-of-Care Diagnostics with Animal Metagenomes
HR21-034	Oklahoma State University	Guinevere Wogan	Epigenetics of Early Stress Exposure: Unraveling a Complex Stress-Induced Polyphenism
HR21-036	Oklahoma State University	Elizabeth McCullagh	Auditory Brainstem Response, an Early Biomarker for Autism Detection
HR21-043	Oklahoma State University	Shuxia Peng	Identification of the allosteric binding sites in Hsp90 chaperone by structural biology
HR21-046	Board of Regents of the Univ. of OK Health Sci. Center	Spenser Perloff	Comparing the effect of a new combination prophylactic regimen for individuals at high risk for obstetric hemorrhage
HR21-047	Oklahoma State University Center for Health Sciences	David R Wallace	Involvement of SIRT1 in pancreatic damage following exposure to environmental toxicants: Diabetes to Pancreatic Cancer
HR21-053	University of Oklahoma	Zhibo Yang	Interactions between Drug-Resistant and Drug-Sensitive Cancer Cells: Mass Spectrometry Metabolomics Studies of Single Cells and Multicellular Spheroids in Coculture Systems

Application No.	Organization	PI	Title
HR21-054	Oklahoma State University	Jerome Hausselle	Effect of Gait Dynamics on Cartilage Damage
HR21-058	Oklahoma State University	Guangping Chen	Three-dimensional culture for drug development and personalized cancer therapy
HR21-064	Oklahoma State University	Gabriel A. Cook	Studying the effects of Glycosylation of Membrane Proteins Involved in Human Disease
HR21-065	University of Oklahoma Health Sciences Center	Rajagopal Ramesh	BRG1 (SMARCA4) status dictates the response of wild-type EGFR lung cancer to EGFR-TKIs
HR21-068	The University of Tulsa	Joanne L Davis	Reducing Suicidal Ideation Through Improving Sleep
HR21-075	University of Oklahoma Health Sciences Center	Maria J. Ruiz Echevarria	Molecular Function of TMEFF2, a prostate tumor suppressor, and its effect on the cell cycle
HR21-076	OMRF	Scott M. Plafker	Determining the metabolic health impacts of a well-formulated ketogenic diet
HR21-081	Oklahoma State University	Chulho Yang	Numerical and Experimental Investigation on Noise-Induced Hearing Loss Caused by Earbuds
HR21-086	Oklahoma State University	S. M. Kennison	Understanding Passive Versus Active Health-Related Risk-Taking
HR21-092	University of Oklahoma Health Sciences Center	Ralf Janknecht	Role of DNPH1 in Melanoma
HR21-093	Oklahoma State Univeristy-Tulsa	Tonya Hammer	Body image and quality of life: A comparison study with group intervention between rural and urban LGBQ+ adults
HR21-095	Oklahoma State University	Aihua Xie	Advanced Infrared Biology of Protein Structure & Dynamics
HR21-100	University of Tulsa	Matteo Avella	A new step in gamete interaction
HR21-109	The University of Oklahoma	Catalin Teodoriu	Development, testing and validation of a ‘smart’ mechatronic device to enhance pre-clinical training for the placement of dental implants and bone biopsy procedures
HR21-113	Hough Ear Institute	Richard D. Kopke	Investigation of Potential Correlations Between Blast-Induced Tinnitus and Maladaptive Neurogenesis
HR21-120	University of Central Oklahoma	Christina Hendrickson	Phytochemical Analysis of Taraxacum officinale to Determine its Anti-carcinogenic Constituents
HR21-121	University of Central Oklahoma	Mohammad Hossan	In-vivo efficacy analysis of bioresorbable flow diverters for aneurysm treatment
HR21-123	OU Hudson College of Public Health	Karla J Finnell	Examining the Complex System of Maternal Stresses among Black Women Living in Formerly Redlined Areas

Application No.	Organization	PI	Title
HR21-125	Oklahoma State University	Jose L Soulages	Lipids and Vitellogenesis in Aedes aegypti
HR21-127	Oklahoma State University	DO YOUNG KIM	Piezoelectric OLEDs for direct ultrasound imaging
HR21-129	University of Central Oklahoma	Lilian Chooback	Enzymes of lysine biosynthetic pathway: targets for the development of novel antibiotic therapies
HR21-135	University of Oklahoma	Mojgan Padash-Barmchi	Validation and Mechanistic Studies of Novel Drug Targets in Cervical Cancer
HR21-137	OUHSC	Vadim A. Ivanov	Proteolytic enzyme inhibitors for treatment of meconium aspiration syndrome in an animal model.
HR21-149	Oklahoma State University	Heather D.N. Fahlenkamp	Development of a tissue-engineered eye model to test drug delivery systems
HR21-158	University of Oklahoma Health Sciences Center	Anthony Burgett	Drug Targeting Oxysterol-Binding Protein (OSBP) for Metabolic Syndrome and Longevity Proposal
HR21-161	University of Oklahoma Health Sciences Center	Shirley James	First Step Towards Effective Propulsion (FSTEP): A novel device for addressing paretic propulsion in individuals with stroke
HR21-167	University of Oklahoma	Wesley T. Honeycutt	Development of Corticosteroid Sensors for Continuous Monitoring Implants
HR21-174	University of Oklahoma Health Sciences Center	Amgad Amin	3D Bioprinted Tissue Engineered Nanofiber Scaffold with Mesenchymal Stem Cells for the Treatment of Articular Cartilage Osteochondral Defects
HR21-178	Rogers State University	Jin Seo	Obesity Control using microRNAs and their Target Genes
HR21-179	Hough Ear Institute	Matthew B. West	Defining the efficacy of a clinical stage oral therapeutic for reducing trauma-induced tauopathy in the CNS

PI: Guangpu Li	**Project Title: Specificity of Rab Isoforms**
HR21-063	**Organization:** University of Oklahoma Health Sciences Center
Rank: 1	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	The goal is to understand the mechanism of membrane localization and function of Rab GTPases in intracellular transport. This project is focused on two Rab isoforms, Rab22 and Rab31 (a.k.a. Rab22b), and investigates their distinct localization and function despite nearly 90% sequence similarity. To this end, our preliminary studies suggest that the C-terminal hypervariable domain (HVD) largely accounts for the distinct localization of Rab22 and Rab31 to early endosomes and the Golgi complex via differential interaction with membrane effectors. Furthermore, Rab22 is shown to control angiotensin II-mediated hypertension in mice. Because Rab22 and Rab31 share the same switch I and II regions for interaction with effectors and regulators, we propose a novel concept that different membrane localization may account for their functional specificity, which may result from quantitative differences in interaction with the membrane-associated effector(s). Along this line, the amino acid differences in the HVD may affect binding affinity for the effector(s) directly or indirectly via conformational changes in the switch regions and consequently influence the Rab localization and function. We will test the hypothesis with three specific aims. Aim 1. To determine the structural domain responsible for differential Rab22 and Rab31 localization. We will narrow down the amino acid residues in HVD that determine the Rab localization by construction of Rab22 and Rab31 chimeras, site-directed mutagenesis and confocal microscopy. Furthermore, we will determine if C-terminal HVD and ISL as well as N-terminal domain, based on structural comparison, constitute a general membrane targeting domain (MTD) for the Rab5 subfamily members by transplantation of Rab31 MTD to Rab5 and vice versa and determine the effect on their intracellular localization by confocal microscopy. Aim 2. To determine the cellular factors responsible for differential Rab22 and Rab31 localization. Our preliminary data show that Rab22 binds more strongly to the early endosome-associated effectors EEA1 and Rabenosyn-5 than Rab31 in GST pulldown assays. We will characterize additional Rab22 and Rab31 chimeras and mutants in these pulldown assays and further quantify each binding affinity by microscale thermophoresis (MST). Then, we will test the roles of these effectors in the Rab localization by RNAi-mediated knockdown or CRISPR-mediated gene ablation. Furthermore, we will screen for novel effectors and characterize their roles in Rab22 and Rab31 localization. Aim 3. To determine if endosome-localized Rab31 chimera or mutant can function like Rab22 in vitro and in vivo. We will establish a HEK293 cell line expressing the angiotensin II receptor AT1R and test Rab22 or the Rab31 chimera/mutant in AT1R endocytosis and recycling. Furthermore, we will generate transgenic mice expressing Rab22 or the chimera/mutant and determine if they can rescue the defective blood pressure regulation in the Rab22 KO mice.
Research Area 1	Cell/Molecular Biology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Yong Cheng	**Project Title: WNK4-mediated Exosome Biogenesis Inhibits Cystic Fibrosis Macrophage Death during Nontuberculous Mycobacterial Infection**
HR21-050	**Organization:** Oklahoma State University
Rank: 2	**Year 1:** $35,431 **Year 2:** $28,884 **Year 3:** $19,251 **Total:** $83,566
Research	Exosomes are nanoscale membrane vesicles with a size between 50 to 150 nm that are released by eukaryotic cells. These vesicles play a critical role in intercellular communications between eukaryotic cells and are key components in the host immunity in response to microbial infections. However, we still know little about exosome biogenesis in host cells in response to invading bacteria. Nontuberculous Mycobacteria (NTM) are opportunistic pathogens that cause infections in individuals with underlying lung disease or depressed immune systems such as cystic fibrosis and chronic obstructive pulmonary disease (COPD). Cystic fibrosis is a genetic disorder in humans that is caused by defective CFTR (Cystic fibrosis transmembrane conductance regulator) protein, a chloride ion channel. The majority of NTM strains (95%) isolated from cystic fibrosis patient lungs are Mycobacterium avium complex (MAC) (M.avium and M.intracellulare) and Mycobacterium abscessus complex (MABSC) (M.abscessus, M.massiliense and M.bolletii). Our preliminary data show that exosome biogenesis was dramatically dysregulated in mouse cystic fibrosis (Cftr-/-) macrophages relative to wild-type (Cftr+/+) macrophages during M.abscessus infection. Therefore, we hypothesize that CFTR-associated intracellular Cl- homeostasis regulates exosome biogenesis in NTM-infected macrophages. In this proposal, we will test our hypothesis using M.abscessus and mouse Cftr+/+ and Cftr-/- macrophages as our study model. We hope our study will facilitate the development of host-directed therapy for cystic fibrosis patients with bacterial lung infections.
Research Area 1	Infectious Disease
Research Area 2	Immunology
Research Area 3	Cell/Molecular Biology

PI: Thanh Thieu	**Project Title: Leveraging deep active-transfer learning to identify low-resource mobility functioning information in public clinical notes**
HR21-173	**Organization:** Oklahoma State University
Rank: 3	**Year 1:** $44,926 **Year 2:** $45,000 **Year 3:** $0 **Total:** $89,926
Research	Secondary use of electronic health records (EHRs) for clinical, administrative, and research purposes have mostly focused on health conditions (i.e. diseases, disorders) and related drugs. The assessment, application, and identification of function in medical EHRs has been almost unexplored. Therefore, there exists a critical need to develop methods and resources to automatically identify functioning information from EHRs. The U.S. Social Security Administration (SSA) exemplifies the use of function to adjudicate their disability benefit programs. My long-term objective is to reduce application backlogs and waiting time for disabled Oklahoman applicants by developing methods and resources to automatically capture functioning evidence from EHRs. In my preliminary study, I have identified Mobility as an important, observable, and self-contained domain of ICF. I also established the need to capture functioning information, created a private corpus at the National Institutes of Health, and built supervised named entity recognition machine learning models to capture mobility functioning concepts with good accuracy (84.9% F1-score). Nevertheless, there exists limitations: (1) it is unknown how well the models perform outside of the NIH on data with different institutional language idiosyncrasies, and (2) the private corpus is unavailable to the public, making it impossible to accelerate research by leveraging the public community. The publicly available National NLP Clinical Datasets (N2C2) provides an answer to the limitations. Unfortunately, the N2C2 data does not have any annotation for mobility, rendering it useless for supervised entity recognition methods. In this proposed work, my specific research goal is to combine deep transfer learning (a modern neural networks machine learning technique) with active learning (an annotation sample selection technique) to build mobility entity recognition models on N2C2 data. The non-existence annotation for mobility information on N2C2 makes it extremely low-resourced for entity recognition purpose. I propose to overcome this obstacle by combining transfer learning with active learning. My plan is to pursue two specific aims: Specific aim #1: Utilizing deep active-transfer learning to train robust mobility entity recognition models on N2C2 with the least effort in human annotation. I project that the resulting models will have comparable accuracy while require less annotation compared to the ones built on NIH private data. Specific aim #2: Build a community web portal to publicize mobility recognition models and mobility annotation in N2C2. I project that scientific publication and software development to identify functioning information from EHRs will multiply after one year from the release date.
Research Area 1	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Nutrition/Psychology/Public Health

PI: Ying He	**Project Title: Epigenetic regulation of opioid addiction by microRNA**
HR21-107	**Organization:** Oklahoma State University Center for Health Sciences
Rank: 4	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	My long-term research goal is to develop effective pharmacological interventions that can prevent or cure opioid use disorders. Our nation is in the midst of a formidable opioid crisis, which claims the lives of nearly 50,000 Americans each year and leaves millions more struggling with addiction. Oklahoma is among the states hardest hit by the opioid epidemic. Current FDA-approved medications for opioid use disorder are underused, and the risk of relapse is high. There remains a critical and urgent need to advance our understanding of the neurobiological mechanisms of opioid addiction. Long-term opioid exposure induces persistent alterations to the function of reward-processing networks in the brain. Current evidence suggests drug-induced epigenetic modifications switch the reward system into a hyperresponsive state promoting future drug seeking and drug taking. While most of the research attention has been paid to how epigenetic modifications promote addiction for psychostimulants such as cocaine, opioid-induced alteration of the epigenetic landscape has largely been lagging behind. microRNA (miRNA) is now recognized as one of the major epigenetic regulators that controls target gene expression at the post-transcriptional level. Emerging evidence has implicated miRNAs in regulating addiction-relevant neuroplasticity in the brain. My preliminary data demonstrate a marked increase of let-7 family miRNAs expression in cellular and mouse models of opioid addiction. Moreover, we previously reported that let-7 family miRNAs contribute to the development of analgesic tolerance. However, it is not known whether let-7 regulates opioid dependence. In an effort to explore addiction neurobiology, the μ opioid receptor (MOR) remains as the focus of intensive research, since it is the primary receptor responsible for both beneficial and adverse effects of the opioids. Indeed, my previous work identified MOR as a direct target of let-7 miRNA, which is subjected to the constitutive translation repression by let-7 miRNA. In this application, I propose to test the hypothesis that let-7 family miRNA is a functional target of morphine to modulate the development of physical dependence in opioid addiction. By characterizing the modulatory role of miRNA in opioid addiction at the molecular, cellular and behavioral levels, specific targeting of these mechanisms holds great promise of designing effective therapies that can benefit patients with opioid addiction. Successful completion of the study will not only generate crucial preliminary data to submit an NIH R01 application, but also lead to a groundbreaking new research area identifying miRNA as the epigenetic and neurobiological mechanism for opioid addiction.
Research Area 1	Physiology/Pharmacology
Research Area 2	Neurobiology
Research Area 3	Cell/Molecular Biology

PI: Katerina Ntourou	**Project Title: Attentional bias to threat, social anxiety, and childhood stuttering**
HR21-052	**Organization:** University of Oklahoma Health Sciences Center
Rank: 5	**Year 1:** $39,498 **Year 2:** $39,215 **Year 3:** $40,250 **Total:** $118,963
Research	Stuttering is a neurodevelopmental speech disorder that has substantial negative impact on children's academic, emotional, and social development as well as their later vocational achievement and financial security. Furthering such negative impact is the fact that stuttering is associated with an increased risk for social anxiety in adolescence and adulthood. In the school-age years, children's stuttering is associated with a seven-fold increase in the odds of developing social anxiety, reaching an alarming 16- to 34-fold increase by adulthood. This is especially concerning given that social anxiety can negatively impact multiple aspects of life, creating substantial economic burden on individuals who stutter and society at large. Although it is likely that environmental events/stressors (e.g., negative peer reactions) contribute to the elevated risk for social anxiety, the role of child-specific/intrinsic factors, which have been assigned causative role in models of social anxiety, cannot be overlooked. Given the above, it is imperative to study risk factors to social anxiety during early childhood (the time when stuttering typically begins) and determine whether they differ between children who do and do not stutter and whether they impact the actual stuttering severity, and reactions to stuttering of children who stutter. To address this imperative, the present applicant proposes the study of such factors: (1) attentional bias to threat (i.e., preferential allocation of attention towards negative stimuli) and its components (vigilance to threat, difficulty disengaging from threat), and (2) effortful control (i.e., ability to inhibit a dominant response to perform a more adaptive subdominant response) with the use of eye tracking, standardized parental-report measures, standardized tests of children's stuttering (stuttering severity, reactions to their stuttering). The proposed project builds on our preliminary findings and conceptual model that relates attentional processes (i.e., attentional bias to threat, vigilance to threat, difficulty disengaging from threat) and temperamental factors (i.e., effortful control) to the onset, development and maintenance of childhood stuttering as well as risk for developing social anxiety. To objectively evaluate these factors, the applicant with employ multiple methods (i.e., eye-tracking, standardized tests of temperament, stuttering severity, and reactions to stuttering). The proposed project is supported by an interdisciplinary team specializing in stuttering, theory/methodology relating to attentional biases to threat in anxiety, eye tracking methodology, and quantitative research design and data analyses. Findings from this investigation will help ground the study of stuttering within the broader context of socioemotional development and help focus future research on issues that inform diagnostic and treatment protocols for childhood stuttering.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Nutrition/Psychology/Public Health

PI: Tiangang Li	**Project Title: Sulfur amino acid metabolism in the pathogenesis of fatty liver disease**
HR21-106	**Organization:** Board of Regents of the University of Oklahoma Health Sciences Center
Rank: 6	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	It is increasingly recognized that non-alcoholic steatohepatitis (NASH) is a prevalent liver disease with heterogenous underlying causes. Now, new evidence suggests that dysregulated hepatic sulfur amino acid metabolism is associated with advanced human NASH and causes markedly worsened steatosis and injury in genetic mouse models. However, significant knowledge gaps exist in our understanding of how sulfur amino acid metabolism modifies NASH severity, and what mechanisms control hepatic sulfur amino acid metabolism in normal physiology and liver diseases. This proposal builds on our discovery that coenzyme A (CoA) metabolism is a key missing link between impaired hepatic sulfur amino acid metabolism and liver fat accumulation and injury in NASH. We aim to establish a novel pathogenic mechanism whereby hepatic availability of cysteine (a CoA synthesis substrate) is critical in maintaining the mitochondrial CoA pool to support fatty acid oxidation. However, dysregulated sulfur amino acid flux in NASH reduces cysteine availability that impairs CoA synthesis. Hepatic CoA insufficiency in turn limits the liver's ability to adapt to increased fatty acid influx, creating a condition termed metabolic inflexibility that promotes mitochondrial dysfunction, steatosis and oxidative stress driving disease progression. Mechanistically, we have identified that impaired methionine adenosyltransferase 1A (MAT1A), which mediates upstream methionine cycle-transsulfuration flux to produce cysteine, contributes to such pathogenic condition by decreasing cysteine synthesis. Further study revealed that the nutrient-sensing transcriptional factor TFEB stimulates MAT1A to promote cysteine and CoA synthesis. We will use liver specific MAT1A gain-of-function and loss-of-function mouse models to establish the significance of MAT1A in regulating hepatic sulfur amino acid, CoA and GSH metabolism, and further investigate how TFEB activation attenuates NASH progression by stimulating the MAT1A-driven sulfur flux. By defining a new pathogenic link of sulfur amino acid metabolism to CoA metabolism, we expect that this study may advance the field by providing not only new insights into the mechanisms driving NASH progression but also molecular basis for developing future therapeutic interventions.
Research Area 1	Physiology/Pharmacology
Research Area 2	Cell/Molecular Biology
Research Area 3	Chemistry & Biochemistry

PI: Junpeng Deng	**Project Title: Mechanism of cytosolic dsNA sensing by SAMD9**
HR21-071	**Organization:** Oklahoma State University
Rank: 7	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Human Sterile Alpha Motif Domain-containing 9 (hSAMD9) and its paralog SAMD9L are myeloid tumor suppressors and antiviral factors. Gain-of-function (GoF) mutations in SAMD9/9L are a common cause for inherited bone marrow failure syndrome, predisposing for myeloid malignancies, but the molecular functions of SAMD9/9L are largely unknown. We have identified a novel double strand nucleic acid (dsNA) binding domain from hSAMD9. We solved the crystal structure of this unique domain in complex with a 22bp dsDNA. Structure-guided mutagenesis identified three basic residues essential for dsNA binding. Mutations of each of these residues abolished the antiviral and antiproliferative functions associated with wild-type and GoF SAMD9/9L variants. Furthermore, the mutations rescued the profound suppression of global protein synthesis by GoF variants. These exciting unpublished data lead to our novel hypothesis that SAMD9&L could function as a unique cytosolic dsNA sensor in innate immunity and anti- proliferation suppression. In this proposal, we aim for further detailed mechanistic studies on this unique dsNA sensing domain from SAMD9 by using structural and functional approaches. The expected outcome will reveal the novel mechanism of SAMD9&L for sensing cytosolic dsNA, which plays an essential role in cellular development, tumor suppression and antiviral defense. The studies will open new windows for developing SAMD9&L inhibitors for treatment of human diseases that are caused by gain-of-function SAMD9&L mutations.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Immunology
Research Area 3	Infectious Disease

PI: Shailendra Kumar Dhar Dwivedi	**Project Title: Targeting NNT-AS1 for Ovarian Cancer Therapy**
HR21-170	**Organization:** University of Oklahoma Health Sciences Center
Rank: 8	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Among the cancers affecting women, ovarian cancer (OvCa) is a leading health concern. A woman's chance of getting ovarian cancer is about 1 in 78, and her chance of dying from it is 1 in 108. Despite improvements in patient care and patient therapy methods, the death rate from ovarian cancer is predicted to increase significantly by 2040. Hence identification, research, and development of newer druggable targets in ovarian cancer is a major priority. Currently most of the cancer research is mainly focused on protein targets, which are encoded by about 1% of the human genome. Our current understanding of the remaining 99% of the genome, which includes noncoding RNA (lncRNAs), is limited. LncRNAs are non-protein-coding transcripts longer than 200 nucleotides, and their involvement in all cancer-related pathways is well documented. In the pursuit to identify new targets for ovarian cancer, we investigated the existing ovarian cancer database from The Cancer Genome Atlas (TCGA) and found that a small fraction of the human genome (gene locus 5p13.2), that contains the lncRNA nicotinamide nucleotide transhydrogenase antisense RNA 1 (NNT-AS1), is amplified in ~45% ovarian cancer patient samples (low gain in 40.1% & high gain in 5.3%). Our recent research shows that lncRNA NNT-AS1 is overexpressed in ovarian cancer cell lines and patient samples and inhibition of NNT-AS1 in OvCa cell lines significantly decreased their tumorigenic potential. Interestingly, expression of NNT-AS1 positively correlates with mRNA expression of the nicotinamide nucleotide transhydrogenase (NNT), and inhibition of NNT-AS1 decreases the NNT mRNA and protein levels. NNT is the main mitochondrial enzyme responsible for the synthesis of NADPH, which plays a crucial role in diverse cellular pathways including reactive oxygen species (ROS) homeostasis in cancer cells, which are known to produce high ROS. Therefore, we hypothesized that NNT-AS1 mediated silencing of NNT in ovarian cancer cells will impair the antioxidant capacity of ovarian cancer cells leading to their death. Since the biology of NNT-AS1 and NNT is not explored, in the current research we aim to study the mechanistic details of NNT-AS1 mediates regulation NNT and the pathophysiological significance of their inhibition in ovarian cancer. Successful completion of the research will provide the mechanistic details of NNT-AS1 mediated regulation NNT and establish the significance of NNT-AS1 in NNT mediated ROS detoxification. Importantly, ROS detoxification leads to enhanced drug resistance, therefore targeting NNT-AS1 can be instrumental in improving the treatment outcome in drug-resistant ovarian cancer patients.
Research Area 1	Cancer Research
Research Area 2	Cell/Molecular Biology
Research Area 3	Chemistry & Biochemistry

PI: Yuan Yang	**Project Title: Multimodal integration of concurrent high-density EEG-fMRI with diffusion and anatomical MRI to determine dynamic information flow in brain circuits – an application to hemiparetic stroke**
HR21-164	**Organization:** University of Oklahoma
Rank: 9	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Abstract. Precise measures and understanding of brain structural and functional changes due to injury, such as a stroke, can lead to better prevention, treatments, and recovery. Advances in non-invasive neuroimaging technologies, such as EEG and MRI, are central to these objectives. However, inherent limitations in each single neuroimaging modality limit neuronal information inference. Our long-term goal, therefore, is to provide advanced multimodal brain-imaging tools to increasing our understanding of brain plasticity that informs better clinical practice. Previous studies have shown functional and structural changes to motor pathways from the brain to the muscles in hemiparetic stroke, indicating an upregulation of cortico-reticulospinal tracts excitability in the contralesional side. However, it is still unknown how somatosensory feedback information can reach the contralesional hemisphere to support the maladaptive usage of cortico-reticulospinal tracts. Answering this question requires an advanced brain-imaging approach that can determine the fast propagation of somatosensory neural information flow across underlying, remaining brain circuits after a stroke. For decades, neural information flows are estimated using functional brain connectivity methods based on brain signal correlation or Granger causality without referring to underlying neural fiber bundles as physical pathways in the brain. As a result, information flow may be estimated between brain regions without a clear route, for which there is no physical pathway connection, or the physical pathway has already been damaged by a stroke lesion while the re-routing occurs in the brain. To address this problem, we propose to develop a new multi-model brain imaging approach namely Neural Information Flow Tracker (NIFT) that integrates concurrent high-density EEG and fMRI with diffusion and anatomical MRI to address the limitations in each single neuroimaging modality. Using electric tactile finger stimulation as controllable external input, NIFT tracks dynamic somatosensory information flow through the underlying physical brain circuits, provide us with a unique tool to study and characterize the changes in the brain after an injury. In short, our primary objective is to establish an advanced new tool for tracking neural information flow in the brain networks (in healthy participants, N=20) and, by that, to improve our understanding of the neural basis of post-stroke motor impairments (in stroke participants, N=20). The specific aims are: 1) to determine normal somatosensory information flow in healthy individuals using NIFT; 2) to determine the change of somatosensory information flow in hemiparetic stroke participants and its relationship with motor impairments. This project will, for the first time, provide a tool to precisely determine changes in structurally defined brain activity post-stroke, and likely to inform targeted interventions for a better recovery after a stroke.
Research Area 1	Biomedical Engineering
Research Area 2	Neurobiology
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: J. Cecil	**Project Title: Investigation of an HCC based Mixed Reality approach to support training of medical residents in microsurgery**
HR21-006	**Organization:** Oklahoma State University
Rank: 10	**Year 1:** $36,718 **Year 2:** $37,597 **Year 3:** $38,508 **Total:** $112,823
Research	As microsurgery is considered more difficult than other surgical fields (requiring more years of training than other surgical fields), the number of medical residents entering this field has also reduced considerably. Traditional modes of surgical training includes practicing on cadavers and small animals. Practicing on cadavers holds the risk of infection to the medical residents. The use of small animals for training has been criticized by animal rights groups; these drawbacks has underscored the need to explore alternate forms of computer based surgical training. The design of a Human Centered Computing (HCC) based Mixed Reality (MR) approach to train residents in microsurgery is the primary objective of this proposal; the investigation of such an innovative approach holds the potential to provide a viable alternative training avenue which addresses the above mentioned drawbacks while providing a novel training approach that is intuitive and user friendly in helping residents improve their surgical skills and being better prepared to perform microsurgery in the operating room. Project activities (to achieve this goal) include designing and building a Mixed Reality simulator based on HCC principles, conducting validation of the training modules and subsequently assessment of knowledge and skills transfer activities. The design of this simulation scenarios within these training modules will be explored based on Human Centered Computing (HCC) principles taking into account various new and established factors such as affordance and cognitive load of the participants (medical residents). The microsurgery residents will be able to 'immerse' themselves completely within the surgical simulation environment during the training activities. Using the proposed approach, they will gain the benefit of an integrated cyber-physical training experience where they can be guided by 3D simulation content (through their headsets) while simultaneously performing the various intricate physical steps of microsurgery on a physical setup in the real world. We will assess knowledge gain and transfer of surgical skills with the involvement of volunteer surgical residents at Dignity Regional Medical Center (Chandler, AZ).
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Biomedical Engineering
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: I-Hsiu Huang	**Project Title: Development of a mucosal vaccine against Clostridioides difficile**
HR21-115	**Organization:** Oklahoma State University Center for Health Sciences
Rank: 11	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Clostridioides difficile is the most common cause of antibiotic-associated diarrhea worldwide. C. difficile causes infections in individuals whose gut microbiota has been disrupted by antibiotic usage. C. difficile can form stress-resistant spores that survive the passage through the stomach to the large intestine of infected individuals. The spores rapidly transform back into toxin-producing bacterial cells resulting in symptoms ranging from mild diarrhea, pseudomembranous colitis, and eventual toxic megacolon if left untreated. The current treatment for C. difficile infection (CDI) relies on antibiotic replacement which can result in multiple relapses due to sustained imbalance in the gut microbiota. The high health care burden created by CDIs has prompted the medical research community to focus on vaccine development. In this proposal, we will develop a novel orally delivered mucosal vaccine against CDIs by encapsulating multiple antigens using biodegradable polymers. In Aim 1 of this study, we will evaluate the potential of using various biodegradable as mucosal vaccine carriers. Our preliminary results using animal models have demonstrated polylysine-based hydrogels are safe, stable, and can induce long-term protective responses against C. difficile challenge. In aim 2 of this study, we will identify and characterize multiple C. difficile surface proteins as vaccine antigens. We hypothesize that vaccine composed of toxin and surface antigens will induce antibodies that not only neutralize toxins but also disrupt C. difficile colonization. Finally, in Aim 3, we will establish a murine model of recurrent infection to test the protective ability of our nanoparticle vaccine. Significance and impact: The development of a novel mucosal vaccine against C. difficile infection will aid in the reduction of medical care cost associated with the disease. Experiences gained from the utilization of novel biodegradable polymers as vaccine carrier can advance future vaccine development for other infectious diseases
Research Area 1	Infectious Disease
Research Area 2	Immunology
Research Area 3	Biomedical Engineering

PI: Joshua T Butcher	**Project Title: Exploring the Effect of an Exercise Mimetic on Brain Function**
HR21-045	**Organization:** Oklahoma State University
Rank: 12	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Exercise is an effective intervention to improve brain health, demonstrating positive effects cardiovascular function and improving cognitive function in all groups of people, regardless of age. Unfortunately, aging-related muscle loss (sarcopenia) is accelerated in adults over 50, reducing overall robustness (fitness, strength, stamina) in the elderly. In parallel with population aging, obesity is an epidemic in the U.S. Obesity restricts activity and accelerates the onset of sarcopenia so that the aged obese carry the greatest burden of the disease. The most effective intervention for obesity and/or muscle loss is regular exercise but the aged obese are often unable to exercise at a level that confers benefit. As such, interventions that can replicate the effect of exercise are a medical necessity. This proposal will test the effect of an exercise mimetic (myostatin inhibition) in a rodent model of obesity, We will determine the source of vascular dysfunction in the brain, both from aging and obesity. Further, based on our preliminary data, we believe we have isolated a specific source of dysfunction, increases in oxidant stress from the NADPH oxidase (NOX) family of enzymes, We intend to use exercise mimetics and direct targeting of NOX1 in obese aged mice to determine if we can improve cerebrovascular health.
Research Area 1	Physiology/Pharmacology
Research Area 2	Infectious Disease
Research Area 3	Nutrition/Psychology/Public Health

PI: Ari Berkowitz	**Project Title: Calcium imaging of multifunctional and behaviorally specialized spinal interneurons during swim, scratch, and flexion reflex motor patterns**
HR21-145	**Organization:** University of Oklahoma
Rank: 13	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	How does the central nervous system select and generate the right movement at the right time? We address this question using the adult turtle spinal cord, which can appropriately generate several types of leg movements without input from the brain and movement-related sensory feedback from the legs—i.e., the spinal cord contains central pattern generators (CPGs) that generate the coordinated outputs, or motor patterns, for several types of leg movements. Using electrophysiological monitoring of individual nerve cells (neurons), we found that most spinal cord interneurons (i.e., neurons that are in between sensory neurons and motor neurons in the neural circuit) are multifunctional—they are activated during both forward swimming and 3 types of scratching motor patterns, and often during leg withdrawal (flexion reflex) as well. Thus, the CPGs for these different kinds of natural leg movements likely overlap. We also described two classes of behaviorally specialized spinal cord interneurons, one type specialized for scratching and another for flexion reflex, which are typically inhibited during other motor patterns. Finally, we found behaviorally specialized motor neurons as well. How do all these types of neurons work together? We will inject into the spinal cord a solution of a virus that contains the gene for a fluorescent indicator of calcium concentration, called GCaMP6f, and later image calcium-related fluorescence (an indicator of neuron activation) of tens of neurons simultaneously within the cut face of the spinal cord during each type of motor pattern in vivo, as well as during altered motor patterns triggered by stimulus combinations. Our data will reveal the proportion and spatial distribution of multifunctional neurons and each type of behaviorally specialized neuron. They will also show how multifunctional and behaviorally specialized neurons dynamically combine when motor patterns are adjusted adaptively. Collectively, our data will provide a real-time picture of how sets of multifunctional and behaviorally specialized spinal interneurons combine to appropriately generate several kinds of natural, coordinated leg movements and adaptive changes in movements. Such insights are not yet available for any limbed vertebrate. Our findings will reveal the likely organization of spinal cord circuits for leg movements for limbed vertebrates generally.
Research Area 1	Neurobiology
Research Area 2	Physiology/Pharmacology
Research Area 3	Cell/Molecular Biology

PI: Yolanda Vasquez	**Project Title: Development of Gold Nanocarriers for the Treatment of Rheumatoid Arthritis Using Photocatalytic Click Reactions**
HR21-031	**Organization:** Oklahoma State University
Rank: 14	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Rheumatoid Arthritis is a disease with no cure that affects approximately 1% of the world populace. This disease is characterized by inflammation, cartilage/bone destruction, and disorders of the cardiovascular, pulmonary, and skeletal systems. Disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate provide effective management of the symptoms. Methotrexate is an effective drug for rheumatoid arthritis, but has side effects that include stomach ulcers and renal, central nervous system, and liver toxicity. In this proposal, the investigators want to address the clinical limitations of methotrexate such as its renal clearance, the availability of the drug at the target tissue, high dosage requirements, and toxicity by developing a gold nanocarrier for the drug. Here, the gold nanocarrier will be chemically bound to methotrexate using a new photocatalytic reaction. The hypothesis is that methotrexate will be less toxic when bound to the gold and result in longer clearance times. The combination of the gold nanocarrier and the methotrexate molecule is expected to have a synergistic effect on the suppression inflammation factors when tested in cell models.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Cell/Molecular Biology
Research Area 3	Cancer Research

PI: Sadagopan Krishnan	**Project Title: Quantitative Understanding of a Multiplex Viral RNA Nano-Bioconjugate for Visual Self-Testing Sensors**
HR21-013	**Organization:** Oklahoma State University
Rank: 15	**Year 1:** $42,683 **Year 2:** $43,619 **Year 3:** $44,587 **Total:** $130,889
Research	This OCAST application seeks to gain quantitative understanding of a multiplex viral RNA nano-bioconjugate design. Preliminary results obtained will help us apply for federal funding with the goal to successfully translate the knowledge to develop a visual self-testing viral infection sensor. For viral infections, particularly an acute respiratory infection, quantitative polymerase chain reaction (PCR) of respiratory secretions and serological enzyme-linked immunosorbent assays (ELISA) are routinely used to detect causative viral nucleic acids and antigens (proteins and antibodies), respectively. However, serological ELISA methods require several lengthy incubations steps, challenges with developing reliable antibodies, tedious protocols, stability issues, and expensive instrument-based detection for results. Similarly, PCR has many limitations such as the need for high purity samples, gene isolation and amplification, highly trained personnel, sophisticated facilities for sample processing, and expensive laboratory instruments not affordable for economically challenged and resource-limited countries; in addition, long reaction times are required. Lateral flow viral infection colorimetric assays are challenged with accuracy problems, routine sample induced artifacts, and lack of multiplex features to increase probability of positive identification and eliminate false negative detection. These present assay limitations highlight the critical need for a robust reliable multiplex pathogen sensor that is inherently sensitive from the multiplex feature, more selective by targeting more than a single marker, user-friendly and affordable globally. Diagnosing viral infections, however, requires ultra-low (femtomolar, attomolar, and even lower) detection limits of RNA markers. Hence, a glucometer compatible amperometric sensor approach that can additionally measure viral infection relevant RNA markers represents an innovative research goal of this application.
Research Area 1	Biomedical Engineering
Research Area 2	Chemistry & Biochemistry
Research Area 3	Infectious Disease

PI: Mary Beth Humphrey	**Project Title: Mesenchymal Stem Cell Regulation by TRPC1**
HR21-119	**Organization:** University of Oklahoma Health Sciences Center
Rank: 16	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Mesenchymal stem cell regulation by TRPC1 10-15% of bone fractures fail to healing leading to non-union bone defects. Understanding how bone healing is regulated is critically important to prevent and to treat non-union bone defects. Risk factors for non-healing include obesity and smoking that are common in Oklahoma. To provide better bone healing, surgeons often use bone particles or powder to fill in the bone defect but this often fails to bring in mesenchymal stem cells (MSC) to promote normal bone formation. In MSC, we have identified a calcium channel protein, TRPC1, that tells MSC to become bone forming osteoblasts or fat forming adipocytes. Our proposed studies will determine how TRPC1 regulates MSC in response to stimulators of bone remodeling. We will also test whether MSCs lacking TRPC1 or treated with TRPC1 inhibitors provide improved healing of a critical bone defect. Results of our studies will improve our understanding of the regulation of MSC cell fate decisions and will provide critical preliminary data for a R01 proposal on the role of TRPC1 and CaSR mediation of bone regeneration during non-union fractures and critical size bone defects.
Research Area 1	Cell/Molecular Biology
Research Area 2	Physiology/Pharmacology
Research Area 3	Biomedical Engineering

PI: Karla Rodgers	**Project Title: Chromatin effects on conventional and aberrant V(D)J recombination**
HR21-142	**Organization:** University of Oklahoma Health Sciences Center
Rank: 17	**Year 1:** $44,777 **Year 2:** $44,776 **Year 3:** $44,786 **Total:** $134,339
Research	B and T lymphocytes of the adaptive immune system express antigen receptors (AgRs), which specifically recognize and function in the elimination of invading pathogens. The lymphocytes express a tremendous array of AgR sequences, referred to as the AgR repertoire, making it possible for diverse pathogenic antigens to be recognized by the adaptive immune system. The AgR repertoires are produced during lymphocyte development by V(D)J recombination. From many available gene segments, this combinatorial assembly process selects and joins two to three gene segments to generate intact AgR genes. As the combinatorial assembly differs between individual lymphocytes, V(D)J recombination also leads to the diverse AgR repertoires expressed by B and T lymphocytes. The V(D)J recombinase, consisting of the proteins RAG1 and RAG2, catalyze the first enzymatic steps of V(D)J recombination. Specifically, the V(D)J recombinase recognizes and cleaves the recombination signal sequence (RSS), which flanks each gene segment. As the RSSs are only semi-conserved, the V(D)J recombinase must be capable of cleaving at a wide range of variant RSSs to generate diverse AgR repertoires. However, there are millions of cryptic RSS-like sites (cRSS) that are located throughout the genome. Erroneous RAG-mediated cleavage at cRSS sites can cause oncogenic chromosomal rearrangements. Therefore, RAG1/2 must be promiscuous to facilitate recombination of poorly conserved RSSs at AgR loci, but it must also be precise to avoid off-target cRSSs. Long standing questions remain as to the contribution of DNA sequence selectivity, along with the effects of the chromatin environment, on the balance between conventional versus aberrant V(D)J recombination events. To address the contribution of DNA sequence selectivity to V(D)J recombination, we developed a high-throughput recombination method to analyze RSS selectivity, in which the relative efficiency of V(D)J recombination on RSS substrate libraries are obtained by analysis of next generation DNA sequencing results. Our preliminary studies have shown preferred sequence motifs and sequence interdependencies between different regions of the RSS that have significant consequences on the level of V(D)J recombination activity. However, how RSS selectivity by the V(D)J recombinase may be affected by the chromatin environment is not clear. In this project, we will utilize our high-throughput recombination assay to determine how the chromatin environment affects DNA selectivity by the V(D)J recombinase at AgR loci, and alters the propensity for off-target RAG cleavage events. Overall, we predict that findings from this project will significantly improve our current understanding of RAG selectivity of RSSs and cRSSs in normal and aberrant V(D)J recombination reactions, respectively.
Research Area 1	Immunology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Genomics & Gene Expression

PI: Michael Criss	**Project Title: Link Between Chronic Adversity and Emerging Adult Mental and Physical Health: An Examination of Underlying Bio-Social Mechanisms and Protective Factors**
HR21-021	**Organization:** Oklahoma State University
Rank: 18	**Year 1:** $34,590 **Year 2:** $38,504 **Year 3:** $38,991 **Total:** $112,085
Research	Emerging adulthood (18-25 years) has been characterized as a formative period for social and neurological development and a critical transitional period for various mental and physical health outcomes. Furthermore, experiences among ethnic minorities at this age may be hampered through exposure to social and environmental adversity, which in turn, may lead to more social weathering, health problems, and adjustment difficulties. As such, this is an optimal time to investigate health disparities. The objectives of the proposed project are to identify potential pathways linking social and environmental adversity, biological processes, and mental and physical health and to elucidate potential relationship processes that serve as protective factors among ethnic minority emerging adults. In particular, Specific Aim #1 will identify pathways linking social and environmental adversity, biological processes, and emerging adult mental and physical health. 2. Specific Aim #2 will determine whether the links among social and environmental adversity, biological processes, and mental and physical health are moderated by supportive relationships (i.e., protective factors) with parents, peers, and mentors. The proposed 3-week study will utilize a multimethod (e.g., surveys, biodata), multisystem (i.e., stress system, immune/inflammatory system, HPG axis), and multi-context (i.e., laboratory, home) design. The sample will consist of 120 African American, Hispanic American, and Native American emerging adult men and women. In Week 1, participants will take part in a 2-hour laboratory visit consisting of surveys and a stress test. Saliva and dried blood spots will be collected. During the home assessment in Week 2, participants will complete three daily surveys assessing social and environmental adversity and three daily saliva collections (twice daily: after waking up and just before bed). In the laboratory assessment in Week 3, participants will complete a series of surveys assessing mental and physical health. This proposed investigation has substantive and applied significance as it addresses important barriers in the field, including the identification of potential underlying bio-ecological mechanisms tied to chronic adversity and health disparities and potential protective factors. Such information will inform interventions targeting at-risk emerging adults. In addition, the proposed project contains several strong, innovative features, such as adopting a multi-method, multi-system, and multi-context approach to biomarkers tied to chronic adversity. Moreover, these data will be used to stimulate NIH supported research in Oklahoma by providing important pilot data.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Physiology/Pharmacology
Research Area 3	Immunology

PI: David Sparling	**Project Title: The Initial Characterization of the Novel Adipokine CRISPLD2**
HR21-005	**Organization:** University of Oklahoma Health Sciences Center
Rank: 19	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Obesity continues to be a worldwide epidemic, with an increase in Type 2 diabetes being a significant side effect. Inflammation of fat tissue is thought to be a vital part of the development of insulin resistance. As such, new understanding of the regulators of fat inflammation are needed. Recent work has identified a novel protein, CRISPLD2, which is increased in fat tissue that is undergoing weight loss. Interestingly, CRISPLD2 has been previously associated with (and may be able to bind) inflammatory signals, and can regulate inflammatory signaling and tissue development. However, the full function of CRISPLD2 in fat tissue has not been determined. We have found that CRISPLD2 levels strongly correlate with insulin sensitivity in adolescents, is regulated during fasting and refeeding, and is increased during fat breakdown. We continue to explore the function and regulation of CRISPLD2. We plan to characterize the function of this protein in affecting fat/immune cell interactions in a cell culture model. We have also created a mouse model that can overproduce CRISPLD2, and will determine if it can be protective against obesity and its outcomes. These aims will allow us to both produce the tools and better characterize the function of CRISPLD2 to continue to look for new targets in the treatment of obesity and Type 2 diabetes.
Research Area 1	Cell/Molecular Biology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Anindya Dey	**Project Title: The role Cystathionine beta-synthase in age-related cognitive impairment**
HR21-166	**Organization:** University of Oklahoma Health Sciences Center
Rank: 20	**Year 1:** $44,093 **Year 2:** $42,368 **Year 3:** $43,170 **Total:** $129,631
Research	Cognition is a combination of processes in the brain that include the ability to learn, remember, and make judgments. Impairment of cognition can have a profound impact on an individual's overall health and well-being. As life expectancy rises, cognitive impairment and dementia have become a leading public health issue in the USA. As such, it is extremely important to develop a mechanistic understanding that may then provide opportunities for mitigation of age-related cognitive impairment. However, to date no strategies exist for the prevention or treatment of aging-induced cognitive decline. In the aging human brain, an imbalance between production of detrimental reactive oxygen species (ROS) and its removal leads to oxidative damage which is associated with cognitive impairment. The smelly gas hydrogen sulfide (H2S) produced by the metabolic enzyme Cystathionine ß-synthase (CBS) is associated with an extended life-span in animals and may play a protective role against this oxidative damage by modification of proteins through persulfidation. In brain, CBS is found predominantly in astrocytes and in this proposal, we want to study the role of age-dependent astrocytic CBS deficiency in the pathogenesis of cognitive impairment in older adults.
Research Area 1	Neurobiology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Cell/Molecular Biology

PI: Steven D. Hartson	**Project Title: Advancement of antiproliferative flavonoids as drug leads by identifying their targets**
HR21-122	**Organization:** Oklahoma State University
Rank: 21	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Cancer is still very much with us, with 40% of all U.S. men and women likely to be diagnosed with cancer at some point in their lives. One-third of these individuals will not survive past year 5. To address this problem, we seek to expand the pipeline of experimental anti-cancer drugs. We will pursue this goal in an OCAST project that will delve into an enormous family of natural plant compounds called "flavonoids." We are inspired by the many successes with other molecules produced in nature: 40% of today's therapeutics derive from biological sources. With these successes as our template, we will use advanced cell biology and biophysics techniques to compare how 11 chemically distinct flavonoids kill leukemia cells. This will provide a biochemical "Rosetta Stone" to decipher the biochemical basis of each flavonoid's anti-cancer activity. These very specific biochemical details will be useful in future efforts to rationally modify flavonoids to improve their cancer-killing potential.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Physiology/Pharmacology
Research Area 3	Cancer Research

PI: Jacob Kirkland	**Project Title: Non-canonical Roles of Homologous Recombination Proteins**
HR21-114	**Organization:** Oklahoma Medical Research Foundation
Rank: 22	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Every cell in the human body has the same sequence of DNA. Our 2 meters of DNA must be packed carefully into cellular nuclei about 5 million times smaller in diameter. Additionally, each cell must decide which genes in its genome to turn on and which genes to turn off. Despite having the same genes, a skin cell is different than a heart cell, and the decision of which genes to turn on and off is what can differentiate them. Many are familiar with the concept of mutations in a crucial gene leading to developmental diseases and cancer. Another way these diseases can form is for genes that should be turned off to mistakenly get turned on or for genes that should be turned off to get turned on. The proteins that control this are called chromatin regulators. Another group called Homologous Recombination proteins were first discovered for their role in repairing broken DNA that can lead to mutations. However recent work from myself and others in yeast has shown that these same Homologous Recombination proteins can control which genes get turned on or off. Homologous Recombination proteins do this by cooperating with chromatin regulators determining how certain genes are organized in the cell nucleus. It is important to understand this additional role of Homologous Recombination proteins in mammals to understand how changes in them lead to developmental diseases and more aggressive cancers. In this study we will use state-of-the-art techniques to study how Homologous Recombination proteins regulate gene expression and DNA organization in mouse cells, to better understand human disease. This study will provide the preliminary data required to acquire Federal NIH funding to accomplish our long-term goals. Furthermore, the results are expected to have a positive impact on Oklahomans because the identified mechanisms will likely provide new pathways to target for therapeutic intervention of cancers with misregulation of Homologous Recombination proteins.
Research Area 1	Cell/Molecular Biology
Research Area 2	Genomics & Gene Expression
Research Area 3	Cancer Research

PI: Chongle Pan	**Project Title: Interpretable machine learning for improved estimation of polygenic risk scores in diverse populations**
HR21-165	**Organization:** University of Oklahoma
Rank: 23	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Polygenic risk scores (PRS) quantify the genetic predisposition of individuals towards complex diseases based on their personal genome information. Our long-term goal is to develop accurate and trustworthy PRS estimation for many complex diseases across populations of all ancestries, which will facilitate the development of a precision preventive medicine strategy that is tailored for individuals based on their PRS for a disease. A variety of statistical approaches have been developed to estimate PRS using the genotype-phenotype associations discovered by genome-wide association studies. Here, we propose to develop a machine learning approach for constructing PRS models. Our preliminary results have demonstrated an improved PRS estimation for breast cancer using deep neural networks (DNN). The main objective of this project is to achieve substantial increases in the predictive performance and interpretability of PRS models in both the European ancestry (EA) population and the non-EA populations for breast cancer, coronary artery disease, and type-2 diabetes. This is significant because more performant PRS models will be able to identify more high-risk individuals with higher confidence. In order to deliver the anticipated benefits of PRS to all ancestry groups, it is critical to close the PRS performance gap between the EA population and the non-EA populations. We will accomplish our objective via the following specific aims: (Aim 1) improve the predictive performance of PRS models in three complex diseases; (Aim 2) interpret the PRS DNN models for building trust and obtaining biological insights; and (Aim 3) develop trans-ancestry PRS models for diverse populations using transfer learning. The innovations in our proposed approach include (i) using deep neural networks with the attention mechanism for PRS estimation; (ii) using a new linearizing neural network architecture for model interpretation; and (iii) using transfer learning to address the training data scarcity challenge in the non-EA populations. At the successful completion of the proposed research, the expected outcome is a systematic evaluation of the technical merits of machine learning methods for estimation of the PRS of three complex diseases in both EA and non-EA populations. This will provide a strong basis for future development of accurate and trustworthy PRS models that can be used in clinical applications, which are expected to have a significant impact on precision preventive medicine.
Research Area 1	Genomics & Gene Expression
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Nutrition/Psychology/Public Health

PI: Weidong Wang	**Project Title: Prokineticin-2 in pancreatic beta cell replication**
HR21-132	**Organization:** University of Oklahoma Health Sciences Center
Rank: 24	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Diabetes affects approximately 400 million people worldwide. Due to a decrease in insulin-producing beta cell number, patients with diabetes are not able to produce enough insulin to control their blood glucose levels. If the number of beta cells in these patients is increased, their blood glucose control can be much improved, thus slowing down or preventing the devastating outcomes of high blood glucose. It is well known that beta cells possess the capacity to greatly increase their numbers by proliferation, the most common route of beta cell regeneration. This suggests the possibility of using such regeneration as a therapeutic approach for diabetes. We have recently discovered that a secreted protein significantly increased the proliferation of cultured human ß-cells. In this grant, we will test whether this protein induces ß-cell regeneration in animals and determine the mechanism by which it induces ß-cell regeneration. Completion of this grant will not only reveal a novel physiological mechanism of ß-cell regeneration but also provide a potential ß-cell regeneration therapy for diabetes.
Research Area 1	Physiology/Pharmacology
Research Area 2	Cell/Molecular Biology
Research Area 3	Genomics & Gene Expression

PI: Bruce Noden	**Project Title: Evaluating Effect of Woody Plant Encroachment on Mosquitoes and Mosquito-borne Viruses in the Southern Great Plains**
HR21-101	**Organization:** Oklahoma State University
Rank: 25	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Zoonotic and human arboviruses are a major source of endemic and epidemic disease in the United States. In the Great Plains region, there is a critical need to identify how land cover change affects: abundance and diversity of mosquitoes that are arbovirus vectors; blood feeding of these mosquitoes on arbovirus reservoir hosts and accidental hosts like horses and humans; and mosquito infection rates for important arboviruses affecting humans, like West Nile virus (WNV). A major form of land cover change occurring in the Great Plains is woody plant encroachment (WPE), an increase in density, cover, and biomass of woody plants in grasslands driven by alteration of land management (e.g., fire suppression). WPE's effects mirror mechanisms by which other types of land cover change (e.g., urbanization) influence arbovirus transmission. WPE changes abiotic conditions (e.g., humidity, temperature), vegetation, and species composition of arthropods and wildlife. A completely unstudied consequence of WPE is its potential foundational role in influencing transmission and large-scale distribution of arboviruses. Our long-term goal is to clarify how WPE affects arbovirus transmission in the Great Plains. The overall aim of this application is to assess relationships between WPE—specifically by eastern redcedar (Juniperus virginiana; ERC), the primary encroaching species in the Great Plains—and the ecology of arbovirus transmission systems in Oklahoma (where the extent of WPE is 5-7x greater than elsewhere in the U.S.). Our central hypothesis is that the numerous WPE-caused changes to ecosystems facilitate spatial expansion and persistence of key arbovirus vectors and hosts, and increase vector-host contact and vector infection rates relative to more open areas. This hypothesis was informed by our initial work showing that ERC expansion influences abundance and WNV-infection of Culex tarsalis, the key regional WNV vector. The hypothesis was also informed by studies showing that ERC affects abundance of key WNV hosts (e.g., American Robin; Turdus migratorius). To test our central hypothesis, we propose the following three objectives: 1. Assess the relationship between WPE and mosquito communities. 2. Determine if WPE affects mosquito host feeding preferences. 3. Evaluate the effect of WPE on arbovirus infection in mosquitoes. At successful completion of this project, results will have a positive impact by informing public health and WPE management efforts that improve human health and well-being in this region. Further, because WPE is occurring nationwide and globally, this study provides a model for future investigations into its effects on other diseases that impact human health.
Research Area 1	Infectious Disease
Research Area 2	Infectious Disease
Research Area 3	Infectious Disease

PI: Franklin Alan Hays	**Project Title: p66Shc Functional Modulation of Mitochondrial Response to Ischemia-Reperfusion Injury**
HR21-134	**Organization:** University of Oklahoma Health Sciences Center
Rank: 26	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	p66Shc is soluble adaptor protein that also produces reactive oxygen species (ROS). This protein is known to be essential in mediating a diverse array of human pathologies including coronary artery disease, diabetes, and stroke. The current project is focused on myocardial infarctions (MI) that result when tissue blood supply is blocked or decreased. This reduces oxygen availability within that tissue resulting in tissue damage and death. From a clinical standpoint, the primary focus is to remove whatever is blocking blood flow, treat the reason it occurred in the first place, and monitor going forward. p66Shc is known to be involved in producing tissue damage at the wound site. Indeed, our studies with zebrafish shows that p66Shc is a major mediator of delayed recovery in cardiac tissue following ischemic-reperfusion (I/R) injury (removing blood flow and then adding it back). How this occurs is unknown though our preliminary data supports two arguments: 1) p66Shc-mediated ROS production is elevated at MI wound sites and 2) p66Shc has functional interactions with the mammalian electron transport chain (ETC). ETC stimulation and over-activation are key mediators of cell death pathways. p66Shc ROS affects CAD and stroke strongly enough that its levels can predict stroke severity or determine CAD presence in patients. Although inhibiting or removing other ROS producing proteins is fatal in mice, p66Shc knockouts are beneficial, without physiological detriments or increased compensatory ROS. The Hays lab is the first to produce full-length p66Shc, putting this project in a unique position to: 1) define mechanism of ROS production 2) validate in vitro mechanistic findings with an in vivo model by illustrating how mechanistic manipulation can benefit pathology, and 3) characterize functional interactions between p66Shc and ETC enzymes. Thus, this project is acutely focused on defining mechanism for a key protein and relating that mechanism to the development of, and tissue response to, myocardial infarctions in vertebrate systems. This project will directly impact cardiovascular disease by identifying mechanistic and structural therapeutic targets that can affect clinical outcomes for ROS-mediated pathology.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Cell/Molecular Biology
Research Area 3	Cancer Research

PI: Amanda Harrist	**Project Title: The Consequences of Adverse Childhood Experiences and Early Weight Trajectory on Obesity , Brain Structure, and Neurocognitive Function in Young Adults**
HR21-103	**Organization:** Oklahoma State University
Rank: 27	**Year 1:** $44,997 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $134,997
Research	Adverse childhood experiences (ACEs) and obesity are interrelated predictors of serious adverse health outcomes, including neurocognitive deficits. These effects are alarming given the high prevalence of ACEs and obesity. The majority of US adults (64%) have experienced at least one ACE and 1/10 adults are projected to be severely obese by 2030. Both ACEs and obesity have been linked to adverse socio-emotional and neurocognitive effects, although prospective data examining these associations over time are rare. The current project addresses this limitation by testing ACEs history, brain morphology, neurocognition, and obesity levels in 60 20- to 21-yr-olds followed from age 6. The timing and history of ACEs will be tested in relation to weight trajectories from childhood to adulthood, including the role of ACEs in explaining links among obesity trajectories, adult brain morphology, and adult neurocognition. Our specific aims are to (1) identify whether 14-year obesity trajectories from early childhood to emerging adulthood are linked to ACEs and neurocognitive performance; (2) examine the path between ACES, neurocognition, and obesity in emerging adulthood; and (3) determine whether volumetric and morphological brain differences mediate links between ACES, neurocognition, and obesity in emerging adulthood.The longitudinal study that will be used to meet these aims is unique in the field of child obesity given that it is a large community sample followed prospectively. Almost 1200 1st grade children (19% Native American) were assessed in 1st-4th grades: Annual biometric assessments (BMI, bioelectric impedance) were conducted and data collected from children/peers/teachers to assess self-regulation, emotional/external eating, and weight-teasing/bullying. In 12th grade, 355 participants were re-assessed, resulting in a 14-yr weight trajectory. In this study, we will recruit 66 past participants who are now in adulthood, with over-sampling of Native Americans. Lifetime incidence of ACEs will be assessed and MRI scans and neuropsychological testing conducted. Although adult obesity has been linked to brain structure and functioning, no studies have linked prospective socio-emotional data and/or ACEs across childhood to future obesity or brain health, as we plan to do. High ACE scores are linked to impaired neurocognition and structural brain changes, and we advance these findings by determining how timing and type of ACEs interact with child obesity trajectories, and which brain and neurocognitive profiles these predict. Our findings will inform the development of neurocognitive interventions tailored to patients based on psychosocial histories and weight trajectories, and are relevant for Oklahoma, where both obesity and ACEs rates are among the highest nationally. Given that the project will involve children, ACEs, and obesity—all critical funding areas—the project will be competitive when we seek federal funding using findings from this study.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Neurobiology
Research Area 3	Immunology

PI: Asish K. Ghosh	**Project Title: Study MER Tyrosine Kinase Signal as a Target in CLL Therapy**
HR21-110	**Organization:** The University of Oklahoma Health Sciences Center
Rank: 28	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Chronic lymphocytic leukemia (CLL) is an adult B-cell malignancy with highly variable disease course. The oral B-cell receptor (BCR)-signal inhibitor therapies (ibrutinib, targets Bruton's tyrosine kinase [BTK]; idelalisib, targets PI3Kd) have been shown to be effective in relapsed/drug-refractory CLL patients. However, when patients relapse there is often evidence for more aggressive disease including transformation to lymphoma, leaving only limited therapeutic options for these patients. Reported rates of ibrutinib discontinuation range from 28–51% after 3-year follow-up, primarily due to disease progression, drug intolerance and adverse events without evidence of BTK mutations. Given this, further knowledge of the nature and extent of other active receptor tyrosine kinase (RTK) signals in CLL cells is critical for development of additional therapies to treat these high-risk CLL patients. Our recent discovery of MER, a RTK of the TAM (Tyro3, AXL, MER) family, in CLL cells may offer such an option. This grant proposal will develop a robust and comprehensive analysis of the status of a novel receptor tyrosine kinase (RTK) MER in CLL which we have generated considerable information on this hitherto undescribed signaling axis in CLL cells. The proposed studies are dedicated in novel and important directions: 1) to further the understanding of MER signal transduction and its association with the disease course; 2) defining the mechanism of MER expression/activation, its functional relationship with the BCR signal in CLL cells; and, 3) defining the role of MER in regulating CLL cell survival and feasibility of targeting this signaling pathway to induce apoptosis both in vitro and in vivo in an established CLL mouse model; In total, the information gained on this novel RTK signaling axis in relation to disease progression and our work on developing increasing rationale for the use of a high-affinity MER-inhibitor alone or in combination with the BCR-inhibitors for CLL treatment has great potential to impact and improve public health.
Research Area 1	Cancer Research
Research Area 2	Cell/Molecular Biology
Research Area 3	Immunology

PI: Chung-Hao Lee	**Project Title: Risk stratification and predictive modeling of tricuspid valve regurgitation for personalized management of infants born with hypoplastic left heart syndrome (HLHS)**
HR21-044	**Organization:** The University of Oklahoma
Rank: 29	**Year 1:** $44,991 **Year 2:** $44,991 **Year 3:** $44,991 **Total:** $134,973
Research	Each year in the United States, 1 out of 3,841 infants are born with hypoplastic left heart syndrome (HLHS). This birth defect requires a three-step non-curative surgery over the first 2-3 years of the infant's life. Reports from the Oklahoma Children's Hospital (OCH - OUHSC) estimate up to 37% of the HLHS newborns will develop an additional heart complication, known as tricuspid regurgitation (TR), during these surgeries – a major risk factor for death between the surgical steps and poor long-term outcomes. Despite 25% of HLHS patients requiring surgical repair of the tricuspid valve (TV) afflicted with TR, there are currently no clinical guidelines to determine if a specific patient is at a higher risk for developing TR. Thus, our goal in this OCAST project is to identify the indicators for TR to establish a patient-specific predictive model for discerning future TV dysfunction. We hypothesize that finding these TR indicators will lead to the development of clinical guidelines to improve the management of high-risk HLHS newborns. We propose two specific objectives to test our hypothesis: 1) to develop a database of the changes in patients' TV features over the first 2-3 years of life to identify the geometric, structural, or mechanics-based TR indicators, and 2) to establish a predictive statistical model for patient-specific risk level assessment. We will accomplish these goals using computational analyses of patient image data that have been established by Principal Investigator (Dr. Lee)'s laboratory at OU Norman. We will also utilize Dr. Lee's expertise in TV tissue mechanics and computational modeling, and Collaborator Dr. Burkhart's experience with HLHS surgeries on infants at the OCH - OUHSC. We will use previously acquired heart valve imaging data, along with the reconstructions of the patient's TV geometry, to quantify mechanics-based and clinical (geometric) metrics of the TV apparatus. These analyses will form a first of its kind detailed, longitudinal patient image database, and by performing basic statistics we will identify the key geometric, mechanical, and structural features of the TV that indicate the development of TR. We will next develop statistical models to predict the likelihood a specific patient will develop TR during their first 2-3 years of life, along with predicting the severity of the TR (i.e., facilitating patient risk stratification). The endpoint of this study will be to advance the state of the art in translational medicine using individualized TV analyses and predictions. The proposed research will provide clinical guidelines for personalized management of TR in HLHS infants. At the same time, it will also serve as the first logical step toward achieving our long-term goal to optimize the invasive surgeries and save lives of newborns suffering from HLHS.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Biomedical Engineering

PI: Khaled Sallam	**Project Title: A new delivery technology for treating chronic Eustachian tube dysfunction and otitis media with effusion**
HR21-130	**Organization:** Oklahoma State University
Rank: 30	**Year 1:** $44,524 **Year 2:** $44,513 **Year 3:** $44,830 **Total:** $133,867
Research	In the United States, each year, nearly 700,000 children have tympanostomy tubes inserted because of chronic middle ear fluid and frequent ear infections. According to a US study the total number of annual office visits related to Eustachian-tube dysfunction (ETD), otitis media with effusion (OME), and tympanic membrane retraction exceeded 4 million in patients of all age groups. Complaints associated with ETD contributed to about 40% of the total visits. Nationally, annual expenditures for treatment of otitis media in children were estimated to have been over $5 billion. Despite the high impact of OME and ETD in children and adults, there is presently no non-invasive approach that treats underlying causes of ETD. Myringotomy, the most commonly used surgical approach in treating middle ear effusions, only addresses the symptoms of OME and ETD. While Balloon Eustachian Tuboplasty is a promising intervention, it is very costly, only works in about 50% adults with ETD and is not approved for use in children. As a result, many patients with persistent middle ear effusions and chronic ETD remain without good treatment alternatives. Recognizing the existing unmet need, we propose to develop a novel delivery system that has potential to target underlying pathological conditions associated with dysfunctional Eustachian tube (ET). Our new delivery concept is based on a combination of a custom-made nasal metered dose inhaler and positive airflow/air pressure-assisted insufflation of the ET/middle ear system. Our research hypothesis is based on findings in the literature that (1) demonstrated the possibility of efficient delivery in difficult-to-access regions of the nasal cavity, (2) therapeutic efficacy from delivering therapeutic formulations into the ET with no observed side effects and (3) clinical benefits of politzerization/insufflation in the treatment of OME. In Aim 1 we will employ our dual needle prototype to evaluate the use of concurrent nasal spray and airflow in delivering a medication to the eustachian tube orifice. Using the nasal phantom model, we will experimentally study the effect of the total injection volume, spray initial size distribution, and assisted-air velocity on droplet size distribution and spray penetration of the nasal cavity. Following optimization of spray characteristics as part of Aim 1, in Aim 2 we will build delivery device prototypes and evaluate them in phantom models. Our team will use proof-of-concept data from the OCAST project to apply for federal funding from agencies such as the NSF and NIH.
Research Area 1	Biomedical Engineering
Research Area 2	Biomedical Engineering
Research Area 3	Biomedical Engineering

PI: Sun Young Lee	**Project Title: Targeting of exosome-based therapy in ocular neovascularization**
HR21-171	**Organization:** Board of Regents of the Univ. of OK Health Sci. Center
Rank: 31	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Exosomes have a great potential for intraocular drug delivery vehicles due to their small size, biocompatibility, and reduced toxicity compared with synthetic nanoparticles. The frequency of anti-VEGF intravitreal injections to treat retinal and choroidal neovascularization (NV) has grown exponentially with the introduction of bevacizumab, ranibizumab, and most recently aflibercept. A total of 2,474,124 intravitreal injections were performed in 2015 in the USA for the Medicare beneficiaries alone. However, the visual outcome of anti-VEGF treatment in clinical practice has been worse than outcomes in clinical trials because of difficulties maintaining sufficient injection frequency. Frequent suboptimal efficacy of anti-VEGF treatment is an additional barrier for poor clinical outcome due to limited binding affinity of anti-VEGF agents to overlying retinal fibrosis or scarring to NV. To address unmet needs for sustained and target delivery of intraocular drugs, we will engineer aflibercept encapsulated exosomes using the targeting exosome delivery system (ASL-exosome) that we developed. The goal of the studies proposed in this application is to elucidate the targeting and functionality of intraocularly delivered ASL-exosomes in ocular neovascularization to explore an exosome-mediated novel drug delivery strategy to treat posterior eye diseases such as age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion. The results from this project will lead to future studies, including testing the utility of bioengineered exosomes as a vehicle for various therapeutic cargos and the application of stem cell-derived exosomes in the treatment of retinal diseases.
Research Area 1	Physiology/Pharmacology
Research Area 2	Biomedical Engineering
Research Area 3	Cell/Molecular Biology

PI: Avishek Mitra	**Project Title: Identifying inhibitors of siderophore, heme and ferrous iron acquisition pathways of Pseudomonas aeruginosa**
HR21-007	**Organization:** Oklahoma State University
Rank: 32	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Pseudomonas aeruginosa (Pa) is the leading cause of nosocomial infections, pneumonias, and deaths in patients with cystic fibrosis (CF). The ever increasing number of infections with multi- or pan-drug resistant Pa has led the World Health Organization to declare Pa a "Priority 1: Critical" pathogen needing new strategies and options for prevention and chemotherapy. Thus, the development of new antipseudomonal drugs, preferably against new drug targets, is urgent. Pa is strictly dependent on acquiring iron nutrient within the host to survive and colonize the host. Iron is used by Pa for countless cellular process and is absolutely essential for survival. Therefore, significant efforts have been made to develop antibiotics to disrupt Pa iron acquisition to block access to this essential nutrient. However, these efforts have only been made to inhibit Pa siderophore-dependent iron acquisition. Siderophores are small molecules produced by Pa to acquire iron within the host, but these molecules can only access 15% of the total iron in the human host. Pa also has heme and ferrous iron acquisition systems which allow access to the other 85% of the iron in the human host. The existence of these pathways has prevented Pa siderophore blockers from being an effective antibiotic therapy because Pa still acquires iron using the ferrous or heme pathways. We propose that to successfully prevent Pa from acquiring iron in the host all iron acquisition systems of Pa need to be blocked simultaneously. However, research has not been done to identify inhibitors of heme and ferrous iron acquisition pathways which is an obvious and major gap in our knowledge. We have developed a method by which we can identify molecules that can specifically block different iron acquisition pathways in any bacterial pathogen. In our proposal we present evidence of how we have successfully used this strategy to identify iron acquisition blockers in Mycobacterium tuberculosis, which is another serious lung pathogen like Pa. Our goal is to use this already established method and identify new molecules that can specifically block siderophore-, heme- and ferrous-dependent iron acquisition by Pa. This strategy will allow us to develop a cocktail of specific inhibitors that block all iron acquisition pathways of P. aeruginosa.
Research Area 1	Infectious Disease
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Augen A. Pioszak	**Project Title: Composition and functions of the human class B GPCR-RAMP interactome**
HR21-017	**Organization:** Oklahoma, University of, Health Sciences Center
Rank: 33	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	This OCAST project will study a family of human cell surface receptor proteins that control many important physiological processes such as bone growth, food intake, blood glucose, stress responses, pain transmission, and cardiovascular system function. These receptors, known as class B G protein-coupled receptors (GPCRs), are intimately involved in several diseases that have a significant burden on the health of Oklahomans including osteoporosis, diabetes, migraine headache, and heart disease. In this project we propose to use advanced biochemistry and pharmacology methods to determine how proteins known as RAMPs control the abilities of class B GPCRs to regulate human physiology in response to peptide hormones. Successful completion of this project will significantly advance our understanding of the roles of class B GPCRs and RAMPs in human health and will provide a foundation of knowledge that will aid the development of new drugs targeting this family of receptors for the treatment of several diseases. In addition, support from OCAST will enable us to advance this project to a stage where it will be competitive for federal research funding from the National Institutes of Health.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Physiology/Pharmacology
Research Area 3	Cell/Molecular Biology

PI: Xuewei Chen	**Project Title: Improving health literacy and preventive care use among rural populations in Oklahoma**
HR21-003	**Organization:** Oklahoma State University
Rank: 34	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	According to Healthy Oklahoma 2020 (the Oklahoma Health Improvement Plan), the Oklahoma State Department of Health calls for innovative research designed to promote health by emphasizing preventive care and enhancing health literacy skills. Limited health literacy is identified as a significant barrier to preventive care use. Delays in seeking preventive care lead to diseases such as cardiovascular disease, stroke, and cancer, which are leading causes of death in Oklahoma. Only 12% of the adults in the United States have proficient health literacy. Moreover, due to structural barriers such as shortage of specialist doctors and limited media exposure, it is harder for rural populations to access and use reliable health information source, especially those with limited health literacy. A significant limitation of research focused on promoting preventive care utilizing through reducing the health literacy barrier is the tendency to recruit samples of participants in more urban areas of the United States, ignoring the unique experiences of underserved population living in more rural areas. Thus, there is a critical need to identify the health information sources used and trusted by this population and to understand their process of comprehending and evaluating the information. In the absence of such knowledge, the development of effective intervention strategies to enhance health literacy and improve preventive care use within this population will likely remain difficult. Our long-term goal is to identify key factors predictive of appropriate health decision making, so that improved strategies can be developed to alleviate health disparities among rural populations. Our overall objective in this application is to identify key barriers under the scope of health literacy to preventive care utilization among rural residents in Oklahoma. Our central hypothesis is that the health information source accessed and trusted by this population often contain misleading information, thereby causing them to decide to not obtain health care services that are recommended. We have based our central hypothesis upon the findings from our previous studies and preliminary data that individuals with low health literacy lack the knowledge and skills to evaluate the quality of health information; moreover, those living in rural areas have limited access to high-quality health information sources. The rationale for this project is that its successful completion would help the development of effective intervention strategies to enhance health literacy and improve preventive care use within this population. We are well-positioned to lead this project because our research team has extensive experience in recruitment and retention of rural populations, intensive data collection methods, analysis of complex data, and published health literacy and health communication research.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Andrew Conner	**Project Title: Functional Network Alterations in Medically Intractable Epilepsy**
HR21-069	**Organization:** University of Oklahoma Health Sciences Center
Rank: 35	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	Localization of eloquent regions is necessary for preoperative workup of epilepsy patients. The Wada test is commonly included in this workup to determine memory asymmetry and language lateralization. However, it is an invasive procedure with associated risks. Resting state fMRI (rs-fMRI) is an emerging alternative that has already demonstrated high concordance with Wada for language lateralization. In contrast, the comparison between rs-fMRI and Wada has not been assessed for memory lateralization to the same degree. In this project, our goal is to determine the rs-fMRI correlate for Wada memory asymmetry in medically intractable epilepsy. Recent studies have identified consistent patterns of functional connectivity (FC) between the hippocampus and default mode network (DMN), which are associated with postoperative memory outcomes. This pattern, known as hippocampal dominance, may be a biomarker of memory lateralization. We hypothesize that hippocampal dominance will be concordant with Wada memory asymmetry in patients with typical memory and language lateralization. We will also perform concurrent electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) recording to assess neurovascular coupling (NVC). NVC has been used in preoperative language lateralization and shown abnormal parameters when discordant with fMRI. Therefore, we hypothesize that patients with discordant memory lateralization on rs-fMRI and Wada will demonstrate abnormal NVC parameters. In this pilot study, we will gather data on the FC patterns, NVC parameters, and their concordance with Wada. This will guide our approach in the next project phase, where we will examine the predictive value of rs-fMRI versus Wada for postoperative memory outcomes.
Research Area 1	Neurobiology
Research Area 2	Biomedical Engineering
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Anne Kasus-Jacobi	**Project Title: Multi-Target Peptide: A Drug to Remember**
HR21-143	**Organization:** OUHSC
Rank: 36	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Alzheimer's disease is a type of disease in which brain neurons become damaged and die over time. As the disease progresses, patients, usually older than 65, experience symptoms such as memory loss, difficulties communicating and performing basic activities like bathing and dressing, personality changes, incontinence, loss of motor functions, and eventually, early death. In 2020, almost 6 millions of Americans were suffering from Alzheimer's disease and 67,000 of them were living in Oklahoma. These numbers will continue to increase as the American population becomes older. The first drug that can slow down this disease has been approved this year and will become available to the patients soon. However, this drug is not very efficient because it only protects against some toxic events that are happening in the brain, but not all of them. With this drug, the neurons continue to die, just a little bit more slowly. To really stop this disease, we will need a much stronger drug with more protective effects. Developing such a drug is our long-term goal. We have found a new compound that has several protective effects that we believe could come together to completely stop the progressive death of neurons. In this project, we propose to first, use chemistry to make this compound even stronger and more stable and second, test the strongest compound in mouse to make sure that it can get into the brain and protect against the most neurotoxic events that take place during Alzheimer's disease. If we are successful, this will be a game changing approach in the search for better treatments for Alzheimer's disease.
Research Area 1	Physiology/Pharmacology
Research Area 2	Neurobiology
Research Area 3	Immunology

PI: John P. Masly	**Project Title: Functional Characterization of a Novel Regulator of Tissue Growth in Drosophila**
HR21-083	**Organization:** University of Oklahoma
Rank: 37	**Year 1:** $44,940 **Year 2:** $44,969 **Year 3:** $44,928 **Total:** $134,837
Research	Understanding the mechanisms that direct cell proliferation and tissue growth— and identifying the genes that function to direct these mechanisms— are major goals of health research. An under-utilized and potentially powerful approach to identifying important regulators of eukaryotic cell proliferation is to compare tissue growth differences that exist among closely related model species and characterize the functional genetic differences. We recently used this approach and identified a novel gene that negatively regulates tissue growth by suppressing cell proliferation. The research objective of this proposal is to leverage natural genetic variation at this locus among fruit fly (Drosophila) species to understand how genetic variation directs cell proliferation differences and to begin a functional characterization of this novel protein by focusing on the effects of sequence substitutions in this protein's putative functional domains. To accomplish this, we will address two specific research aims. First, we will identify the base-pair substitutions at this gene that specify differences in cell proliferation. We will accomplish this by first taking advantage of genome sequencing technologies that allow us to identify gene regulatory domains that are involved in enabling expression of this gene during the crucial periods of tissue growth. We will then use genome editing approaches to target these open regulatory regions and "swap" species-specific regulatory sequences to identify the causative substitutions that regulate cell proliferation. In parallel, we will also perform similar genome editing experiments for species-specific substitutions in the functional domains of the protein-coding region of this gene. Second, we will study the function of this novel protein by performing experiments to test whether the protein is secreted or functions within the cell, and then perform a series of experiments to identify its potential protein interactors. Once we have obtained candidate interacting proteins, we will use newly acquired, state-of-the-art mass spectrometry technology to identify these protein interactors and validate potential interactions with the strongest candidates using standard molecular techniques. The study of the molecular basis of species-specific differences in tissue growth in Drosophila is widely applicable to the study of tissue growth and morphology in other species, including humans and their primate relatives. In particular, variation among several highly conserved genes appears important for control of tissue growth among multicellular organisms, and defects in many of these genes have been implicated in some forms of cancer. The proposed work is thus relevant to public health because the information learned from this study can be applied to understanding how change in genes important for regulating cell and tissue growth translate into human diseases.
Research Area 1	Cell/Molecular Biology
Research Area 2	Genomics & Gene Expression
Research Area 3	Cancer Research

PI: Karen Wozniak	Project Title: Mechanisms of Action of Novel Antifungal Macrocycle Derivatives
HR21-012	**Organization:** Oklahoma State University
Rank: 38	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Cryptococcus neoformans is a fungal pathogen that causes meningitis in approximately 225,000 individuals with AIDS each year, resulting in over 181,000 annual deaths. C. neoformans is inhaled and then escapes the lungs and spreads to the central nervous system where life-threatening meningitis occurs. There are currently only four classes of antifungal drugs available to treat this infection. These medications are not very effective, they are highly toxic, and the organism is developing resistance against these drugs. Therefore, novel antifungal drugs are desperately needed. Our collaborator has made compounds that can kill C. neoformans. We have selected 10 promising candidates with anti-cryptococcal activity to move forward with for these studies. Our preliminary data show that these compounds affect fungal cell shape, and therefore we hypothesize that these compounds affect the fungal cell wall and fungal cell membrane, leading to lysis of the organism. To test this, we will first examine changes in fungal genes after treatment. Next, to identify how these compounds work, we will identify C. neoformans strains that are resistant to treatment in order to identify how these compounds kill C. neoformans. We will next test the ability of these compounds to kill C. neoformans in cell culture. Finally, the most promising compounds from the cell culture experiments will be tested as a treatment in a mouse model of cryptococcal disease to determine if these compounds can be used as a new therapy for C. neoformans infections.
Research Area 1	Infectious Disease
Research Area 2	Cell/Molecular Biology
Research Area 3	Immunology

PI: Paul DeAngelis	**Project Title: Safer Sugar-based Sepsis Therapeutics**
HR21-146	**Organization:** University of Oklahoma Health Sciences Center
Rank: 39	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Bacterial infection causes many specific diseases, but quite often the body over-reacts to the 'danger' signals derived from microbes causing sepsis and septic shock with symptoms including extremely low blood pressure and organ failure. Sepsis affects about 270,000 people in the US per year and is often a deadly condition (1 out of 3 persons who die in hospitals) according to the CDC. In sepsis, the innate immune system in blood (which defends the body before antibodies are created) can cascade out of control in at-risk patients creating a hyper-inflammatory state and organ damage. Our team is exploring the molecular mechanisms and utility of a new class of synthetic sugar-based molecules that are very similar to heparin (a drug derived from pig intestine that is frequently used in hospitals to control bleeding) to suppress this excess inflammation and tissue destruction. In this project, we will analyze the relationship between the new sugar's structure and function in biochemical, blood, and animal model systems of sepsis to fine-tune its abilities to reduce septic shock. Our translational goal is to modulate the patient's defenses using an approach targeting regulatory systems without triggering side effects like hemorrhage thus yielding more selective and safer therapies for sepsis.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Cell/Molecular Biology
Research Area 3	Infectious Disease

PI: Hugo R. Arias	**Project Title: DM505, A positive allosteric modulator of alpha7 nicotinic acetylcholine receptors for novel non-opioid anti-pain therapy**
HR21-082	**Organization:** Oklahoma State University - Center for Health Sciences
Rank: 40	**Year 1:** $44,948 **Year 2:** $44,709 **Year 3:** $44,662 **Total:** $134,319
Research	Our preclinical project has two main objectives: (1) First, we will determine whether neuropathic pain induced by either the chemo drug oxaliplatin (OXA) or by sciatic nerve ligation (CCI) develops co-morbidities such as depression and anxiety in mice from both sexes. (2) Subsequently, we will use DM505 for the treatment of neuropathic pain and associated anxiety/depression, and determine if the effectiveness of this drug differs between male and female mice. In this regard, three different non-invasive behavioral determinations will be performed in the following sequence: (a) the extent of cold- (OXA) and mechanical-hypersensitivity (CCI) in treated mice from both sexes as well as the antinociceptive activity of DM505 in these mice; (b) the extent of anxiety in mice with chronic pain as well as the anxiolytic activity of DM505 in these mice; and (c) the extent of depression in mice with chronic pain as well as the antidepressant activity of DM505 in these mice.
Research Area 1	Neurobiology
Research Area 2	Physiology/Pharmacology
Research Area 3	Cell/Molecular Biology

PI: William Kyle Simmons	**Project Title: The past is prologue: Assessing whether glucocorticoid and immune epigenetic biomarkers link childhood adversity to adult psychosocial stress**
HR21-180	**Organization:** Oklahoma State University Center for Health Sciences
Rank: 41	**Year 1:** $44,978 **Year 2:** $44,540 **Year 3:** $44,624 **Total:** $134,142
Research	The COVID-19 pandemic has laid bare the pressing need to identify both phenotypic and biological characteristics that place individuals at elevated risk for poor outcomes upon exposure to psychosocial stressors such as those experienced globally during a pandemic or any number of emerging society-wide threats. Accomplishing this, however, requires ready access to exceedingly rare datasets containing a well-characterized cohort of participants who have been tracked through periods of psychosocial crisis, and for whom biological samples are available from before the advent of the crisis period. Phenotypic data and biospecimens previously collected from participants in the Holistic Assessment of Tulsa's Children's Health (HATCH) study offer a unique opportunity to identify biological predictors of vulnerability to psychosocial stress. HATCH, which began in 2017, is a longitudinal clinic-based study of low-income women recruited during pregnancy with extensive continuing data collection. The central hypothesis of our proposal is that early life adversity, and the epigenetic changes it causes in key immune and glucocorticoid gene pathways, makes individuals more susceptible to psychosocial stress during periods of crisis. This hypothesis is built on the well-replicated findings that adverse childhood experiences (ACEs) such as abuse, neglect, and family dysfunction result in enduring changes to the hypothalamic-pituitary-adrenal (HPA) axis that lead to altered glucocorticoid signaling and immune system changes that promote both heightened acute inflammatory responses and chronic inflammation. These persistent biological changes to human stress and immune signaling pathways arise from epigenetic modifications (e.g., gene methylation) that alter gene expression, protein building, and eventually, behavior. These epigenetic changes link ACEs to well-documented dysregulated stress responses, the adoption of health-harming coping behaviors (smoking, substance abuse, overeating and obesity), and the mental and physical health conditions observed in large-scale epidemiological studies (e.g., cardiovascular disease, autoimmune diseases, suicide, and depression). We will thus measure methylation of key genes in glucocorticoid (HPA stress axis) and immune signaling pathways in dried blood spot samples collected from HATCH participants prior to the COVID-19 pandemic outbreak. This will allow us to determine the relationship between HPA and inflammatory gene methylation and subsequent psychosocial coping during the COVID-19 pandemic, and whether HPA and inflammatory gene methylation better predict psychosocial coping during the COVID-19 pandemic than ACEs alone. By completing these aims, we will determine whether a person's methylation status alone, or in conjunction with ACEs history, can help predict risk to personal and society-wide crises, thereby laying the groundwork for improving screening and treatment both in clinical practice and public health.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Genomics & Gene Expression
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Alexandra C N Kingston	**Project Title: The Helmet-like Armor of Snapping Shrimp may Mitigate Blast-Induced Neurotrauma**
HR21-091	**Organization:** The University of Tulsa
Rank: 42	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Exposure to shock waves leads to neurotraumas, including blast-induced traumatic brain injuries (bTBI), which are a considerable danger to human health. Currently, one of the greatest challenges to mitigating bTBI in humans is the lack of armor with the ability to protect brains and other soft tissues from transient high-amplitude pressure waves, more commonly known as shock waves. Snapping shrimp (Crustacea: Decapoda: Alpheidae) present a unique opportunity to study the mitigation of bTBI as they regularly produce and experience shock waves. Recently, I discovered snapping shrimp have a helmet-like structure, the orbital hood, that dampens shock waves. I hypothesize that orbital hoods prevent brain damage and preserve cognitive function in snapping shrimp. The goal of this proposal is to study how orbital hoods mitigate bTBI in snapping shrimp by examining: 1) cognitive function of snapping shrimp following exposure to shock waves; 2) brain damage caused by shock waves; and 3) the mechanism by which their armor dampens shock waves. This research will establish snapping shrimp as a model for research on the prevention of neurotraumas and inspire new approaches to the engineering of armor designed to protect human brains from shock waves and thus the debilitating effects of bTBI.
Research Area 1	Neurobiology
Research Area 2	Cell/Molecular Biology
Research Area 3	Physiology/Pharmacology

PI: Lawrence Rothblum	**Project Title: Ribosome Biogenesis as a Therapeutic Target in Cancer**
HR21-150	**Organization:** Board of Regents of the University of Oklahoma Health Sciences Center
Rank: 43	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	The ribosome is the site of synthesis of the cell's proteins. Ribosomes are composed of proteins and ribosomal RNAs (rRNA). How ribosome biogenesis is regulated is a central question in cell biology. The rate-limiting step in this process is transcription of the ribosomal RNA genes (rDNA) by RNA polymerase I (Pol I) in the nucleolus of the cell. Transcription by Pol I can represent as much as 70% of the nuclear RNA synthesis in rapidly growing cells, e.g. cancer cells. A tumor cell may produce several thousands of ribosomes per minute. This is a bottleneck in cancer cell proliferation; the rate of ribosome production. An abundance of ribosomes is needed to sustain cell growth and proliferation. It is therefore not surprising that many anti-cancer drugs interfere with RNA Pol I or RNA Pol II transcription leading to preferential targeting of dividing cancer cells. Interestingly, many commonly used chemotherapeutic drugs inhibit rRNA synthesis and/or processing, e.g. Actinomycin D and 5-Fluorouracil (5-FU). Actinomycin D (Cosmegen) is both an antibiotic and DNA intercalating molecule. Although Actinomycin D (Cosmegen) is a potent inhibitor of cell proliferation. However, its off-target effects limit its use in cancer chemotherapy to a few cancer types, e.g. Wilm´s tumor and Ewing´s sarcoma. Be that as it may, the result of the inhibition of ribosome biogenesis is striking on the cellular level. The nucleoli shrink and re-organize within one hour. This is accompanied by a process referred to as nucleolar stress which results in the death of cancer cells, but not normal cells. This phenomenon has refocused interest in the relationship between nucleolar function, rDNA transcription, nucleolar stress and cancer. Moreover, several recent reviews have documented the dysregulation of Pol I transcription in cancer cells and/or the desirability of targeting Pol I in those cells. This project focuses on the molecular mechanism of rDNA transcription. Our work is centered on an essential and unique, Pol I associated factor required for rDNA transcription - specifically Rrn3. Our goal is to interfere in its ability to function. We have shown that interference of the interaction of Rrn3 with Pol I inhibits ribosome biogenesis and induces the death of cancer, but not normal, cells. The work proposed herein is significant as it will validate the direct inhibition of Pol I assembly as a target for cancer drug discovery. Further, these studies will develop the information necessary for the development of small molecule inhibitors of rDNA transcription that will serve as a cancer chemotherapeutic.
Research Area 1	Cancer Research
Research Area 2	Cell/Molecular Biology
Research Area 3	Genomics & Gene Expression

PI: Anupama Munshi	**Project Title: Breast milk-derived exosomes for delivery of radiosensitizers for breast cancer**
HR21-040	**Organization:** University of Oklahoma Health Sciences Center
Rank: 44	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Effective treatment of breast cancer remains a formidable clinical challenge. The advent of molecularly-targeted therapies and immune checkpoint inhibitors has shown limited efficacy in breast cancer treatment. Further, inefficient delivery and accumulation of anticancer drugs in tumor depots combined with dose-limiting toxicity contributes to disease relapse, drug resistance, and metastasis culminating in patient death. Thus, testing of new therapeutic strategies and drug delivery systems are warranted for improving treatment outcomes. In the present application, we propose developing and testing of tumor targeted (tt)-multifunctional exosomes (tt-Mfn-Exo) as a radiosensitizer for breast cancer therapy. We hypothesize that exposure of the tt-Mfn-Exo to radiation therapy, which is a standard of care for breast cancer, will result in enhanced antitumor activity. To achieve this objective, exosomes derived from bovine breast milk (colostrum) will be loaded with gold nanoparticles (GNP) carrying siRNA targeted to an oncogenic protein, HuR. The release of the siRNA from GNP is controlled by a pH responsive linker thereby minimizing unrelated-related toxicity to normal cells. Further, the siRNA-GNP loaded exosome is decorated with a tumor-targeted transferrin (Tf) ligand for enhancing tumor-specific drug delivery and reducing cytotoxicity to normal cells. Finally, inclusion of GNP enables in amplifying the radiation effects by heating the tumor milieu, inducing DNA damage and cell death. Preliminary studies from our laboratory demonstrated the feasibility of isolating exosomes various biological fluids and ability to load the exosomes with GNP and other therapeutics. Additionally, siRNA-based knock down of HuR in breast cancer cells showed growth inhibitory effects in vitro. Based on our preliminary data, we hypothesize that tt-Mfn-Exo will efficiently target and deliver HuR siRNA to tumor cells and produce antitumor activity. Additionally, we hypothesize GNP will radiosensitize tumors resulting in enhanced antitumor activity both, in vitro and in vivo. To achieve this goal we will conduct preclinical studies in vitro and in vivo breast tumor models.
Research Area 1	Cancer Research
Research Area 2	Genomics & Gene Expression
Research Area 3	Physiology/Pharmacology

PI: Song Fang	**Project Title: Towards Monitoring Month Breath During Sleep Leveraging Off-the-shelf Sensors**
HR21-112	**Organization:** University of Oklahoma
Rank: 45	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Respiration is one of the human body's vital functions. Occasionally when nasal obstruction happens or we need more oxygen, the nose may be supplemented by the mouth. Over time, people whose mouth breathing goes untreated may suffer from health problems and subsequent problems, including abnormal facial and dental development, hoarseness and halitosis, speech impediment, social restriction and other side effects. Thus, early detection of mouth breathing is essential to prevent and minimize its negative effects on the overall development of individuals. Artificial observation of mouth breathing is burdensome and inconvenient, while camera-based methods often require strong computing power to process live video frames and fail when the mouth does not show in the presence of camera or is covered by the quilt. This project aims to achieve real-time detection of mouth breathing during sleep leveraging off- the-shelf sensors (e.g., geophones, wireless transceivers) without depending on visual techniques. Such mouth breathing information could help a user to timely correct mouth breathing before it becomes a habit, and also provide valuable evidence for diagnosis of mouth breathing associated diseases. Specifically, during sleep, the breathing activity (i.e., inhalation and exhalation) as well as chest fluctuations can cause subtle environmental changes, which can be captured and analyzed to distinguish mouth breathing from nose breathing. Compared with traditional mouth breathing detection methods, which usually require the patient to wear dedicated and expensive sensors, the proposed techniques are non-invasive, and the utilized sensors are easily obtained and have low cost. This project aims at (i) developing a geophone- based sleeping monitoring system that can accurately detect mouth breathing during sleep; (ii) developing a wireless-based sleeping monitoring system that would send alert and analysis report when mouth breathing during sleep is detected; and (iii) conducting comprehensive real- world experiments to evaluate the impact of the proposed techniques.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Nutrition/Psychology/Public Health

PI: Gary J Gorbsky	**Project Title: Effects of Microplastics and Nanoplastics Contamination on Mammalian Cell Function**
HR21-098	**Organization:** Oklahoma Medical Research Foundation
Rank: 46	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	The problem of plastic pollution in the environment is large and growing. Plastic contamination at of various sizes and chemical composition are found in almost all modern environments including land, atmosphere, and water, both marine and fresh. Plastics often contain additives such as stabilizers, strengtheners, flexibility agents, dyes, and other compounds that can be released into the environment. Plastics can also absorb and concentrate environmental toxins such as organic compounds and heavy metals. Plastics have been found to contaminate human food and water sources. Despite their potential serious effects, ubiquitous distribution, growing abundance, and likely entry into the body, relatively little is known about the effects of plastic contaminants on the function and physiology of mammalian cells. To fill this gap in our understanding, we will treat mammalian cells grown in culture dishes in the laboratory with a variety of microplastics and nanoplastics. The terms microplastic and nanoplastic are used to describe particles of different sizes, none of which are visible to the eye. We will use a variety of microscopic observations and biochemical analyses to determine how plastics harm human cells. We will also test the effects of materials that leach into water from commonly used plastics such as disposable water bottles. Our studies will identify biochemical pathways in cells specifically vulnerable to perturbation by the presence of plastic pollution. They will also show which types, sizes and shapes of plastics are most harmful to human cells. Our studies guide potential practices for reducing the toxic effects of plastic pollution.
Research Area 1	Cell/Molecular Biology
Research Area 2	Genomics & Gene Expression
Research Area 3	Physiology/Pharmacology

PI: Caroline Markey	**Project Title: TREATMENT EFFECT OF 9-VALENT HPV VACCINE IN HPV POSITIVE WOMEN**
HR21-087	**Organization:** Board of Regents of the Univ. of OK Health Sci. Center
Rank: 47	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	This is a prospective cohort study evaluating the possible treatment effect of the 9-valent human papillomavirus (HPV) vaccine series in women with HPV positive pap smears. The HPV vaccine was initially approved in 2006 and was available to women ages 15- to 25 years-old, aimed at preventing HPV 16 and 18 infection and related disease. Since that time, the vaccine has been expanded to include a total of 9 high-risk subtypes. Vaccine eligible patients have increased from only young women up to the age of 27, to men as well as women up to the age of 45. Although there are no specific guidelines recommending global vaccine administration in this older age group, these patients can derive benefit from vaccine administration. HPV vaccination has been shown in multiple studies to be effective at preventing HPV infection and related diseases in HPV naive patients. Some studies have also suggested a decreased recurrence of type-specific HPV related disease after treatment, when administered the HPV vaccine following cervical excisional procedures. The aim of this project is to evaluate the possible treatment effect of the 9-valent HPV vaccine when administered to high-risk HPV positive women between the ages of 30-45 years-old.
Research Area 1	Immunology
Research Area 2	Infectious Disease
Research Area 3	Cell/Molecular Biology

PI: Martin McCullagh	**Project Title: Allostery in Flavivirus NS3: A Target for Selective Antivirals**
HR21-066	**Organization:** Oklahoma State University
Rank: 48	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Approximately 2/3rds of the world population is at risk of infection by at least one of the 35 mosquito-borne flaviviruses known to cause disease in humans, such as Zika and dengue viruses. This problem has only increased over the past few years with reported cases of Zika and dengue in the United States including in Oklahoma. There are currently no therapeutics available to treat patients infected by flaviviruses despite the severe morbidity and mortality that they cause each year. The development of broadly active antiviral therapeutics to treat flavivirus infections requires improved knowledge of the molecular mechanisms that these viruses use to replicate their genomes. This project will address this deficiency by defining the molecular mechanics of an enzyme, NS3h, that is key to flaviviral replication. We propose the following: 1) Identify key molecular-level components of the RNA and ATP-binding mechanisms of flavivirus NS3h. NS3h utilizes ATP binding and hydrolysis to power translocation along and unwinding of viral RNA. We have previously reported results from all-atom molecular dynamics (MD) simulations and quantum mechanical calculations of dengue NS3h (Davidson et. al PLOS Comp. Bio., 2018 v14 e1006103) that identify key components of the ATP hydrolysis reaction. This work also identified critical components of the RNA-translocation mechanism. These simulations provide us with a baseline understanding of all critical states of the protein. Additional simulations are proposed to investigate the thermodynamics and mechanism of transition between these states. 2) Identify allosteric paths in flavivirus NS3h that transduce energy from ATP binding and hydrolysis to perform RNA translocation. The ATP and RNA pockets are coupled through allosteric paths. We have recently developed a novel suite of analysis techniques to inform us about this process (Lake et al. J. Chem. Theory Comput. 2020 v16 3385-3395). We will employ this technique to identify regions of the protein that are critical for coupling the ATP and RNA pockets. 3) Develop mutations that perturb the allosteric mechanism of NS3h. To demonstrate the accuracy of the proposed allosteric mechanism, we will propose and test mutations that target the paths found in aim 2. This will be done using both in silico simulations and in collaboration with an experimentalist. These have been performed on dengue NS3h and have corroborated our preliminary findings (Du Pont et al. J. Biol. Chem., 2020 v295 1551-1564). Combined, this work will produce unprecedented molecular-level insight into the translocation mechanism of flavivirus NS3 helicases. Key components of this mechanism represent new targets for antiviral development.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Infectious Disease
Research Area 3	Cell/Molecular Biology

PI: Eric Wickel	**Project Title: Exploring the complex interplay between device-measured daily movement behavior and health: a prospective cohort study.**
HR21-072	**Organization:** The University of Tulsa
Rank: 49	**Year 1:** $44,712 **Year 2:** $38,166 **Year 3:** $19,517 **Total:** $102,395
Research	Daily movement behaviors, including physical activity, sedentary behavior, and sleep, are key targets in health research, but are inherently difficult to measure and interpret under free-living conditions. Self-report tools are widely used in health research, but are prone to recall bias, which may result in imprecise time-use estimates across physical activity intensities (light, moderate, and vigorous) and unique sedentary/stationary postures (sitting, standing, and lying). Furthermore, existing studies tend to use cross-sectional study designs, which are unable to establish causality, and traditional analytic methods that are unable to account for the compositional nature of daily behavior. To advance time-use research, a critical need exists for prospective cohort studies using innovative wearable devices and novel analytic methods to determine the interactive effects of daily movement behavior on health outcomes. The proposed 3-year longitudinal, observational study will include 250 adults aged 25 to 55 years who work full-time within the Tulsa area. Baseline data collection will occur in years 1 and 2, while follow-up data collection will occur 1-year later in either year 2 or 3. At baseline, participants will complete a 7-day activity monitoring protocol while wearing two accelerometers; one worn on the wrist (Actigraph) and the other attached to the thigh (activPAL). Actigraph data will be processed to estimate daily time in light, moderate, and vigorous activity, whereas activPAL data will be processed to report daily estimates of sedentary time, time spent in sedentary/stationary postures, time spent in 30+ minute sedentary bouts, mean sedentary bout duration, and sleep duration. After a 1-year period, participants will complete a follow-up 7-day activity monitoring protocol using the same wearable devices. Daily exposure variables from the Actigraph and activPAL will be summarized as mean weekly, weekday, and weekend values at baseline and follow-up. Descriptive variables and primary (blood pressure and body size) and secondary (self-reported comorbidities, quality of life, and depressive symptoms) health outcomes will be collected at baseline and follow-up. Summary statistics (mean, standard deviation) will be calculated across descriptive variables, while compositional data analysis will be used to: 1) characterize the composition of daily movement behavior, 2) determine the influence of reallocating time between daily movement behaviors on health outcomes, and 3) determine how longitudinal changes in daily movement behavior influence health. Outcomes from this project will include scientific publications and presentations, which will be the basis for preliminary data for external grant submissions. Our interdisciplinary team is well-positioned to complete this project given our experience with wearable devices and expertise in the development and application of mathematical, statistical, and computational methods in bioinformatics.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Physiology/Pharmacology

PI: Namik Kirlic	**Project Title: Interoceptive Processing in Adolescents Exposed to Early Life Stress**
HR21-141	**Organization:** Laureate Institute for Brain Research
Rank: 50	**Year 1:** $44,962 **Year 2:** $44,863 **Year 3:** $44,784 **Total:** $134,609
Research	With one in four children affected, early life stress and trauma (ELS) are a serious and persistent problem in the United States and, in particular, the State of Oklahoma. ELS is the single strongest predictor of mental illness in childhood, and has been found to result in physical health problems later in life. Several decades of previous research have identified a range of short- and long-term consequences of ELS exposure, prompting broader ELS assessment and efforts to treat mental and physical illness from an ELS-informed perspective. However, the current evidence-based psychological and pharmacological intervention are significantly less effective for ELS-exposed individuals seeking mental health treatment. This is likely due to the fact that we do not fully understand how ELS changes the way brain processes information, and which brain systems are most affected by ELS. Because ELS consists of environmental (i.e., external) events that impact both the body and the brain, we need to understand interoception in affected individuals, that is, how they integrate bodily responses, such as heart rate, respiration, and pain with prior experience, beliefs, and moment-to-moment thoughts to form and regulate emotional states and guide behaviors. Previous research has not studied this brain-body connection to try and characterize how ELS-related mental illness emerges, especially during sensitive developmental period of adolescence. Our central hypothesis is that dysfunction in brain-body processing plays a crucial role in the development and maintenance of ELS-related mental illness. If confirmed, this will open new avenues for development of novel interventions to modify interoceptive dysregulation and relieve the long-term pain and suffering in traumatized adolescents. Specifically, we aim to determine (1) the impact of ELS on brain and behavioral measurements of brain-body processing, and (2) the degree to which symptom and behavioral changes relate to brain function during processing of bodily sensations. We propose to recruit 87 adolescents, 47 with significant history of ELS and 40 of their healthy counterparts. Participants will complete a series of tasks designed to measure awareness of and responses to varying bodily sensations. Behavioral, physiological, and brain levels of measurement will be used to achieve a comprehensive assessment of interoceptive processing. The data gathered by this proposal will be used to apply for future large-scale grant funding aimed at experimentally probing brain-body processing as a disease modifying process for youth affected by ELS. This work will be particularly informative for how brain-body interventions, such as mindfulness training, can be further optimized to improve outcomes in this high-risk population.
Research Area 1	Neurobiology
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Hongliang Li	**Project Title: The Therapeutic Potential and Molecular Mechanism of a Novel Decoy Peptide Inhibitor in Polycystic Ovary Syndrome**
HR21-148	**Organization:** University Of Oklahoma Health Sciences Center
Rank: 51	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Polycystic ovary syndrome (PCOS) is characterized by laboratory and/or clinical features consisting of hyperandrogenism with menstrual irregularities, anovulation, infertility, and obesity. PCOS is characterized by a variable and erratic elevation of testosterone (T) of unknown etiology. The gonadotropin-releasing hormone (GnRH) in the upstream hypothalamic-pituitary-ovary (HPO) axis is a key regulator of PCOS, triggering the synthesis of luteinizing hormone (LH) from the pituitary and leading to the release of T in the ovary. We have novel data demonstrating that agonistic autoantibodies to GnRH receptor (GnRHR-AAb) are present in some women with PCOS. GnRHR-AAb induction in the rat leads to characteristic phenotypes related to PCOS. We also found GnRHR-AAb can be neutralized by specifically designed proteolysis-resistant decoy peptides, which form the basis for developing pharmacological interventions. However, the molecular mechanisms responsible for GnRHR-AAb induced PCOS are not fully clarified. In addition, the therapeutic potential of GnRHR decoy peptides in the new PCOS animal models are not been evaluated. Our hypothesis is that GnRHR-AAb is produced and interacts with hypothalamic/pituitary GnRHR to inappropriately alter the synthesis and pulsatile release of LH, thus leading to pathophysiological events associated with PCOS including hyperandrogenism, polycystic ovaries, and insulin resistance (IR). A novel inhibitor will prevent the binding of GnRHR-AAb to the target receptor and normalize the HPO axis, thus alleviating the PCOS phenotypes. The central hypothesis will be tested by pursuing three specific aims: 1) Explore the therapeutic potential of a novel inhibitor and its effects on the immunological and functional properties of PCOS-related GnRHR-AAb in two large infertile cohorts, 2) Explore the molecular mechanisms of a novel inhibitor to reverse GnRHR-AAb induced LH biosynthesis and secretion in gonadotroph LßT2 cells, 3) Investigate whether blocking the GnRHR-AAb effects via a novel inhibitor can improve reproductive and metabolic dysfunction in the new PCOS animal models. We will pursue these aims using an innovative combination of clinical biobank samples and a novel animal PCOS-like model expressing GnRHR-AAb to explore the pathophysiology and molecular mechanisms of PCOS including LH and T production, IR, and ovarian function. The proposed research is significant because it will determine the prevalence of anti-GnRHR AAb in PCOS and non-PCOS infertility cohorts and establish the mechanism by which these antibodies participate in the development or progression of PCOS. These results will have a positive impact by developing a diagnostic test to differentiate forms of infertility and to better understand their underlying differences in pathophysiology. Furthermore, the results are expected to have a positive impact because they will provide pre-clinical data for novel therapeutics for the autoimmune sunset of PCOS.
Research Area 1	Immunology
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Physiology/Pharmacology

PI: Gary Yen	**Project Title: Early Detection of Oral Cancer Through Deep Neural Network and Edge Computing**
HR21-124	**Organization:** Oklahoma State University
Rank: 52	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	According to NIH, the 5-year survival rate for oral cancer diagnosed early is 75% compared to 20% for diagnosed late. Increased awareness and early intervention to those at greatest risk are believed the most effective means to save lives from oral cancer. Unlike tumors of the kidney, prostate, or other internal organs, oral cancers are readily accessible. In this proposal, our long-term objective is exploiting the modern technologies of high-resolution image sensing, AI for machine learning, and cost-effective edge computing as a viable alternative to address this long lasting threat to personal oral health through early detection. Aided with big data analytics and eXplainable AI on the learnt process, we believe this study will improve medical knowledge and build a data proven instrument for improving outcomes for oral cancer. This study will develop a novel model for the early detection and region of interest (ROI) marking of cancer in the buccal region of the oral cavity using a texture-map branch-collaborative Convolutional Neural Network (CNN) based on extracted texture features. The network model comprises of two integrated, yet complement, branches, namely an early detection branch and a ROI marking branch. Given the fluorescent images available at our disposal, the preliminary experimental results have produced a model with a sensitivity of 0.9687 and specificity of 0.7129. The developed CNN model will then be implemented in various resource-constrained edge devices, including cell phones and tablets. The collective data will be archived, analyzed and fed into an eXplainable AI module to extract meaningful knowledge. The proposed work will involve three specific tasks: •Task 1- Developing a CNN for early detection: The main goal in this task is to automatically evolve CNNs for early detection given the oral images available. Various CNN architectures (e.g., ResNet-50, Inception, Xception, ResNeXt-50, CB-CNN) and texture feature image transformations (e.g., transform-based, model-based, graph-based, entropy-based, learning-based approaches) will be considered. •Task 2- Incorporating the trained CNN within a Branch-Collaborative Network for ROI marking: Effective image segmentation branch that greatly improves the ROI marking in the proposed model will be thoroughly investigated. Due to the conflicting nature of targeted utilities on early detection and ROI marking, a multi-criteria decision making on the CNN design in maximizing sensitivity at the cost of reasonable specificity loss would be sought for. •Task 3- Edge device implementation and eXplainable AI: A filter level compression on the developed CNNs will be proposed to allow three to four orders of magnitude reduction in computing power and memory capacity to run the developed oral cancer early detection and ROI marking in resource-constrained edge devices. The CNN developed will be further validated and updated with the biochemical/medical knowledge and practices.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Nutrition/Psychology/Public Health

PI: Dean Dawson	**Project Title: Mps1-interacting proteins that promote tumor cell survival**
HR21-099	**Organization:** Oklahoma Medical Research Foundation
Rank: 53	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	A key to the development of effective anti-tumor therapeutics is identifying compounds that selectively inhibit the growth of tumor cells but do not critically damage normal cells. MPS1 is a gene that is essential for multiple processes in normal cells. MPS1 encodes a protein that is a kinase. Kinases are cellular regulators that act to turn other proteins on or off to perform their cellular jobs. MPS1 performs several cellular jobs, but among its most well-known jobs is regulating the cell machinery that partitions the chromosomes into each daughter cell during cell division. In tumors, certain genes are often turned on to abnormally high levels. MPS1 is one of these genes. Recent studies have shown that tumors require this over-expression of MPS1 to survive. This phenomenon is called MPS1-addiction. In the laboratory, cells isolated from these tumors die when they are exposed chemical compounds that reduce MPS1 activity, but normal cells are more tolerant of the reduced levels of MPS1. This MPS1-addiction of tumor cells has made MPS1 a target for the development of anti-tumor therapeutics. Current compounds that affect MPS1 act in a very general way – they impede its ability to regulate all of its partners. Ideally, an anti-tumor compound would only inhibit the ability of MPS1 to keep tumor cells alive and not affect its other jobs that are also important for normal cells. To identify these compounds, it is first necessary to learn which cellular functions, regulated by MPS1, are the functions required by tumor cells for their survival. This is the goal of our project. First, we will perform a screen to find genes that work with MPS1 in keeping tumor cells alive. We will sensitize tumor cells to the loss of genes that function with MPS1 by slightly turning down MPS1 function with a chemical inhibitor. Then we will identify other genes, which when inactivated at the same, time kill the cell. Then, in a second series of experiments, we will analyze the genes identified in our screen for those that work together with MPS1 and will identify the biological jobs they perform. These experiments will refine our understanding of why MPS1 is required for tumor cell survival and will empower the development of compounds that strategically block the ability of MPS1 to keep tumor cells alive without preventing it from performing its essential roles in normal cells.
Research Area 1	Cell/Molecular Biology
Research Area 2	Cancer Research
Research Area 3	Genomics & Gene Expression

PI: Christopher L. Sansam	**Project Title: Role for Acetylation in DNA Replication Origin Site Selection**
HR21-126	**Organization:** Oklahoma Medical Research Foundation
Rank: 54	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	In every round of cell division, tens-of-thousands of replication forks work in concert to replicate or copy, the human genome. This process of DNA replication is controlled by time and restricted by three-dimensional space, and is highly regulated so that the right number of forks fire at the right time and place. The initiation of too many forks or too few forks can lead to the accumulation of genetic mutations that increase health risks associated with cancer and human developmental disorders. The mechanisms that determine which origins are selected for firing in vertebrates are not well understood. One essential protein, TICRR/TRESLIN, is limiting for DNA replication and has been shown to regulate S-phase length. We have previously shown that the interaction of TICRR with the epigenetic reader protein BRD4 is important for the three-dimensional spatial control of replication forks. BRD4 is part of a bromodomain and extra-terminal (BET) family of proteins that proteins associate with chromatin by binding preferentially to acetylated lysine residues on histones. Here, we propose a research strategy to define the role of histone acetylation in replication origin selection. Our central hypothesis is that histone acetylation recruits limited replication initiation factors, which in turn impacts selection of replication origins. Genomic mapping of initiation factor localization as well as identification of early firing origins will be used to determine the role of histone acetylation in selecting replication origins to fire.
Research Area 1	Cell/Molecular Biology
Research Area 2	Cancer Research
Research Area 3	Genomics & Gene Expression

PI: Karl Hansen	**Project Title: The role of very long chain polyunsaturated fatty acids in male fertility**
HR21-172	**Organization:** Board of Regents of the University of Oklahoma Health Sciences Center
Rank: 55	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	Infertility is one of the most common medical problems, affecting 10-15% of couples worldwide. Abnormalities in the semen are an important contributing factor in up to 30-40% of couples with infertility. Unfortunately, for most of these men, no underlying cause is identified. A major obstacle is our poor understanding of the factors leading to male factor infertility. As a result, current standard therapies for male factor infertility such as ovarian stimulation (OS) of the female partner with intrauterine insemination (IUI) and in-vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) primarily involve treating the female partner rather than addressing the underlying etiology. Other limitations of these therapies include the low success rate of OS-IUI (7-10%/attempt) and the expense and invasiveness associated with IVF with ICSI. Moreover, IVF is cost prohibitive for many couples. Low cost, low risk and effective treatments for male factor infertility are a pressing need. Prior studies by our group in humans and animal models have suggested that very long chain polyunsaturated fatty acids (VLC-PUFA) are important for normal sperm structure and function. VLC-PUFA are essential fatty acids that contain = 28 carbon atoms and are synthesized by elongation of dietary essential fatty acids by a number of elongases and desaturases, and are subsequently incorporated into sperm membrane sphingolipids. Male knock-out mice lacking enzymes necessary to synthesize VLC-PUFA are infertile, an effect that is at least partially mediated by decreased sperm concentration, but likely involves functional aspects as well. Most recently, our group has demonstrated a significant positive correlation between sperm lipid VLC-PUFA concentration and sperm concentration, morphology and importantly, live birth rate following standard treatment in couples with unexplained infertility. However, we currently lack a clear understanding of the mechanism by which sperm VLC-PUFA concentration impacts fertility. To address these questions, our team will utilize a transgenic mouse model of male factor infertility which lacks the ability to synthesize VLC-PUFA. Our proposal will determine if VLC-PUFA replacement can restore fertility in this knockout mouse model, and mechanistically, examine the effect of VLC-PUFA deficiency on sperm function through a series of in vitro fertilization experiments. The proposed experiments will define the steps in the reproductive pathway that are dependent on the presence of VLC-PUFA in sperm, and thus has substantial potential for clinical translation that advances the diagnosis and treatment for male factor infertility.
Research Area 1	Cell/Molecular Biology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Genomics & Gene Expression

PI: Marimuthu Andiappan	**Project Title: Earth-Abundant Iron- and Copper-Based Photocatalysts for Continuous Syntheses of Pharmaceuticals through C-N, C-S and C-O Coupling Reactions**
HR21-131	**Organization:** Oklahoma State University
Rank: 56	**Year 1:** $44,571 **Year 2:** $44,543 **Year 3:** $44,548 **Total:** $133,662
Research	Approximately 25% of all the reactions performed in the pharmaceutical industry consist of cross-coupling reactions, such as carbon-carbon (C-C), carbon-nitrogen (C-N), carbon-sulfur (C-S), and carbon-oxygen (C-O) cross-couplings. The cross-couplings have been traditionally carried out by homogeneous palladium (Pd) catalyzed batch processes using environmentally unfriendly solvents. The National Science and Technology Council (NSTC) has recently identified the continuous manufacturing of pharmaceuticals as one of five manufacturing areas of emerging priority of the USA. Continuous manufacturing of pharmaceuticals has the potential to (i) reduce manufacturing costs by up to 40-50 percent, (ii) improve drug product quality, (iii) reduce waste generation, and (iv) reduce the manufacturing facility space by 10 to 100 times. Additionally, continuous processes are safe, agile, and robust. Therefore, pharmaceutical manufacturing by continuous processes also has the potential to mitigate the public health threats arising from drug shortages. Given these advantages, heterogeneously catalyzed cross-couplings have been of great interest since they can be used as a platform to switch cross-couplings from the conventional batch mode to the continuous flow mode. In this proposal, our research goals are to (1) develop inexpensive and earth-abundant iron (Fe)- and copper (Cu)-based photocatalysts as efficient catalysts with activity and stability superior to that of conventional homogeneous palladium (Pd)-based catalysts for C-N, C-S, and C-O cross-coupling reactions, and (2) based on these photocatalysts, design efficient cross-coupling flow processes using green solvents to produce pharmaceuticals. Fe and Cu are inexpensive, earth-abundant, and less toxic compared to Pd. Our central hypothesis is that light with the wavelength that matches the dielectric Mie resonances of Fe- and Cu-based photocatalysts can be utilized as a powerful tool to tune and greatly enhance their catalytic activity. This hypothesis is based on a novel photocatalytic approach recently demonstrated in the literature by the PI and coworkers. The heterogeneous photocatalytic approach proposed in this project has the potential to reduce the manufacturing cost significantly and increase the rate of production of pharmaceuticals. Successful completion of the project will have a major impact on the pharmaceutical industry in Oklahoma.
Research Area 1	Chemistry & Biochemistry
Research Area 2	Biomedical Engineering
Research Area 3	Physiology/Pharmacology

PI: Gaurav Kumar	**Project Title: Unravelling the complex functions of B Cell Maturation Antigen in neuro-autoimmunity**
HR21-169	**Organization:** Oklahoma Medical Research Foundation
Rank: 57	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Multiple Sclerosis (MS) is a chronic immune-mediated disease of the central nervous system (CNS) characterized by neuronal damage, resulting in loss of motor and sensory functions. MS is considered to be one of the most common causes of disability, especially in young adults between 20 years and 40 years of age. According to the national multiple sclerosis society (NMSS), more than 2.3 million people are affected by MS worldwide, and the incidence continues to increase with a female to male ratio of 3:1. The burden of this complex disease is associated with reduced quality of life, increased pain, cognitive dysfunction, increased disability progression and increased mortality. In MS, the immune system, which is designed to protect the body from outside infections, gets dysregulated and mistakenly starts attacking our own neurons in the CNS. A variety of manifestations and symptoms can be seen in MS patients. Till date, there is no cure for MS, and most therapies functions to either slow the disease progression or speed the recovery from MS symptoms. Currently, there are many pharmacological agents that are used for the treatment of MS, and these disease-modifying therapies have significantly improved the management of this disease. Therapies that limit the immune-mediated inflammation have so far shown promising results in decreasing the attack rate. Despite several treatment options, a relevant proportion of MS patients continues to experience worsening of the disease and turn out to be non-responders to the therapy. Among the therapies, atacicept was developed to target the inflammatory cells of the immune system. The specific and selective effects of atacicept, on particularly the inflammatory immune cells made this drug appear as a promising candidate for targeting the pathogenic cells in MS and leaving the beneficial immune response intact. However, an increase of disease activity was seen in MS patients on atacicept therapy, and therefore, the clinical trial of the therapy was suspended. At present, reasons for the observed increase in disease activity with atacicept therapy remains to be completely understood and is currently a matter of investigation. Our proposed project aims to understand the reason behind the failure of atacicept in MS, using an experimental mice model that mimics MS disease. Our goal is to better understand the mechanism of the action and functioning of this drug to unravel the interlinked effects of atacicept on various cells of the immune system. It is very important to understand why some therapies worsen MS disease. The lessons learnt from the failure of the therapy may provide insight into the etiology of the complex MS disease.
Research Area 1	Immunology
Research Area 2	Cell/Molecular Biology
Research Area 3	Neurobiology

PI: Stephanie Sweatt	**Project Title: Nonsuicidal Self-Injury: Development of a Personalized Mobile Intervention**
HR21-004	**Organization:** Oklahoma State University
Rank: 58	**Year 1:** $44,987 **Year 2:** $43,390 **Year 3:** $44,745 **Total:** $133,122
Research	Short-term, accessible treatment for individuals engaging in nonsuicidal self-injury (NSSI) are limited. NSSI is a significant physical and mental health concern that may result in tissue damage, depression, anxiety, and suicidal behaviors. Historically, NSSI was thought to only occur within clinical populations; however, NSSI is a significant public health problem. Self-injurious behaviors are such a serious and pervasive health concern that a diagnosis of Non-Suicidal Self-Injury has been proposed for inclusion in a future diagnostic manual for mental disorders. While NSSI interventions have been developed, the du-ration and cost of treatment limit implementation. There is no existing short-term mobile intervention for NSSI that targets its potential mechanisms (e.g. emotion regulation). In the proposed study, we aim to 1) adapt an existing emotion regulation-based treatment with personalized feedback using an ecological momentary intervention (Adapted Mobile Intervention for NSSI; AdMIN) and 2) conduct a pilot RCT of AdMIN to assess its efficacy for reducing NSSI. During Phase 1, the mobile intervention utilizing personalized feedback and emotion regulation strategies will be developed. Following its development, community participants who engage in NSSI will pilot AdMIN and provide feedback regarding acceptability, credibility, utility, and feasibility. AdMIN will assess NSSI frequency and severity, provide personalized feedback to individuals about why they engage in NSSI, provide alternative strategies for regulating emotions, reducing impulsivity, and promoting behavior change, and will offer psychoeducational information about NSSI and referrals and resources for services. Phase 2 is a randomized control trial assessing community members engaging in NSSI to determine the efficacy of AdMIN. Participants (n = 60) will be randomly assigned to one of two groups: healthy skills + EMA control group or targeted emotion regulation skills + personalized feedback + EMA treatment group. Participants will complete questionnaires and psychoeducation and 1 week of EMA to assess baseline NSSI. Then, participants will complete modules depending on their randomized group for 2 weeks. Following Phase 2, all participants will complete EMA for 1 week to assess NSSI urge and engagement post-intervention. Following this, participants will complete 1-month follow-up session to report NSSI frequency and severity and provide additional feedback about the treatment's feasibility, transportability, and acceptability. This research will provide a personalized 2-week mobile treatment easily deployable to a variety of settings. This approach would constitute an early step in research that will lead to the development of a clinically useful targeted intervention for the reduction of NSSI behaviors and utilizes a short-term mobile intervention for NSSI that will bridge NSSI and emotion regulation research with personalized feedback interventions.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Nutrition/Psychology/Public Health

PI: Ann Louise Olson	**Project Title: PFKFB3-dependent regulation of adipocyte mRNA and protein expression**
HR21-025	**Organization:** Board of Regents of the University of Oklahoma Health Sciences Center
Rank: 59	**Year 1:** $42,575 **Year 2:** $44,215 **Year 3:** $44,215 **Total:** $131,005
Research	Adipose tissue is the only tissue in our bodies that can expand as a direct function of positive energy balance. The nutrient signaling that promotes adipocyte expansion is unknown. The purpose of this proposal is to test the hypothesis that glucose metabolism specifically regulates the synthesis of important proteins and enzymes that are required to maintain healthy glycemic control. In this proposal we will learn how glucose metabolism is important for helping adipocytes produce and maintain all of the functioning proteins that they need to store nutrients in the fed state and release these stored nutrients during fasting. This process is essential for maintaining healthy metabolism and preventing the development of insulin resistance and type 2 diabetes.
Research Area 1	Cell/Molecular Biology
Research Area 2	Physiology/Pharmacology
Research Area 3	Chemistry & Biochemistry

PI: Tieming Liu	**Project Title: Designing a User-Friendly Diabetic Retinopathy Screening App Using Routine Lab Results for Rural Primary Care Providers**
HR21-117	**Organization:** Oklahoma State University
Rank: 60	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Diabetic retinopathy (DR) is the leading cause of vision loss and blindness among American adults. However, the recommended ophthalmic exam for diabetic patients has an alarmingly low adherence rate, only 50%-60%, especially in rural communities. Many patients do not seek proper medical attention because DR is asymptomatic in the early stages. Moreover, ophthalmic equipment for DR exams is predominantly limited to urban areas, restricting access by patients in rural communities. As a result, many patients, especially in rural areas, miss the most effective period to halt DR progression and prevent vision loss. Efforts to improve the adherence rate by bringing fundus-image-based DR screening tools to primary health settings have been hindered by the relatively high cost of retinal cameras. Moreover, retinal imaging is technically challenging, potentially hindering its adoption in resource-limited settings, like rural primary care clinics. The rising prevalence of DR, coupled with barriers to DR screening in rural communities, creates a critical need to develop innovative non-image-based approaches that are cost-effective and widely available for DR screening. The objective of this project is to develop a user-friendly and cost-effective artificial intelligence DR screening app (DiRSA) for primary care physicians (PCPs) using demographic, comorbidity data, and routine lab results. Our approach differs from existing image-based DR detection tools (e.g., IDx-DR and Google's Verily) in that it does not require fundus images. Our preliminary study conducted in OCAST Project HR18-017 demonstrates that the accuracy of our approach is close to the fundus-image-based DR screening tools. Our approach is cost-effective and easy to use because primary care lab results and comorbidity data are not difficult to obtain for diabetic patients. It is promising to break the barrier to ubiquitous diabetic eye care in rural communities and increase the compliance rate of the ophthalmic exams among asymptotic patients. Timely identification of asymptomatic patients with on-going DR pathology will enable physicians to advise them to seek accurate examinations and early treatments. Consequently, it will save thousands of people, especially those living in rural areas, from preventable blindness and mitigate the threat of a dramatic increase of costly treatments for late-stage DR.
Research Area 1	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Biomedical Engineering

PI: Handan Acar	**Project Title: Peptide-based tool for controlling immunogenic cell death**
HR21-153	**Organization:** University of Oklahoma
Rank: 61	**Year 1:** $34,679 **Year 2:** $34,679 **Year 3:** $34,679 **Total:** $104,037
Research	In 2018 NIAID Strategic Plan for Research on Vaccine Adjuvants, the Blue Ribbon Panel recommended to "Expand [fundamental immunology and adjuvant] discovery efforts beyond TLRs, to include adjuvants that trigger inflammasome components Immune and nonimmune cells have specific receptors that recognize tissue damage-associated patterns. This recognition can “activate” the cells to produce similar patterns or other molecules (such as inflammasomes) to amplify immune response (inflammation). Damage-related immune responses are characteristic of the most potent adjuvants and vaccines. We know one way of release of damage-associated molecular patterns (DAMPs) is through holes that form in the cell membrane of distressed and dying cells. However, we still do not know the specifics of how these patterns are released to invoke potent immune responses. Previous research has attempted to release associated molecular patterns by initiating cell damage with radiation (as in radiotherapy) and temperature (as in photothermal therapy). In these studies, the responses were found to be potent enough to activate our immune system against the damaged cells; this is particularly useful to help the body fight e.g. cancer. Nevertheless, the imprecise duration, location, and amplitude of these therapies lead in many cases to more harm than benefits. No technology exists to manage the release of these patterns for a controlled immune response, despite the urgent clinical need. Acar Lab are experts in peptide design and engineering for various biomedical and materials science applications. By carefully mimicking the small parts of the natural proteins that create pores on cell membranes, we designed PAIIR – a pair of small molecules made of natural amino acids. We showed these molecules insert into the cell membrane, aggregate, and damage the membrane to release the most potent molecular patterns in various types of cells. In this proposal, we will expand our understanding of the effects of PAIIR in various cell types, study how PAIIR creates immune protection, and examine PAIIR’s effects as part of an influenza vaccine. The development of such technology in Oklahoma will naturally create new health care industry in the State, as well as improve health care in the State and beyond.
Research Area 1	Biomedical Engineering
Research Area 2	Immunology
Research Area 3	Cell/Molecular Biology

PI: Abhrajit Ganguly	Project Title: H2S Regulation of Airway Epithelial Programming and Injury during Neonatal Development
HR21-067	**Organization:** University of Oklahoma Health Sciences Center
Rank: 62	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Premature babies frequently require treatment with supplemental oxygen. Excessive oxygen – termed hyperoxia - can produce free radicals that inflict serious damage to the neonatal lung causing a chronic lung disease called bronchopulmonary dysplasia (BPD). Antioxidant defenses in premature babies are immature and not enough to counter the toxic effects of oxygen. Hydrogen sulfide (H2S) is an odorous gas that is poisonous and deadly in large quantities. In small quantities, however, H2S is an integral compound for proper cell function. Recent studies have demonstrated that administering small quantities of H2S can partially protect the developing lung from the toxic effects of hyperoxia. How H2S exerts these downstream effects however is not completely understood. We will explore whether protective H2S signaling in the newborn lung occurs through a novel biochemical modification on proteins called persulfidation, recently been touted as the principal mechanism through which H2S protects cells. Understanding the underlying mechanisms through which H2S protects the neonatal lung from oxygen toxicity will lead to the development of targeted therapeutic approaches to prevent BPD.
Research Area 1	Cell/Molecular Biology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Andriy Yabluchanskiy	**Project Title: Prevention of cognitive decline in older adults with peripheral artery disease**
HR21-162	**Organization:** University of Oklahoma Health Sciences Center
Rank: 63	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Vascular cognitive impairment is a major health concern in the aging US population. Alarming epidemiological data show that a significant percentage of the elderly population in the US has poor vascular health, which associates cognitive decline. Among the age-related diseases of the vascular system, peripheral artery disease (PAD) has attracted much attention recently. There is a strong body of evidence that PAD significantly worsens cognitive decline in older adults. While the prevalence of PAD is high in older adults, the mechanisms by which PAD worsens age-related cognitive decline is poorly understood. Moment-to-moment adjustment of cerebral blood flow via neurovascular coupling (NVC) is essential for maintenance of normal brain function. Our recent pre-clinical studies show that impairment of NVC responses and cognitive impairment are causally related and that endothelial dysfunction plays a critical role in this impairment. Although PAD is characterized by a significant endothelial dysfunction, its effects on NVC remain unexplored. Our overall hypothesis is that in elderly PAD patients, systemic microvascular endothelial dysfunction promotes neurovascular uncoupling, which leads to cognitive decline. Our hypothesis is testable in the following aims: Aim 1a) Determine the relationship between microvascular dysfunction, neurovascular uncoupling, and cognitive impairment in PAD patients. We will measure and correlate microvascular function to the NVC responses and cognitive function in PAD patients; Aim 1b) Test whether physical exercise improves microvascular function, NVC responses, and cognitive function in aged PAD individuals; and Aim 2)Test the hypothesis that circulating factors from the peripheral blood of PAD patients change the function and phenotype of cerebral microvascular endothelial cells (CMVECs). We will treat human CMVECs with serum samples from PAD patients and evaluate whether oxidative stress and inflammation predict the magnitude of NVC responses and cognitive function in these patients. Our studies will investigate clinically highly important consequences of a disease that is highly prevalent in elderly Americans, exploring the mechanistic role of circulating factors, oxidative stress and key endothelial pathways that regulate NVC. Identifying the role of microvascular endothelial dysfunction in the adverse neurovascular and cognitive outcomes of PAD could identify novel strategies for mitigating these deleterious complications.
Research Area 1	Physiology/Pharmacology
Research Area 2	Cell/Molecular Biology
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Bing Yao	**Project Title: Computer Simulation Enabled Machine Learning for Early Detection of Heart Disease**
HR21-079	**Organization:** Oklahoma State University
Rank: 64	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Medical decisions in clinical practice are generally based on rough estimations of outcomes from clinical trials, which do not fully incorporate the time-varying disease characteristics or patient-specific variations. Additionally, early-stage symptoms of heart disease occur intermittently, and most patients, especially those from rural communities who have limited access to world-class cardiac care, ignore such symptoms and approach a heart specialist at late stages. This may incur a significantly heavier financial burden to the patients, and may further delay the delivery of timely and effective medical treatment. Computational modeling of the human heart has contributed tremendously to advance the quantitative understanding of the cardiac dynamic processes, providing a vital opportunity for optimal medical decision making. However, most cardiac simulations lack the ability to incorporate variabilities among individuals, and little has been done to integrate personalized computer models with machine learning algorithms for automatic disease diagnosis. What is particularly lacking, is an innovative strategy to effectively incorporate patient data from medical sensing and imaging into cardiac simulation, and further utilize the virtual heart to provide important assistance to medical doctors and also help patients for self-monitoring with modern mobile devices. Our long-term goal is to help improve cardiac research driven by the vision of precision cardiology through innovative healthcare data analytics and personalized computational modeling. The objective of this proposed project is to develop a decision-making tool by integrating cardiac simulation with advanced healthcare data analytics for early disease diagnosis, which will be accomplished by pursuing two specific aims: 1) Sensitivity Analysis and Model Calibration: sensitivity analysis will be conducted to identify the most influential model parameters and an active-learning statistical framework will further be developed for model calibration. 2) Simulation-Aided Machine Learning for Early Disease Diagnosis: The calibrated cardiac simulation model will be integrated with real-world medical data through advanced deep learning infrastructures for early disease diagnosis. This is expected to have an important positive impact because it will provide a unique opportunity to understand, investigate, and predict disease-altered cardiac electrodynamics, and further optimize medical decisions tailored to each patient at early stages through integrating computer simulation with advanced machine learning algorithms.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Nutrition/Psychology/Public Health

PI: Rashmi Kaul	**Project Title: Hepatitis C virus Associated Inflammation and Cancer Development**
HR21-042	**Organization:** Oklahoma State University Center for Health Sciences
Rank: 65	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Hepatocellular carcinoma (HCC) is a leading cause of cancer death in the world and is strongly linked to chronic liver disease and cirrhosis. Hepatitis C virus (HCV) infection is the prime cause of rising incidence of HCC in developed countries including the United States. The chronic sequelae of HCV-infection include progressive hepatic fibrosis, cirrhosis and HCC. No viable vaccine is currently available for HCV prevention and new antiviral drugs to cure early HCV infection do not seem to reduce occurrence of HCC. Incidence of HCV-related HCC has been found to be higher in males. Clinical observations indicate that chronic HCV-infection appears to progress more rapidly in males than in females suggesting estrogen levels and estrogen receptors (ERs) play an important role in hepatic defense and development of HCC, especially since ERs are expressed in the liver. Estrogen is known to modulate immune responses, thus enabling women to clear the virus more efficiently and delay the onset of cirrhosis. It is also known to modulate the expression of the complement regulatory protein CD55 that is upregulated by HCV to aid in immune evasion. However, the precise mechanism of estrogen protection against HCV-related cirrhosis in females and worse prognosis of HCV-related cirrhosis leading to HCC development in males is largely unknown. Our recent published data suggests that there are gender-differences in the basal expression of ERs in human liver and ER subtype expression significantly decreased in males with chronic HCV-mediated cirrhosis and HCV-mediated HCC. Therefore, we hypothesize that “endogenous estrogen via interaction with ERs, modulate innate immunity involving CD55 expression that in turn will interfere with HCV core protein-mediated viral pathogenesis”. To test our hypothesis, we propose two specific aims: In the first - Study the gender-specific correlation of wildtype and variant ERa with CD55 in chronic HCV mediated cirrhosis and HCV–related HCC, and in the second - Determine whether estrogen-mediated modulation of CD55 occurs via ERa, altering the pathogenesis of HCV core protein in hepatoma cells. These studies will provide insights into the role of gender-specific inflammation/cancer biomarkers in HCV- related pathogenesis during HCV cirrhosis and cancer development at the molecular level and help in developing tailored novel therapies to intervene in HCV-driven inflammation and carcinogenesis.
Research Area 1	Infectious Disease
Research Area 2	Cancer Research
Research Area 3	Immunology

PI: Radhika Santhanam	**Project Title: Better Health for Oklahomans by Reducing Technostress through Active Computer Workstations and Digital Wearables**
HR21-077	**Organization:** University of Oklahoma
Rank: 66	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $44,993 **Total:** $134,993
Research	Better Health for Oklahomans by Reducing Technostress through Active Computer Workstations and Digital Wearables Technostress - stress that is caused by interacting with information technology devices - is becoming a serious health problem for individuals. The aim of the project is to investigate whether active computer workstations, such as standing and treadmill desks, and digital wearables that monitor a user's physiological signals, are helpful to alleviating technostress. Researchers identify events in our interactions with technology that generate technostress, such as interruptions through pop-up message. With the proliferation in information technology usage in organizations in Oklahoma and elsewhere, technostress and consequent health problems have increased in scope. Therefore, technostress requires immediate attention by researchers to develop methods to alleviate its adverse impact on health. High levels of stress directly impact a person's health and is a demonstrated risk factor for anxiety, depression, and chronic diseases. Per the statistics from the Oklahoma State Health Department (2019), the prevalence of these chronic conditions in Oklahoma is already above the United States national average; hence, public health measures to prevent them should address technostress. Our study proposes that active workstations and digital wearables can influence an individual's affect and cognitive engagement in helping them cope with technostress. Affect underlies the individual's emotional experiences and can be described as positive affect (e.g., enthusiasm) or negative affect (e.g., frustration). Decreasing negative affect and enhancing positive affect of an individual can help modulate the intensity of the stress experienced by that person. From earlier studies, we find that body postures and movements impact individuals' affect and their cognitive alertness, and therefore can be leveraged as stress moderators (Labonté-Lemoyne, Santhanam, et al. 2015). Furthermore, stress can be minimized if the individual is alerted through a digital wearable that monitors stress to take a break from their stressor. We conducted a pilot study, and our findings provides preliminary evidence for our hypotheses. e will conduct a rigorous experiment with study participants who are residents of Oklahoma. Participants will use active computer workstations or digital wearables in experimental conditions that will allow us to test our proposed ideas. We will record physiological signals and collect participants' perceptual responses. Our analysis will indicate effectiveness of proposed interventions in alleviating technostress of individuals. We have strong support from an interdisciplinary team of seasoned researchers, and infrastructure support. Our research contributes to the emergent science on technostress and public health, suggesting methods to alleviate impact of stressors, while demonstrating the value of active workstations and digital wearables.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Biomedical Engineering
Research Area 3	Neurobiology

PI: Rita K. Miller	**Project Title: The mechanisms by which acetylation regulates stu2 and microtubule function**
HR21-039	**Organization:** Oklahoma State University
Rank: 67	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Acetylation is a post-translational modification in which an acetyl moiety is attached to a lysine residue of a protein. As lysines carry a positive charge, acetylation can neutralize the positive charge of the targeted lysine. This can switch a protein on or off, drastically altering its function. Microtubule-binding proteins regulate critical microtubule-dependent processes implicated in neurological pathologies such as Alzheimer's disease and Lissencephaly, and in the occurrence of chromosomal instability during cancer. Microtubules are protein polymers comprised of alpha beta tubulin subunits. It is well established that microtubules are key components of the mitotic spindle that separate the genetic material. They also serve as the tracks for the transport of essential cargo in the cell. Stu2/ ch-TOG / XMAP215 is major family of microtubule regulatory proteins that control microtubules. Very similar versions of Stu2 are found in a wide variety of organisms, including humans. Stu2 is the yeast version of this human Tumor Overexpressed Gene that is mutated in many colon and hepatic cancers. Stu2 functions at three locations in the cell: at the plus end of the microtubule, at the microtubule attachment site of the chromsosome that is known as the kinetochore, and at the and the microtubule organizing center in yeast. However, its regulation is these sites is poorly understood. Specifically, a significant gap in our knowledge exists about how acetylation regulates microtubule associated proteins. Recently, the Miller lab demonstrated that Stu2 is modified by acetylation. However, the roles that acetylation plays in regulating Stu2 are not known. This Project fills this knowledge gap by identifying the functions and mechanisms of Stu2 acetylation at the kinetochore and the microtuble organizing center. For this, genetic, biochemical, and cell biological approaches will be used. Understanding this regulation of Stu2 will provide insights that will be valuable for understanding mechanisms of chromosome instability in diseases such as birth defects and cancer.
Research Area 1	Cell/Molecular Biology
Research Area 2	Cancer Research
Research Area 3	Cell/Molecular Biology

PI: Chenang Liu	**Project Title: AI-enabled real-time imaging and diagnosis technique for effective drug delivery in solid tumor treatment**
HR21-060	**Organization:** Oklahoma State University
Rank: 68	**Year 1:** $44,836 **Year 2:** $44,971 **Year 3:** $44,953 **Total:** $134,760
Research	Cancer and the related diseases have posed serious health risks to millions of people in the U.S. [5]. Although the progress in cancer treatment research is very significant in recent decades, unfortunately, the survival rate is still relatively low. To further improve the effectiveness of solid tumor chemotherapy and increase the five-year survival rate of difficult cancers, currently a key research direction is to utilize nanomedicines such as liposomes and then enable image-guided drug delivery (IGDD). Compared with the other common medical imaging techniques, as a safe, cheap, and accessible technique, recent studies have shown that ultrasonic imaging is a very promising option for enabling IGDD in cancer treatment. However, its weak tissue contrast and the commonly existing interference information still significantly limit the practical application for online visualizing of localized drug release or determining the chemotherapy distribution. To achieve more trustworthy IGDD and enable broader applications, motivated by the recent advancement in artificial intelligence (AI), the overall objective of this project is to develop an AI-enabled IGDD technique based on ultrasonic imaging for real-time target localization and characterization of drug delivery in solid tumor. To realize this objective, this project will focus on two crucial specific aims: 1) Aim 1: Develop an intelligent feature extraction and modeling approach using advanced data analytics and machine learning for ultrasonic images to monitor the in vivo drug delivery. This aim is expected to implement an ultrasonic image-oriented approach for IGDD, which is able to identify the tumor region in images automatically, extract the effective image feature intelligently, and correlate the image features with the progress of drug delivery accurately. Completion of this aim will demonstrate the ability to perform non-invasive monitoring of drug distribution in tumors and other related organs using the proposed AI-enabled ultrasonic imaging approach. 2) Aim 2: Enable AI-assisted real-time evaluation and feedback of the therapy process, and develop a prototype toolbox by integrating the developed AI-enabled techniques, which is expected to further improve the capability of the proposed imaging technique in clinic practice. Completion of this aim will demonstrate the capability of the developed AI-enabled imaging technique for the determination of therapeutic efficacy in solid tumors. Overall, the outcome of this research will lead to a better understanding of tumor drug delivery. The proposed methodology integrates the recent advances in IGDD, image processing, and machine learning to provide a smart, affordable, user friendly, trustworthy, and safe clinical solution for cancer patients, particularly for the at-risk populations. Furthermore, this technique will also have great potential to speed up new drug/liposome development in this area due to the assistance of AI.
Research Area 1	Cancer Research
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Biomedical Engineering

PI: Pamela Lovern	**Project Title: Blocking myostatin to improve vascular cell function and enhance blood flow in diabetic skeletal muscle**
HR21-057	**Organization:** Oklahoma State University
Rank: 69	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Diabetes is a very common (and increasing) problem for the citizens of Oklahoma, especially type II or "adult-onset" diabetes. One serious complication of diabetes is peripheral artery disease (PAD). In PAD, arteries in the limbs become blocked, causing insufficient blood flow to the extremities (especially the feet). People with diabetes and PAD have difficulty walking without pain. In the most severe cases, the pain is present even at rest, and patients have wounds that fail to heal and turn gangrenous. When this happens, the patient's limb has to be amputated. Currently, most treatments for PAD are surgical (stents or bypass surgery). Surgery is invasive, expensive, and may not provide long-term benefits. Interestingly, the circulatory system can undergo processes called "angiogenesis" and "arteriogenesis," in which new capillaries form and small arteries grow around blocked arteries to provide an alternate path for blood flow. Stimulation of angiogenesis and arteriogenesis could be an effective treatment for diabetic PAD patients by increasing oxygen delivery to their limbs. Unfortunately, studies have found that diabetes reduces people's ability to develop new blood vessels in their muscles. Currently, it is not known exactly how diabetes does this. Therefore, the goals of our lab's research are to understand 1) how angiogenesis and arteriogenesis are controlled and 2) how diabetes interferes with these processes, so that we can develop new treatments to stimulate them. One treatment commonly recommended for diabetic PAD patients is exercise, because it can stimulate both angiogenesis and arteriogenesis. However, patients with severe PAD may not actually be able to exercise due to their disease. Therefore, in this OCAST application we plan to study how a new treatment that mimics exercise (myostatin inhibition) affects angiogenic and arteriogenic growth factor production and blood vessel growth, and to determine whether myostatin can reverse the effects of diabetes on these processes. Myostatin is a protein that limits muscle growth; when it is inhibited, muscles grow larger, similar to the effect of exercise. Until now, the effects of myostatin inhibition on angiogenesis and arteriogenesis have not been studied. However, early results from our lab show that myostatin inhibition can have beneficial effects to increase growth factor levels, and can also increase the number of capillaries in muscles. Therefore, we propose that blocking myostatin will improve blood vessel growth in experimental type II diabetes and PAD. These studies will help us understand how diabetes limits angiogenesis and arteriogenesis, and will lead to new treatments for Oklahomans with diabetes and PAD.
Research Area 1	Physiology/Pharmacology
Research Area 2	Cell/Molecular Biology
Research Area 3	Genomics & Gene Expression

PI: Clinton Jones	**Project Title: Alzheimer's disease associated pathology is accelerated by herpes simplex virus 1 infections**
HR21-061	**Organization:** Oklahoma State University
Rank: 70	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Alzheimer's disease (AD) is a progressive neurodegenerative disease that causes memory loss, cognitive deficits, and behavioral changes. AD accounts for nearly 70% of all dementia cases. Approximately 5.8 million Americans aged 65 and older are affected by AD, and the incidence of AD is expected to triple by 2050. Strikingly, women are twice as likely to develop AD than men suggesting sex-specific factors drive this disease. The traditional hypothesis for AD progression states beta-amyloid (Aß) plaques initially appear, causing hyper-phosphorylation of the tau protein, culminating in neurofibrillary tangles and neuronal death (neurodegeneration). Overall, the steps leading to AD are also linked to inflammation, which is frequently detected in brains of people with AD. Numerous clinical trials focused on reducing A? plaques failed suggesting other cofactors may play pivotal roles in development of AD. Hence, alternative hypotheses were proposed to augment AD progression. One intriguing hypothesis that has received attention is certain microbial infections can function as cofactors for AD progression. Support for this premise comes from the finding that Aß peptides possess antimicrobial activity and protect against human herpes virus replication. Herpes virus DNA, including Herpes simplex virus 1 (HSV-1), is detected in Aß plaques of people with AD suggesting HSV-1 accelerates AD development. HSV-1 establishes a life-long latent infection in the nervous system of nearly all humans. Stressful stimuli periodically induce reactivation from latency, which culminates in virus shedding, neuronal death, and recurrent disease. Notably, HSV-1 infection in the nervous system also induces inflammation, an important component of AD progression. Our new and exciting studies revealed that aged female mice latently infected with HSV-1 display enhanced neuronal senescence and inflammation relative to age-matched male mice or young mice. Consequently, we hypothesize that HSV-1 is an important cofactor during AD development. The objective of this proposal is to directly test whether the HSV-1 latency-reactivation cycle accelerates AD like pathology in a well-established mouse model of AD. We will also test whether stress-induced reactivation from latency enhances AD pathology in this novel mouse model. Finally, studies designed to confirm that HSV-1 infection preferentially causes neurodegeneration and neuroinflammation in aging female mice will be performed in a well-established mouse model of AD. Completion of these studies will provide novel insight into the role that HSV-1 has on increased AD prevalence in women.
Research Area 1	Infectious Disease
Research Area 2	Neurobiology
Research Area 3	Cell/Molecular Biology

PI: Robert Hal Scofield	**Project Title: Physical, Emotional, and Cognitive Effects of Brain Training Programs in Sjogren's Patients**
HR21-055	**Organization:** University of Oklahoma Health Science Center
Rank: 71	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Autoimmune disease encompasses a large group of disorders (approximately 80 different illnesses) in which the immune system attacks the body itself. The immune system protects us from foreign invaders such as viral and bacterial pathogens by releasing antibodies and other mediators that are specifically targeted to eliminate the threat. However, the cells of the immune system sometimes lose the ability to distinguish the body's cells from foreign cells and attack itself. Approximately 5 to 8 percent of the US population is affected by one of these numerous autoimmune diseases making autoimmunity the third most common disease category after cancer and heart disease. The NIH's Office of Research on Women's Health has declared autoimmune diseases to be the 4th most predominant cause of disability in women since 75% of autoimmune diseases affect women in a much larger prevalence than men. Among the autoimmune diseases, Sjögren's syndrome (SS) affects approximately 1% of the US population, roughly equivalent to those living with breast cancer, with 9 out of 10 of those affected being women. Of those classified as having Sjogren's Syndrome, 44.4-50% complain of cognitive dysfunction commonly called brain fog that can predate glandular symptoms by up to two years. The most common complaints consist of poor attention and concentration, especially in the presence of many distractions, memory deficits, and lowered cognitive ability. Also reported are deficits of attention, information processing speed, executive function, verbal and visual memory, visual-spatial perception, and lower scores in motor reaction time when running a battery of cognitive testing on pSS patients. As humans learn and interact with their environment, neural connections form in the brain. As more and more of these networks appear, the most robust and productive connections retain function, while other connections are pruned away to increase the strength of the primary connections. One theory as to the cause of brain fog is the immune system in the brain over prunes neurons, effectively reducing connections, and causing diminished functionality. Cognitive training relies on a process similar to physical rehabilitation. By exercising different neural networks, cognitive training programs claim to use the brains' neuroplasticity to strengthen and reform connections that have diminished. Studies have shown improvements, not only in cognitive function, but also decreased anxiety and depression, improved insomnia, and reduction in fatigue in other cohorts. All of which plaque the lives of Sjögren's patients and decrease their quality of life. Positive results have been witnessed with as little as 15 minutes a day, 3 days a week, for 8 weeks in normal population studies. We propose to increase this to 5 days a week for 12 weeks for our population to get more robust effects. We predict an increase in quality of life in Sjogren's patients who participate in cognitive remediation therapy.
Research Area 1	Immunology
Research Area 2	Nutrition/Psychology/Public Health
Research Area 3	Cell/Molecular Biology

PI: DJ McMaughan	**Project Title: Addressing psychiatric hospitalizations among autistic adolescents and emerging adults: The role of social inclusion and community mental healthcare resources**
HR21-108	**Organization:** Oklahoma State Univeristy
Rank: 72	**Year 1:** $40,620 **Year 2:** $39,088 **Year 3:** $37,109 **Total:** $116,817
Research	Adolescents and emerging adults with autism experience higher rates of psychiatric hospitalizations compared to their peers. Psychiatric hospitalizations are avoidable with community services yet rank among the top ten causes of hospitalization among autistic youth and account for over $100 million each year. Reducing psychiatric hospitalizations is important because hospitalization is: the most intensive and expensive intervention, an indicator of poor quality care, traumatic for autistic youth, and increases the risk of suicide. In the proposed community engaged, Mixed Methods Research project our goal is to address high rates of psychiatric hospitalizations and costs among autistic adolescents and emerging adults by understanding how social inclusion and community mental healthcare are associated with this phenomenon. We will co-create and deploy a survey of social inclusion and community mental healthcare using two samples of people from the autistic community in Oklahoma: 20 community members (autistic adults and caregivers who will help create the survey) and 300 participants (150 autistic adolescents and emerging adults and 150 caregivers). We will also analyze Oklahoma hospital discharge data to create a state-wide picture of the impact of social inclusion and community mental healthcare on psychiatric hospitalization costs.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Yuchen Qiu	**Project Title: Developing a Fourier Ptychography based Microscopic Scanning System to Facilitate the Diagnosis of Thyroid Carcinoma**
HR21-010	**Organization:** The University of Oklahoma
Rank: 73	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	In United States, many people have palpable thyroid nodules, especially in the iodine-sufficient regions. Although most of these nodules are not harmful to the patients, a certain percentage of them are aggressive (malignant nodules) and the patients need to receive further treatment. In order to diagnose malignant nodules, pathologists need to use a needle to penetrate into patients' thyroid and obtain the cytological nodule specimens (fine needle aspiration, FNA). During the specimen obtaining procedure, one pathologist must be on site to ensure that the quality and quantity of these specimens (rapid on-site assessment, ROSE). Although commercial slide digitizers are available, they cannot be deployed to every operating room and small clinics, which is due to the high cost, low scanning speed, and large volume of these digitizers. In order to overcome this limitation, we plan to develop a novel Fourier Ptychography based microscopic digitizer to achieve low cost and fast slide scanning. This new technique obtains a series of images under low magnification (2x or 4x) objective lenses. These captured images can be combined together to achieve high resolution equivalent to 20x or 40x objective lenses. Since the image is obtained under low magnification, the field of view (i.e. the area for which one shot can cover) is vastly enlarged. Thus only a small number of shots can cover the entire slide and the digitization speed can be greatly enhanced. Meanwhile, the low magnification objective lens has a very large depth of field (the range for which the imaged sample stays clear), which can vastly reduce precision requirement of the moving stage. The cost of the digitizer will therefore be much cheaper than the conventional scanner. If we can successfully develop this novel system, the on-site nodule sample obtainment can be performed by a technician, and the digitized sample images will be transferred to pathologists' office for diagnosis (telepathology). Therefore, pathologists do not need to walk among different operating rooms and the examination efficiency will be vastly improved. This low cost system is affordable for small clinics. Hence these on-site sample assessment can be conducted in remote areas where only small clinics are available. Our new imaging system can also be used for imaging other cancer tissues.
Research Area 1	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 2	Biomedical Engineering
Research Area 3	Cancer Research

PI: Christian Lemon	**Project Title: Thermosensory Processing**
HR21-102	**Organization:** Univ. of Oklahoma
Rank: 74	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Flavor is associated with food selection and preference behaviors in humans. Flavor is contributed by multiple sensory modalities including taste, olfaction (smell), and somatosensory sensations such as food temperature. Cooling frequently arises in the mammalian oral cavity during mouth openings and food sampling due to the high resting temperature of oral skin. Nonetheless, oral temperature has been rarely considered in neurobehavioral studies on ingestive behavior. Because of this, knowledge on how temperature sensing mechanisms in the mouth play into food preferences has lagged behind advances in taste and smell. Relatedly, there are gaps in our understanding of how trigeminal neurons, which underlie the sensing of oral temperature, distinguish pleasant cooling from aversive cold. A long-term objective of the proposed studies is to establish an experimental platform for studying the role of thermosensation in orosensory-guided preference and ingestive behaviors in mice. Mice are a genetic model system for elucidating neurobiological mechanisms. For behavioral tests, we have designed and built an adapter that independently controls the temperatures of fluids inside multiple sipper tubes presented individually to mice by a lickometer. When coupled with this adapter, the lickometer can perform brief-access fluid exposure tests that intend to gauge how lingual temperature sensations influence sensory/tongue control of licking ingestive behavior. Using this device, Aim #1 will measure how change in fluid temperature affects mouse preferences to lick fluid stimuli. This aim will test wild-type and gene-deficient mice to address how genetic silencing of specific temperature-sensing mechanisms on trigeminal fibers impacts oral thermal preference. We will focus on two mechanisms associated with the detection of cooling temperatures. These mechanisms are evidenced by prior data to influence behaviors to cooling in other contexts. In Aim #2, we will apply neurophysiological recording methods to gene-targeted mice to understand how silencing one of these mechanisms affects the neural processing of oral cooling and cold in oral thermosensory neurons in mouse brain. Our hypothesis is that separate thermosensory mechanisms and neural pathways participate in neurobehavioral preference and avoidance reactions to oral cooling. Our hypothesis is supported by our published and pilot results. These projects aim to provide an initial account of how temperature sensing and thermosensory mechanisms in the mouth contribute to ingestive behaviors and hedonics in mice, shedding light on the role of temperature in flavor preferences. Collected data will form the basis for future studies on interaction between thermosensory mechanisms and taste during ingestive responding. Ultimately, defining how thermosensation ties into oral preference behaviors is needed to delineate how flavor impacts ingestive decisions linked to human health and disease, such as obesity.
Research Area 1	Neurobiology
Research Area 2	Physiology/Pharmacology
Research Area 3	Cell/Molecular Biology

PI: Christina R. Bourne	**Project Title: Dissecting the molecular basis of bacterial plasmid addiction systems**			
HR21-176	**Organization:** University of Oklahoma			
Rank: 75	**Year 1:** $44,242	**Year 2:** $0	**Year 3:** $0	**Total:** $44,242
Research	The pervasive spread of antimicrobial resistance (AMR) genes throughout bacteria is a serious public health threat. The most common mechanism for transmission of these AMR genes is by a DNA plasmid. This plasmid does not become part of the genome of the bacteria, and instead it encodes special toxin-antitoxin "addiction" systems to force the bacterial cells to replicate and maintain this plasmid. Innovative strategies have tried to manipulate these addiction systems and "cure" the bacterial cells, but the rules that dictate how the "addiction" works are not clear, and the results were inefficient and unpredictable. We have already made important discoveries in the toxin-antitoxin field, and will use this gained expertise to tackle systems on AMR plasmids. Our proposal is seeking to better define the molecular basis for toxin-antitoxin addiction, and those insights should illustrate how to improve anti-addiction approaches for treating bacterial infections. We will determine how much of the toxin protein molecule is already present when the plasmid is lost, if the paired antitoxin can be removed, if additional toxin proteins can be made from any residual mRNA present, and if the variability in outcomes resulted from different toxin types and their activity in different types of bacteria. These insights will propel an innovative new way to combat the spread of AMR genes, which will improve treatment options and outcomes for people and the "One Health" objectives.			
Research Area 1	Infectious Disease			
Research Area 2	Cell/Molecular Biology			
Research Area 3	Chemistry & Biochemistry			

PI: Jim Smay	**Project Title: Threshold Strength Ceramic Dental Crowns by Direct Ink Writing 3D Printing**
HR21-118	**Organization:** Oklahoma State University
Rank: 76	**Year 1:** $40,387 **Year 2:** $39,471 **Year 3:** $40,593 **Total:** $120,451
Research	This project seeks to improve the performance of all-ceramic dental crowns and bridges through three-dimensional (3D) printing of functionally graded ceramics. While current technology in all-ceramic crown materials and processing have brought these devices very close to the "gold standard" of porcelain on metal crowns, there are some brittle fractures that might be avoided if a residual compressive stress were engineered on the external surfaces of the prosthetic. By 3D printing ceramic gel inks, the composition of the ceramic can be controlled within the printed object. Along with composition control comes variation in the sintering behavior of the ceramics. If a layer of low thermal expansion ceramic is used on the external surfaces, much like in tempered glass, this outer shell will be placed in a state of residual compression upon cooling. This compressive stress will prevent the formation of cracks below a threshold strength hence, improving performance of the crown. Initially the research will pursue printing and characterization of regular geometries, such as disks and bars, to test the best spatial arrangement of the materials during printing and sintering. Finally, the best strategy will be incorporated into the complex geometry of crowns and bridges. One additional aspect of this work will be to explore grading of color in the prosthetic to help clinicians better match crowns to the color variations of natural teeth.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Chemistry & Biochemistry

PI: Kenneth Humphries	**Project Title: Cardiac glycolysis affects systemic glucose homeostasis**
HR21-037	**Organization:** Oklahoma Medical Research Foundation
Rank: 77	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	The heart has an unrelenting requirement for energy that necessitates high metabolic activity. It is relatively unknown, thought, how cardiac metabolism affects systemic parameters such as glucose homeostasis. This is an important gap in knowledge because of potential roles that cardiac function may play in metabolic disorders such as diabetes. We previously discovered that the content and activity of the primary regulator of cardiac glycolysis, phosphofructokinase-2 (PFK-2), is disrupted by diabetes. This prompted us to investigate the role of PFK-2 in cardiac metabolic flexibility and diabetic cardiomyopathy. We have been using transgenic mouse models that have either constitutively active or decreased cardiac PFK-2 activity, corresponding to increased or decreased cardiac glycolysis, to determine how their hearts respond to metabolic stress. Remarkably, we discovered that these cardiac-specific transgenic mice have unique systemic effects when they are challenged with a high fat diet (HFD). In general, mice that have constitutively active PFK-2 (GlycoHi mice) have resistance to the adverse systemic effects of HFD while mice with dominant-negative PFK-2 (GlycoLo mice) do poorly. This suggests that cardiac PFK-2 activity has effects on whole body glucose homeostasis and insulin sensitivity and that decreasing cardiac glycolysis may exacerbate the detrimental effects of HFD. The goal of this proposal is to test the hypothesis that cardiac PFK-2 activity has systemic effects on glucose metabolism via endocrine activity. Aim 1 will determine if cardiac PFK-2 activity directly affects systemic glucose homeostasis. We have now generated a cardiomyocyte specific PFK-2 knockout mouse (PFK2CM-/- mice) that will allow us to directly test this possibility. Control and PFK2CM-/- mice will be fed HFD to induce insulin resistance and hyperglycemia. Sub-Aim1A will determine how knocking down PFK-2 affects cardiac metabolism. Sub-Aim 1B will determine the systemic effects of cardiac PFK-2 knockdown. Aim 2 will determine the mechanism by which cardiac glycolysis affects systemic glucose homeostasis. We will use control, GlycoHi, GlycoLo, and PFK2CM-/- mice, either on control or HFD, to measure cardiac endocrine factors. We will measure circulating natriuretic peptides and known cardiac proteins that affect peripheral tissues. The results of these experiments will determine if PFK-2 mediated changes in cardiac glycolysis affect glucose homeostasis via known or novel mechanisms. Given the epidemic occurrence of obesity and type 2 diabetes, it is essential for human health to understand the underlying causes. Results from this study will provide new and essential information on the role of cardiac metabolism in this process and will be an impetus for further studies on this topic.
Research Area 1	Physiology/Pharmacology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Antonius Oomens	**Project Title: Focusing the immune response to enhance efficacy, safety, and cross-protection of a single-cycle live RSV vaccine**
HR21-073	**Organization:** Oklahoma State University
Rank: 78	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	RSV is a respiratory virus that causes pediatric bronchiolitis and pneumonia, with >100,000 deaths in children worldwide, and also causes significant morbidity and mortality in the elderly. Yet a vaccine is not available. A1960s vaccine trial in very young seronegative children, using inactivated virus, failed to protect and instead induced virus-enhanced lung disease (VED) upon exposure to RSV. From this and other trials, we have learned that in children that have never encountered RSV, many subunit and inactivated vaccine approaches can result in dangerous VED-like responses. In contrast, live-attenuated vaccines have never resulted in VED. Live vaccines can also induce broad immunity, including local mucosal immunity in the respiratory tract, and can be applied needle-free (intranasally). Thus live vaccines are believed to be the major vaccine approach for seronegative children. The most recent trials show however that it is exceedingly difficult to obtain the optimal level of attenuation and to render a live vaccine safe enough. Vaccine safety is arguably the single largest challenge for a live vaccine, given that all the target groups, infants, young children, the elderly, and the immune-compromised, have weak or suboptimal immune responses. Based on this premise, we designed a live-attenuated vaccine primarily to have a solid and stable safety profile. This vaccine, RSV-Mnull, is genetically manipulated to be live but completely block virus spread within a recipient, and to avoid the formation of new virus variants that might regain virulence. The prototype RSV-Mnull was tested in animal models and found to be safe, as expected. Preliminary data with the initial RSV-Mnull prototype also showed encouraging efficacy results with full protection in mice and partial protection in baboons. With a stringent safety profile established, the next phase is to optimize the efficacy of RSV-Mnull, to achieve a vaccine with an optimal efficacy-to-safety balance. To do so, in this proposal, we develop a combination approach that further enhances the efficacy of RSV-Mnull. This approach is a prime-boost vaccination in which RSV-Mnull is the prime vaccine, which ensures we will not induce VED. The boost consists of novel RSV-based virus-like-particles (VLP) which are specifically designed to direct the RSV-Mnull primed immune response to the most neutralization sensitive areas of the major viral antigens. Inherent in the VLP design also is the induction of antibodies that will recognize divergent RSV strains. In summary, our unique approach should both boost and focus the antibody levels, protect against the different strains of RSV, and thus impart strong efficacy. If successful, this combination vaccine approach should exceed previous formulations for seronegative children and may also be applicable to other immune-compromised target populations.
Research Area 1	Infectious Disease
Research Area 2	Biomedical Engineering
Research Area 3	Immunology

PI: Myron Hinsdale	**Project Title: Novel Role for Neuritin in Adipogenesis**
HR21-085	**Organization:** Oklahoma State University
Rank: 79	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Obesity and type II diabetes are at epidemic levels in the U.S. Understanding how adipose (fat) tissue develops, grows and is maintained is critical to helping these patients. Lipodystrophy is a disorder recognized by the National Institutes of Health as critical for more research and therefore deserving of investigation, the advocacy group Lipodystrophy United showcases that this disease impacts Oklahoma as well. This disease is the opposite of obesity characterized by a selective, progressive loss of fat (adipose) tissue from various body locations called "adipose tissue niches". In addition, these patients develop a variety of metabolic abnormalities some of which can be life threatening and include increased blood lipids, and diabetes accompanied by fat tissue inflammation. When patients lose metabolically active fat tissue, they subsequent develop disturbances in storage and release of energy and lose the mechanical "padding" function of fat tissue. The extent of fat tissue loss usually determines the severity of the associated metabolic complications suggesting that treatments targeted at modification of the fat stores can be therapeutic. There is no cure and current treatment is quite limited. These patients have an extremely low quality of life. Fat tissue wasting occurs in other diseases as well such as in cancer that is estimated to cause 20% of cancer deaths and HIV patients undergoing treatment. It's called cachexia. In lipodystrophy, the fat tissue inflammation is speculated to inhibit fat cells from surviving. Since fat is an important endocrine tissue its levels greatly affect how the body handles glucose where excess fat causes diabetes AND loss of fat causes diabetes. Understanding the regulation of the fat deposits therefore could significantly impact many important diseases. We have developed a novel lipodystrophic mouse model by altering the sugar molecules on proteins that surround cells. These are similar to the branches on a tree where the trunk is the protein and the branches are the sugars. These branches have significant roles in the function of the “tree” that is essentially the proteins around cells that are within tissues. These branches are important in cellular attachments and cellular responses to growth factors and inflammatory protein factors. Using these mice we can study human lipodystrophy and our findings suggest that these sugars are important to the function of proteins and cells in the steps of fat cell development and survival. We have recently published our results and using these mice we have discovered an important candidate protein that may impact fat tissue development, and we need to follow-up studies to confirm its role in this process. This is novel and ground breaking since this protein has never been linked to fat tissue. We think understanding the way this protein works will provide a way to treat patients that have fat tissue abnormalities including obesity, lipodystrophy, and cachexia.
Research Area 1	Cell/Molecular Biology
Research Area 2	Physiology/Pharmacology
Research Area 3	Neurobiology

PI: Edgar A. O'Rear	**Project Title: Post-Mechanical Trauma, Autoimmune Reactions to Red Blood Cells as Markers**
HR21-111	**Organization:** University of Oklahoma
Rank: 80	**Year 1:** $44,960 **Year 2:** $44,441 **Year 3:** $44,792 **Total:** $134,193
Research	Blood flowing through certain medical devices injures blood components causing complications for patients and shorter circulatory lifespans for their red blood cells. Lifespans as short as 30 days, compared to a normal of 120 days, have been found for red cells from patients with a left ventricular assist device (LVAD), an auxiliary pump that lightens the load for heart failure patients. Blood damage is attributed to non-physiologic forces or shear stresses associated with flow through mechanical circulatory support pumps, prosthetic heart valves and other cardiovascular equipment. Mechanical trauma to blood in LVAD patients, even at low levels described as "subclinical hemolysis", has been linked to complications like thrombosis and red cell loss. Our group has discovered that mechanical trauma to red cells causes an autoimmune reaction with binding of immunoglobulin G(IgG). IgG activates the complement cascade resulting in a molecular complex attacking the cell membrane and causing hemolysis. We propose to investigate contributions of the complement system by studying component species C5b and CD35. C5b has been chosen from the many species in the complement system because it is common to both the classical and alternative pathways. We are interested in CD35(CR1) also as it can act to modulate the complement system. IgG and complement are opsonins that signal elimination of cells by phagocytosis(ingestion by white blood cells) with removal in the liver and spleen. We will conduct experiments to look at phagocytosis of injured red cells and the effect of shear on CD47 which inhibits phagocytosis. Damage to cells will be mimicked in well-defined flow fields using laboratory equipment and blood from healthy volunteers. The equipment includes a viscometer and microfluidics flow channels. These units allow us to control the magnitude and duration of forces the cells experience. Fluorescently tagged antibodies will be employed with flow cytometry to probe the effects of trauma on C5b, CD35 and IgM. With the assistance of a company in Oklahoma City, the immune response will be examined for red cells that have passed through actual commercial LVAD heart pumps of two different types. An additional component of the project will be to obtain data on IgG binding after turbulent flow to improve prediction of cell damage by computer simulations. Knowledge about these immunological markers offers a basis for an innovative and sensitive method of evaluating the well-being of patients on LVADs or of predicting their susceptibility to complications. Currently, there is no good method for determining sublethal damage to red blood cells. As such, we believe immunological tests may also become a new standard replacing hemolysis for patient monitoring and design improvements of cardiovascular devices. As leaders in this technology, we have the opportunity to create with VADovations a testing service for device performance.
Research Area 1	Biomedical Engineering
Research Area 2	Physiology/Pharmacology
Research Area 3	Cell/Molecular Biology

PI: Marianna Patrauchan	**Project Title: Targeting carbonic anhydrases in calcification and virulence of P. aeruginosa**
HR21-011	**Organization:** Oklahoma State University
Rank: 81	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Soft tissue calcium (Ca) deposition disrupts the function of tissues and leads to severe diseases, such as calciphylaxis, broncholithiasis, arteriosclerosis, and renal stone formation. However, there are currently no clinically viable therapies available to prevent or treat soft tissue calcification. The origins and the contributing factors of calcification are poorly understood and are commonly associated with calcium misbalance and human carbonic anhydrase (CA) activity. These metalloenzymes catalyze the reversible hydration of carbon dioxide to bicarbonate, accumulation of which may lead to the formation of CaCO3. CAs can also be produced by bacterial pathogens. Several calcification-related diseases have been associated with chronic bacterial infections, raising the possibility that the involved bacterial pathogens contribute to the formation of calcium deposits in infected tissues via the catalytic activity of their CAs. Pseudomonas aeruginosa is an opportunistic pathogen causing high-mortality biofilm-associated chronic infections, including cystic fibrosis, endocarditis, meningitis, pneumonia, that each can exhibit calcification during late stages of development. The PI established that P. aeruginosa PAO1 produces Ca deposits when growing at the levels of Ca similar to those in lung liquids of CF patients. We identified three functional ß-class carbonic anhydrases: psCA1, psCA2, and psCA3, produced by PAO1, and characterized their catalytic activities and inhibitors. We hypothesize that the ability of P. aeruginosa to deposit extracellular Ca is due to the catalytic activity of one, two or all three psCAs and that this ability enhances P. aeruginosa ability to form biofilm, resist antibiotics, persist in a host, and cause infections. To test these hypotheses, we propose to characterize the role of three psCAs in Ca deposition in P. aeruginosa; determine whether psCAs-dependent Ca deposition enhances P. aeruginosa biofilm formation, resistance, and pathogenicity; and evaluate the potential of pharmacological inhibition of psCAs on Ca deposition and pathogenicity. This study will have an important and significant impact on both the fundamental aspects of P. aeruginosa physiology including its metabolic activities and biofilm formation, as well as clinical aspects of the pathophysiological role of psCAs in calcification. Since P. aeruginosa ß-CAs share no sequence or structural similarity with the a-CAs, the only CAs expressed in humans, they represent an excellent target for drug development. Therefore, elucidating the role of these enzymes in pathogen-initiated calcification will potentially provide a novel direction in therapeutic developments aiming to prevent or mitigate the progression of calcification in the context of P. aeruginosa infection.
Research Area 1	Infectious Disease
Research Area 2	Cell/Molecular Biology
Research Area 3	Physiology/Pharmacology

PI: Jay Hanan	**Project Title: Chemical Free Advanced Local Pesticide Validation System**
HR21-138	**Organization:** Oklahoma State University
Rank: 82	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	The UVC wavelength part of the UV spectrum is capable of inactivating or killing viruses and bacteria. This sanitization property has been widely used for UVC disinfection mainly in food and medical industries. During the pandemic involving COVID-19 some devices were developed utilizing UVC lamps or LED lights for air sanitization or purification. Although it is scientifically well accepted UVC, with enough exposure time can inactivate viruses. When it comes to the application of low power LED-UVC lights with short exposure times, there is not enough scientific research on effectiveness. The proposal aims to conduct scientific research to determine the minimum required combination range of intensity and exposure time to disinfect a typical virus and project that effective range for other similar virus types like SARS-CoV-2. This study is essential because in miniaturized or portable disinfecting devices there are many practical limits on total weight, battery life, ergonomics, and safety. All these limit possible exposure intensity and exposure time. The project aims to provide the necessary data to optimize and validate a new portable sterile air technology. Testing will be done on pathogens such as viruses to verify that they are inactivated through use of the ultra-violet radiation used within the device. The project will establish an innovative test method for UV-C LED exposure effectiveness on disinfecting viruses and airborne particles. Our preliminary study showed inactivation of 99.9% of microorganisms. This was from a small number of the tests. More statistical significance is needed for a science based development of medical devices. The outcome of the effectiveness of UV-C exposure on air sanitization from lab testing will be validated on a medical breathing aid device. The expectation is laboratory results will require several adaptations when utilized on the exposure chamber of air breathing devices. The sanitization VU-C chamber will be custom designed to take the most exposure power from the LED source and increase the residency of input air to be exposed beyond the necessary level required for complete cleaning of air from pathogens. The ultimate outcome of this research and teams effort with the help of OCAST is validation of an air cleaning technology for a portable device that can create a world where anyone, irrespective of respiratory condition, can travel anywhere safely without fear of contracting a harmful airborne virus or bacteria, simply because they need to breathe!
Research Area 1	Biomedical Engineering
Research Area 2	Infectious Disease
Research Area 3	Cell/Molecular Biology

PI: Xia Lei	**Project Title: Targeting CTRP for macrophage-based therapy in diabetes**
HR21-089	**Organization:** Oklahoma State University
Rank: 83	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Adipose macrophage infiltration has been shown to be highly associated with insulin resistance in obesity and diabetes. Recently, macrophages represent an attractive therapeutic target for the treatment of various diseases. To develop a novel macrophage-based therapy in diabetes, factors which are secreted from macrophages and are involved in the macrophage-adipocyte crosstalk need to be explored. C1q/TNF-related proteins (CTRP), a highly conserved family of 15 secreted proteins, has recently been found to play an important role in regulating the function of adipose tissue. Most of CTRP family members are expressed in adipose stromal cells. Furthermore, it has been reported that most of them are expressed in human peripheral blood mononuclear cells and mature macrophages, indicating their potential impact on adipocyte function. Our long-term goal is to study the regulation of CTRP family members in macrophage-adipocyte crosstalk. In our previous studies, we found genetic deletion of CTRP1 and CTRP9 increased insulin resistance, whereas the deletion of CTRP5 and CTRP6 improved insulin sensitivity in obese mouse models. The objective of this proposal is to understand the detailed mechanisms by which these CTRP family members communicate between macrophages and adipocytes and develop a potential therapeutic for insulin resistance. Therefore, we propose to utilize genetic tools (CRISPR/Cas9 system) to specifically activate CTRP1 or CTRP9 gene in macrophages and evaluate their effects on adipocyte insulin sensitivity in macrophage-adipocyte co-culture system, or knockout CTRP5 or CTRP6 gene and evaluate their effects on macrophage polarization, as well as to evaluate their effects on adipose tissue and whole-body insulin sensitivity via macrophage infusion in vivo. The program will be carried out in three specific aims: Aim 1, Determine the effect on adipocyte insulin sensitivity by macrophages with CTRP1 or CTRP9 activation; Aim 2, Determine the effect on macrophage polarization by knocking out CTRP5 or CTRP6 gene; Aim 3, Develop macrophage-based cell therapy to ameliorate insulin resistance. The proposed research is significant, because it will not only contribute to a fundamental understanding of the mechanisms underlying macrophage-adipocyte communication, but also lay the groundwork for the development of potential therapeutics for diabetes via infusion of genetically modified macrophages.
Research Area 1	Immunology
Research Area 2	Cell/Molecular Biology
Research Area 3	Physiology/Pharmacology

PI: Charles Rice	**Project Title: Correlating BPEI PEGylation with PAMP Neutralization**
HR21-104	**Organization:** University of Oklahoma
Rank: 84	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Innate immunity has considerable specificity and can discriminate between individual species of microbes. In this regard, pathogens are "seen" as dangerous to the host and elicit an inflammatory response capable of destroying the microbes. This immune discrimination is achieved through the recognition of microbe-specific molecules (e.g., lipopolysaccharide, lipoteichoic acid, and peptidoglycan) by toll-like receptors on host cells. Lipopolysaccharide, lipoteichoic acid, and peptidoglycan arising from dangerous bacteria are known as Pathogen-Associated Molecular Pattern (PAMP) molecules. PAMPs impede wound healing by lengthening the inflammatory phase of healing and contributing to the development of chronic wounds. Preventing PAMPs from triggering the release of inflammatory cytokines will restore the optimal inflammatory response. However, successful drugs are elusive because PAMPs originate from many different species of Gram-negative and Gram-positive bacteria. Therefore, the need exists for a universal broad-spectrum therapeutic against LPS, LTA, and PGN bacterial PAMPs.The objective of this project is to correlate PEGylation of 600 Da BPEI with its anti-PAMP properties. The central hypothesis is that increased steric effects from PEGylating 600 Da BPEI improves the neutralization of PAMPs. We will test our central hypothesis with the following specific aims: Aim 1: Correlate PEGylation with PAMP binding affinity; Aim 2: Correlate PEGylation with inhibiting PRR activation. Data arising from these aims will be significant because they are expected to provide strong scientific justification for the continued development of anti-inflammatory agents applied to acute and chronic wounds. This project has added significance because the data will be used to evaluate the strategy of using this agent to bind bacterial PAMPs and prevent cytokine release; a strategy that enables other subsequent research and thinking. The proposed work is innovative because we fill the technological gap with multi-purpose agents that disable PAMPs, dissolve biofilms, and overcome antibiotic resistance mechanisms, making them superior to existing technology. The rationale is that PEG-BPEI, as a universal agent to target PRR agonists, could combat inflammation and mitigate dysregulation of healing that is often observed in chronic wounds. This is based on published and preliminary data. We envision our discoveries as topical agents applied to acute and chronic wounds because, in addition to the active moiety of the agent preventing cytokine release, it also disables antibiotic resistance mechanisms and disrupts the biofilm matrix. This versatility of this agent suggests that it may be an ideal therapeutic agent for use in the hundreds of millions of non-chronic skin or soft-tissue infections (SSTIs), and the 4.5 million chronic wound infections, that occur each year.
Research Area 1	Infectious Disease
Research Area 2	Immunology
Research Area 3	Chemistry & Biochemistry

PI: Yujiang Xiang	**Project Title: Smart Linkage for Optimized Specific Upper-Limb Muscle Rehabilitation**
HR21-048	**Organization:** Oklahoma State University
Rank: 85	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	For stroke patients or patients with muscle injury, muscles partially or completely lose activations/responses. While many researchers investigate the science of stroke or muscle injury prevention, others develop methods for muscle rehabilitation. Over time, recovery is common among these patients. One method of making rehabilitation more effective for the patient is to use robotic devices. These can increase the number of repetitive training exercises that a therapist could use during rehabilitation. There are two types of rehabilitation robots on the market: end-effector type and exoskeleton type. Both require complicated control, and the cost of these devices is high. This project will build a portable, low-cost, and easy-to-use four-bar linkage end-effector rehabilitation robot for specific upper-limb muscle rehabilitation. The basic idea is to move the arm through the guiding coupler point trajectory to exercise specific muscle groups. A real-time human-in-the-loop simulation will be developed to optimize the four-bar linkage driving torque, speed, and link lengths for best muscle exercise. Both passive and active rehabilitation modes are built in the system. Prototypes will be constructed to test the proposed rehabilitation device, design, and control methods.
Research Area 1	Biomedical Engineering
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Physiology/Pharmacology

PI: Wei Yue	**Project Title: Regulation of OATP1B1 and OATP1B3 by lysine acetylation and lysine deacetylase inhibitors**
HR21-128	**Organization:** University of Oklahoma Health Sciences Center
Rank: 86	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Organic anion transporting polypeptides (OATP) 1B1 and OATP1B3 (abbreviated as OATP1B1/3) are liver-specific drug transport proteins that mediate uptake, from blood into the liver, of a diverse array of endogenous compounds, environmental toxins, and many clinically important drugs (e.g., lipid-lowering statins, cardiac glycosides, antidiabetic and anticancer agents, antibiotics, immunosuppressants). OATP1B1/3 are important determinants of transport-mediated drug-drug interactions (DDIs) resulting in severe side effects, such as statin-induced rhabdomyolysis, a sometimes-fatal muscle toxicity. Dysfunction of OATP1B1/3 significantly contributes to altered drug disposition and adverse drug events. Our long-term goal is to delineate the molecular mechanisms underlying drug/toxin disposition through OATP1B1/3. Although it is evident that factors (drugs, aging, disease) modulating OATP1B1/3 function could cause drug-drug or drug-disease interactions with OATP1B1/3 substrates, unfortunately, our ability to predict such mechanism-based interactions is hampered due the dearth of information on OATP1B1/3 regulation. In particular, epigenetic regulation and protein-lysine acetylation, a major post-translational modification known to control function of numerous proteins, has not been investigated for OATP1B1/3. Our novel preliminary data show that OATP1B1 protein is lysine-acetylated at multiple residues; mutagenesis mimicking hyper-acetylation of OATP1B1 and treatment with inhibitors of lysine deacetylases (KDACs) reduce OATP1B1/3 transport function, supporting that lysine-acetylation is pivotal in regulating OATP1B1/3 function. The goal of this application is to determine the cellular and molecular mechanism(s) governing OATP1B1/3 regulation by lysine acetylation and by lysine deacetylase inhibitors. We propose to test the central hypothesis that OATP1B1/3 are lysine-modified and that transport function of OATP1B1/3 are regulated by KDACs. A combination of proteomics, biochemical, drug transport, and genetic engineering approaches will be utilized in cell lines and in the physiologically relevant sandwich-cultured primary human hepatocytes. The outcomes of these experiments will identify lysine-acetylation as a novel mechanism regulating OATP1B1/3 function. The knowledge gained from these studies will be invaluable toward the rational design of novel drugs and inhibitors to optimize drug therapy while avoiding unwanted drug interactions. This work will enhance our ability to predict altered OATP1B1/3 function by lysine-deacetylase modulators (e.g., drugs/candidates that are HDAC inhibitors/activators and liver disease states).
Research Area 1	Physiology/Pharmacology
Research Area 2	Cell/Molecular Biology
Research Area 3	Chemistry & Biochemistry

PI: Joe zhao	**Project Title: Effects of SARS-CoV-2 Spike Protein on Hematopoietic and Cardiovascular Systems**
HR21-160	**Organization:** OUHSC
Rank: 87	**Year 1:** $32,959 **Year 2:** $33,089 **Year 3:** $32,139 **Total:** $98,187
Research	The coronavirus disease COVID-19 is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 was initially considered as a pulmonary disease affecting the lung primarily but is now viewed as a general blood vessel condition causing symptoms throughout the body (1, 2). SARS-CoV-2 infects cells via its surface Spike (S) protein. Upon entry into host cells, it takes over the host's functions and produces viral proteins including S protein and viral RNA for virus replication. The virus-caused damages can be attributed to the functional activities of the expressed viral proteins and the adverse response of the host to the foreign proteins. Our preliminary study indicates that S protein can cause cell fusion when overexpressed in cultured cells. We thus hypothesize that expression of S protein is partly responsible for pathogenesis of SARS-CoV-2 and some side effects of DNA/RNA-based COVID-19 vaccines. In this study, we will employ mouse models to investigate how expression of S protein affects the hematopoietic and cardiovascular system in mice. We have generated various tools and reagents to carry out the study. This study will have major implications for understanding the long-lasting consequence of COVID-19 and the potential side effects of COVID-19 vaccines.
Research Area 1	Cell/Molecular Biology
Research Area 2	Infectious Disease
Research Area 3	Chemistry & Biochemistry

PI: Rittika Shamsuddin	**Project Title: Developing a Decision Support System Prototype for Predicting the Effect of Medicinal Addictive Drugs on Individuals**
HR21-056	**Organization:** Oklahoma State University
Rank: 88	**Year 1:** $44,804 **Year 2:** $41,036 **Year 3:** $42,311 **Total:** $128,151
Research	Medicinal addictive drugs, such as opioids and cannabinoids, are the solutions to complex ailments (such as chronic pain, cancer therapy, depression, etc.) that have plagued people for many years. Hence, many of these drugs (such as marijuana) are being legalized through the United States faster than it takes scientific research to produce conclusive studies about how these drugs can affect the individuals in this country. Also, different clinicians have different levels of training and experience and thus, will be influenced to different extents by external factors (such as pharmaceutical sales promotions) when prescribing a drug. Additionally, in places where there is a lack of clinical practitioners, such as rural Oklahoma, proper implementation of guidelines when prescribing medicinal addictive drugs can be questionable. These factors combined are creating a substantial portion of the general population, who i) have little understanding of how the medicinal addictive drugs can affect them, ii) are already predisposed to substance abuse even before a medicinal addictive drug is prescribed due to previous exposure, and iii) are being cared by clinical practitioners who rely heavily on pharmaceutical companies' advocacy of certain drugs. This is especially true for people in Oklahoma. This is supported by various national statistics and the occurrence of the opioid crisis. Thus, in this application we propose the development of a prototype for a clinical decision support system (DSS) that will quantify how an addictive substance will affect an individual patient (before the drug is prescribed), and notify clinicians about the potential individual risks accordingly. The DSS prototype, once developed, can be tested for deployment in real clinical settings through clinical trials, which we plan to fund via a subsequent NIH R01 grant. This prototype will be developed using interpretable machine learning (ML) techniques to aid clinicians describe the threats of substance abuse as it pertains to the specific individual, rather than just general cautions against drug abuse. The DSS will be developed in three stages. The first stage will develop a risk index that can quantify the severity and propensity of individuals to develop substance abuse based on their biological reactions to certain drugs. The second stage involves summarizing the background and medical history of the patients into low-dimensional, interpretable patient profiles that are easy to work with and understand. The final stage will experiment with deep learning prediction models, the patient profiles and the risk index to develop a candidate DSS that can then be implemented in real life clinical setting. To complete this project, we will collaborate with Oklahoma State University's Center for Health Systems Innovation to obtain the data and clinical expertise. Its completion will lead to healthcare innovations and further funding opportunities.
Research Area 1	Biomedical Engineering
Research Area 2	Biomedical Engineering
Research Area 3	Instrumentation/Data Sciences/Clinical Evaluation

PI: Meng Zhao	**Project Title: The role of mitochondrial redox signaling in iNKT cells**
HR21-140	**Organization:** Oklahoma Medical Research Foundation
Rank: 89	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	iNKT cells are a special group of T cells-a major type of white blood cells. iNKT cells are rapid responders during inflammation and infection, and play important roles in many pathological conditions. iNKT cells develop into three functional groups, NKT1, NKT2 and NKT17, which have different functions, and this represents an alternative mode of T cell development. We have discovered that one of these subgroups, NKT1 cells, have higher free radicals than other T cells, and we have evidence that suggest these free radicals come from mitochondria, the power plant of the cell. When expressed at the right time, place and amount, free radicals can be beneficial to the cells instead of causing damage. In this study, we will test if mitochondria-derived free radicals are important for iNKT cell development and functions. We will create new mouse models which have different levels of mitochondria-derived free radicals in T cells, low/intermediate/high, and examine the presence of iNKT cell subgroups and the response of iNKT cells after stimulation. We aim to identify free radicals as important byproduct from the energy production in mitochondria to regulate iNKT cells. If our hypothesis is correct, changing free radical levels can be a new strategy to promote or dampen NKT1 related functions as therapeutics.
Research Area 1	Immunology
Research Area 2	Chemistry & Biochemistry
Research Area 3	Physiology/Pharmacology

PI: Guoliang Fan	**Project Title: Motion Capture on-the-fly for Cognitive Load Assessment**
HR21-096	**Organization:** Oklahoma State University
Rank: 90	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	With the global aging of the worldwide population, there is no denying that AD/dementia will become a prevalent disease in the next few decades. Since AD/dementia patients exhibit a loss of independence, it greatly burdens the patients of course, but also their families and the entire healthcare system. Dementia-related healthcare costs were estimated at $290 billion in 2019 and are projected to reach $ 1.1 trillion in 2050. Like any degenerative disease, physical or cognitive, early detection is key in developing efficient protocols to early intervene or slow down the progression of the disease. However, there is still a critical need for robust and practical early detection protocols. Gait is a very common daily activity, but also a complex process and motor task that integrate a variety of sensory information and sophisticated cognitive functioning. Cognitive impairment, such as AD and other forms of dementia usually result in changes in gait behavior, even before it can be diagnosed through traditional neurological assessments. Recently, segmental accelerations have been correlated with dementia, as early as three years before the first positive neurological assessment. However, the data collection and processing techniques often used are labor-intensive and may not be applicable in a clinical setting. The overall objective of the project is to develop a novel method of ubiquitous gait analysis applicable outdoors or in a real-world setting and to quantify cognitive load by gait kinematics which is the key to find the early sign of cognitive impairment. Our core hypothesis is that the temporal variability of the ankle, knee, and hip joint ranges of motions exhibit a high enough discriminatory power to detect cognitive load while walking. The rationale is that these joints drive the whole-body kinematics and are directly related to traditional parameters such as stride length and swing time. Recent studies have also shown that the variability of gait parameters is more efficient at characterizing changes in gait behavior than average values. The innovation of the proposed project lies in two distinct aspects. First, for the first time, we will collect both indoor and outdoor kinematics data and assess the effect of real-life environment on the relationship between gait variability and different cognitive loads. Second, we will develop an innovative UAV (unmanned aerial vehicle or drone)-based motion capture system, called MOFLY, which will allow us to ubiquitously collect motion data in an outdoor or indoor environment. We expect that MOFLY can reveal and capture more informative gait changes related to cognitive load in a virtually unconstrained environment, compared with traditional gait analysis in a laboratory setting. The success of this project will lead to a portable and affordable gait-based cognitive load assessment system for early detection and risk assessment of AD and dementia.
Research Area 1	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 2	Biomedical Engineering
Research Area 3	Nutrition/Psychology/Public Health

PI: Susan Schroeder	**Project Title: Endogenous Retroviral RNA Expression in Influenza and COVID-19**
HR21-094	**Organization:** University of Oklahoma
Rank: 91	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	To be ready for the next pandemic virus, we need rapid diagnostics and effective therapies to manage the symptoms in severe cases. Immune dysregulation is the hallmark of severe cases of viral disease for COVID-19 and many upper respiratory viruses such as influenza. Factors such as smoking contribute to severe outcomes in viral respiratory diseases. Current diagnostics for COVID-19 indicate whether or not the RNA viral genome is present but do not indicate the probability of severe disease. This research will focus on understanding the biological basis for the combined effects of influenza infections and cigarette smoke and the concurrent expression of Human Endogenous Retroviral (HERV) RNA in the immune response. The hypothesis is that HERV RNA have a beneficial role in regulating the immune response and can serve as a biomarker for severe outcomes. HERV W RNA is expressed in response to COVID-19 and is a potential biomarker for severe outcomes. Our preliminary data suggest that HERV W RNA are overexpressed in influenza but less expressed in the combination of influenza infection and smoking. HERV RNA profiles are currently used as a diagnostic biomarker for cancer immunotherapy. We envision a COVID-19 assay that indicates not only whether the viral RNA genome is present but also whether RNA indicators of dysregulated immune responses are present and thus could predict the probability of a severe case. This information would be important for managing clinical resources in pandemic crises. It is not yet known why a variety of different HERV RNA types are expressed in different cell types in response to different stresses. We will first focus on HERV RNA in human bronchial epithelial cells in response to influenza and cigarette smoke extracts. We will use new nanopore sequencing technology to determine the changes in mRNA expression, splicing, and natural methylations that can affect protein binding. RNA nanopore sequencing is a single molecule method that provides direct detection of sequence-specific methylated RNA bases. The long nanopore sequencing reads eliminate any ambiguity about splicing isoforms. Both RNA methylation and splicing change in viral and host RNA during viral infections, and these changes regulate gene expression and the immune response. We will compare the results of our experiments with databases of RNASeq data, such as the Human Lung Cell Atlas and the COVID-19 Cell Atlas. This project will be pursued in collaboration with the Metcalf lab at University of Oklahoma Health Sciences Center and the sequencing centers on the Norman campus and the Oklahoma Medical Research Foundation. The successful completion of the project will provide insight into the role of HERV RNA in the innate immune response. The project will provide basic science research on viral RNA and help train the future workforce in biotechnology in Oklahoma so that Oklahoma remains ready to respond to viral outbreaks.
Research Area 1	Genomics & Gene Expression
Research Area 2	Infectious Disease
Research Area 3	Chemistry & Biochemistry

PI: Sundararajan Madihally	**Project Title: 3D Printed Drug Release on Cell-Based Tissue Model**
HR21-084	**Organization:** Oklahoma State University
Rank: 92	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	National Cancer Institute (NCI) statistics show that cancer causes significant death in the United States. Although chemotherapeutic agents such as Doxorubicin have been used, they have significant side effects. We hypothesize that a combination of low quantities of directed delivery of molecules with controlled-release induces higher cell death while minimizing side effects. We will test the hypothesis using i) novel 3D bioprinting to deliver doxorubicin or resveratrol, ii) co-axial electrospinning using poly(e-caprolactone) (PCL) and gelatin (GT) to deliver resveratrol/doxorubicin, and iii) Holo-transferrin derivatized PEG-liposome nanoparticles for targeted siRNA and monoclonal antibody delivery. We want to explore these systems in two cell types: 1) non-adherent K562 cells (derived from chronic myelogenous leukemia), and ii) adherent MCF-7 cells breast cancer cells. Our goal is to understand i) selective depletion of cancer cells with intact vasculature and ii) how adhesion of cells alters the release rate. Developments in three-dimensional (3D) cultures show that 3D space regulates localization and concentration of a variety of signals with the entire cell surface, similar to the in vivo environment. Using novel chitosan-gelatin (C-GT) based injectable hydrogel formulations and bioprinting, we will fabricate in vitro 3D cancer tissue using MCF-7 cells and endothelial cells. Our goal is to compare the two approaches in building a 0.5mm thick tissue. Our preliminary results show that the proposed activities are feasible. The knowledge derived from this proposal will be of broad significance to many areas of medicine and biomedical sciences. Reduction in dosage of doxorubicin will have a direct impact on clinical treatment. Our investigation into the role of vascularized 3D culture models will have a significant impact on future studies related to cellular behavior. Since bioprinting is a novel automated approach, it holds great promise for the mass production of 3D tissue constructs in a scalable and reproducible manner. Screening drugs on such 3D platforms greatly enhances the understanding of drug action, mimicking what could happen in the human body.
Research Area 1	Biomedical Engineering
Research Area 2	Physiology/Pharmacology
Research Area 3	Cancer Research

PI: Randy Morgenstein	**Project Title: The intersection of cell shape, size and metabolism**
HR21-059	**Organization:** Oklahoma State University
Rank: 93	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	A fundamental question in cell biology is how cell shape is achieved. This is important for cells of all size scales, as human cells and many bacteria come in a variety of shapes and sizes that are important for their function. For some bacterial pathogens, cell shape has been linked to pathogenicity, yet there is still much to be learned about how cells regulate their shape and the role that this has on virulence. Therefore, the way that bacteria control their shape is important for human health from a variety of angles. Escherichia coli provides an ideal model organism to study cell shape control given that it is genetically tractable, has functional fluorescent fusion proteins to many proteins, and can be imaged in high numbers to provide statistically relevant information. The broad goals of this work are to: 1) determine the cross talk between cell elongation and division machineries, 2) understand the role of central carbon and cysteine metabolism in cell shape, and 3) use quantitative biochemical, biophysical, and microscopy techniques to understand the effects of gene knockdowns and suppressors on the cell. We expect to uncover universal cell shape control mechanisms that can provide inferences into novel drug development and can be used to modify the shapes of pathogens to render them less virulent.
Research Area 1	Infectious Disease
Research Area 2	Cell/Molecular Biology
Research Area 3	Genomics & Gene Expression

PI: Emily Roberts	**Project Title: Assistive Technology Interventions for Dementia Homecare Environments**
HR21-029	**Organization:** Oklahoma State University
Rank: 94	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	This research builds on previous work in the development of an innovative assistive technology in response to increasingly significant homecare issues facing individuals with dementia and their family caregivers. In the United States, 5.5 million Americans have Alzheimer's disease or some form of dementia and by mid-century, the number of people living with dementia in the United States is projected to grow to 13.8 million. About half of the persons with dementia currently live at home, 43% require occasional support, 47% daily support, and 10% continuous support; with most of this support provided by informal family caregivers who often experience what has been called the "unexpected career of caregiver", facing multi-faceted, complex, and stressful life situations. Caregivers face on-going significant risk throughout the ebb and flow of providing care as individuals with dementia may lose grasp of their understanding of their circumstances, relying heavily on caregivers for all aspects of their physical and emotional support, as well as prompting and cueing through instrumental activities of daily living (IADLs) such as meal preparation, housekeeping, laundry and dressing. This level of care can be intense and physically demanding and the effects of being a family caregiver across the trajectory of care may result in high rates of burden and psychological morbidity, as well as social isolation, physical ill-health and financial hardship for caregivers. In addition, individuals with various degrees of cognitive decline may experience very different needs through a day or in a different setting. This highly personalized set of needs requires a flexible and versatile approach that can be customized and adapted for each individual in a specific setting. Other smart-home/smart-environment technologies and tools of specific functionalities partially address those challenges, however, there is currently a lack of low-cost, portable, versatile and programmable tools that can relieve the physical and emotion burden from caregivers by automatically providing timely, needed and individualized IADL cueing to care recipients throughout the homecare environment. This project will test the context, delivery and interface of a wearable assistive technology for navigation and cueing for individuals living with dementia in their home which will be programmable by their caregiver.
Research Area 1	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 2	Neurobiology
Research Area 3	Nutrition/Psychology/Public Health

PI: Vijay Somalinga	**Project Title: Deciphering metabolic pathways utilized by Streptococcus sanguinis during blood dissemination and endocardial growth: Roles of SSA_2154 (carbonic anhydrase), SSA_0809 (enamine deaminase) and SSA_0908 (substrate binding protein).**
HR21-157	**Organization:** Southwestern Oklahoma State University
Rank: 95	**Year 1:** $42,249 **Year 2:** $44,346 **Year 3:** $42,673 **Total:** $129,268
Research	Streptococcus sanguinis is one of the leading cause of subacute infective endocarditis in susceptible population. High mortality rates, the emergence of antibiotic resistance and the lack of clear knowledge of how S. sanguinis persists in blood during bacteremia and endocardial growth has warranted studies to better understand the metabolic pathways employed by this pathogen during infection process. Although numerous studies have focused on virulence factors required for adherence, colonization and biofilm formation, studies involving metabolic pathways essential for S. sanguinis mediated bacteremia and endocardial growth is lacking. Previous studies in other pathogens have shown that nucleotides are limiting in blood and organisms should de novo synthesize nucleotides to survive in blood. Purine and pyrimidine biosynthesis requires the activity of carboxylases that are dependent on bicarbonate for its activity. Bicarbonate to CO2 interconversion in a cell is carried out by an important enzyme, carbonic anhydrase (CA). In addition to providing bicarbonate to important carboxylases, several studies have shown that bacterial CA's play an important role in pathogenesis. We recently identified and partially characterized SSA_2154, a ß-CA from S. sanguinis. We suspect that SSA_2154 may play an important role in the growth and persistence of S. sanguinis during infection process. Studies have shown that bacteria also rely on amino acid catabolism during infection process. S. sanguinis genome sequencing has revealed the absence of genes required for the synthesis of several amino acids including tryptophan. We recently identified a substrate binding protein, SSA_0908 with homology to proteins involved in aromatic amino acid transport. Sequence analysis and homology modeling studies revealed that SSA_0908 may be involved in binding and transport of aromatic amino acid in S. sanguinis. Amino acid catabolism results in the production of toxic enamine/imine/aminoacrylate intermediates which are detoxified by a class of enzymes known as enamine deaminases. Given the importance of amino acid uptake and catabolism in S. sanguinis, we mined the genome of S. sanguinis for enamine deaminase using a well-characterized homolog from C. jejuni and identified SSA_0809 with sequence and structural homology to other well characterized enamine deaminases. We have already demonstrated the preliminary deaminase activity and identified preliminary crystallization conditions for SSA_0809. The proposed study will be the first to delinate the roles of SSA_2154, SSA_0908 and SSA_0809 in the physiology of S. sanguinis. To our knowledge, we are the first group to identify the presence of enamine deaminase homolog in S. sanguinis, and to show that the homolog is capable of enamine deaminase activity. Our preliminary study opens up new avenues to further characterize the role this protein plays in S. sanguinis.
Research Area 1	Infectious Disease
Research Area 2	Chemistry & Biochemistry
Research Area 3	Cell/Molecular Biology

PI: Ratnakar Deole	**Project Title: Characterization of lactic acid bacterial isolates showing antimicrobial activity against food pathogens.**
HR21-159	**Organization:** Oklahoma State University-Center for Health Sciences
Rank: 96	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Alternative intervention strategies for fighting bacterial pathogens is extremely important due to the rise in their multidrug resistant forms, imposing a serious problem to public health. Antimicrobial resistance is associated with misuse of antibiotics which may side/toxic effects not only to the host but also reduce/eliminate natural microflora associated with the host. Use of probiotics (beneficial microorganism) is a popular approach to mitigate the problem. Most probiotics belong to the order of lactic acid bacteria (LAB). LAB have the potential to provide significant health benefits such as antibacterial activity against pathogens, causing improvement in lactose metabolism, anti-mutagenic properties, anti-carcinogenic properties, reduction in serum cholesterol, anti-diarrheal properties, immune system stimulation and improvement in inflammatory bowel disease. There are specific criteria for determining which organisms are probiotic; the safety of the microbe in question and its viability and metabolic activity within the human digestive tract are important concerns. Some LAB produce gene-encoded inhibitory proteins called bacteriocins, that have varying inhibitory spectra and these properties allow for the development of applications towards roles in food safety or preventing spoilage. The PI of this project has isolated twelve LAB isolates from organic produce. These isolates show promise as probiotic candidates as their cell free extracts show antibacterial activity against both or one the food pathogens Salmonella enterica ATCC 25566 and Listeria monocytogenes ATCC 19116. The objective of the project is to analyze the genomic characteristics that influence beneficial traits and outcomes of the probiotic cultures. Analyze the factors that dictate survival, colonization, and beneficial interactions with the human host which will facilitate substantiation of the probiotic characteristics.
Research Area 1	Infectious Disease
Research Area 2	Genomics & Gene Expression
Research Area 3	Physiology/Pharmacology

PI: Jameca Price	**Project Title: A Novel Urine Biomarker to Identify Bladder Infections in Pregnant and Non-Pregnant Women**
HR21-116	**Organization:** Board of Regents of the Univ. of OK Health Sci. Center
Rank: 97	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Bladder infections are among the most common human diseases, and large numbers of urine specimens are processed daily in clinical microbiology laboratories. The majority of test results are negative, leaving positive specimens for further processing. Most such tests are relatively simple and reliable but require an overnight incubation of cultures before results are available. An additional rapid screening test would be advantageous if it greatly reduced preterm labor caused by late diagnosed bladder infections in addition to the time spent on specimens. The detection of elevated urine Neutrophil gelatinase associated lipocalin (NGAL) levels may aid in diagnosing a bladder infection. A rapid report of results leading to UTI diagnosis would be useful to the physician and patients to avoid unnecessary therapy. We consider that another marker for rapid and accurate diagnosis of a bladder infection would be valuable for early initiation of treatment in women with suspected bladder infections pending urine culture result. The goal of the study is to determine if urine NGAL levels can be used as an appropriate biomarker to detect a bladder infection in adult women including pregnant and non-pregnant prior to having positive urine culture results.
Research Area 1	Infectious Disease
Research Area 2	Instrumentation/Data Sciences/Clinical Evaluation
Research Area 3	Chemistry & Biochemistry

PI: Kelly E. Allen	**Project Title: Mechanical transmission of Trypanosoma cruzi by brown dog ticks**
HR21-070	**Organization:** Oklahoma State University
Rank: 98	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Trypansoma cruzi is the kissing bug-borne parasite causing Chagas disease in people living in the Americas. An estimated 6 million people are infected. Chagas disease is a lifelong condition which affects the heart and sometimes the digestive system. Approximately 30% of infected people will die from the disease; 1.5 million people are currently suffering from associated cardiac complications. Dogs are considered reservoirs of infection for kissing bugs in Latin America. The role of dogs as reservoirs of infection in the United States is not understood, but locally acquired canine Chagas cases are well described in southern regions. In the U.S., there are an estimated 300,000 people infected with T. cruzi based on presence of antibodies (indicating exposure) in blood donors. However, Chagas disease is often insidious and may go undiagnosed and therefore prevalence estimations may be low. Chagas disease in the U.S. is considered a neglected tropical infection by The Centers for Disease Control and Prevention (CDC). Brown dog ticks are a common tick species that are notorious for establishing in-home infestations. As ticks feed, they concentrate blood meal by regurgitating excess fluid back into the host. Brown dog ticks are known to move between hosts and blood-feed intermittently. The tick group preferentially feeds on dogs, but is documented to feed on and transmit pathogens to humans. It is not known if intermittently feeding brown dog ticks can acquire T. cruzi from infected dogs and mechanically transmit the blood-borne parasite to other dogs and possibly humans. Mechanical propagation of T. cruzi among dogs in endemic areas would serve to increase populations of canine reservoirs available to kissing bug vectors, thus amplifying the number of kissing bugs in the environment. As a consequence, the risk of T. cruzi transmission to humans in the area increases. Thus, there is a critical need to fill this knowledge gap and empirically examine the potential role of this tick group in the epidemiology of Chagas disease to better protect human health. The first aim of the proposed work is to investigate proportions of adult brown dog ticks which are PCR positive for T. cruzi after partially feeding on experimentally infected guinea pigs (to mimic intermittent feeding on infected dogs). The second aim is to determine if ticks partially fed on guinea pigs with T. cruzi infections mechanically transmit the parasite to uninfected recipient guinea pigs after infestation. The third aim is to assess temporary viability of T. cruzi within brown dog ticks by demonstrating growth of the parasite from partially fed ticks in culture medium. Insecticidal treatments targeting kissing bugs are not effective against ticks. Adequate tick control requires the use of acaricidal compounds. As a consequence of this work, I expect to identify brown dog ticks as mechanical vectors of T. cruzi that serve to amplify infected kissing populations in Chagas endemic areas.
Research Area 1	Infectious Disease
Research Area 2	Cell/Molecular Biology
Research Area 3	Infectious Disease

PI: Adel Pezeshki	**Project Title: Role of mTOR/IGF-I and gut microbiome in isoleucine and valine induced growth in piglet model of small for gestational age infants**
HR21-154	**Organization:** Oklahoma State University
Rank: 99	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $45,000 **Total:** $135,000
Research	Impaired development of a fetus during pregnancy results in low birth weight (LBW) with developed growth disabilities in early life, which is associated with long-term health issues such as obesity and cardiovascular diseases. The overall objective of the proposed research is to gain insights into the underlying mechanisms of action of diets with partially replaced protein with isoleucine (Ile) and valine (Val) in postnatal growth of small for gestational age (SGA) infants. The rationale for replacing part of protein with Ile and Val include: 1) there is likely a link between high protein consumption and complications such increased urea nitrogen and acidosis and obesity in SGA infants, 2) LBW neonates have lower levels of branched-chain amino acids (BCAA), 3) among BCAA, leucine (Leu) has been considered as the main AA associated with "early protein hypothesis", and 4) Ile and Val have less insulinogenic index than Leu and both can supply energy after being oxidized. Insulin-like growth factor I (IGF-I) is down-regulated and gut microbiota colonization is modified in SGA infants. The effect of AA on IGF-I is believed to be mediated through activation of hepatic mammalian target of rapamycin (mTOR). While there is compelling evidence on the important role of IGF-I and large intestine microbiota in regulation of growth in neonates, it is unknown whether hepatic mTOR/IGF-I signaling and large gut microbiome are regulating the Ile/Val induced growth in LBW infants. Based on strong preliminary data from our laboratory, we hypothesize that higher Ile/Val to Leu ratio improves the growth of SGA infants through enhanced hepatic mTOR/IGF-I signaling and alterations in large gut microbiota composition. We will test this hypothesis with the following aims: 1) to determine the role of hepatic mTOR/IGF-I signaling in regulation of Ile/Val induced growth in piglet model of SGA infants, 2) to determine the role of large intestine microbiota in regulation of Ile/Val induced growth by depletion of large intestine microbiota in piglet model of SGA infants. Using protocols established by our team, we will determine the growth rate, bone growth, hepatic mTOR/IGF-I signaling, fecal microbiota, BCAA transporters, catabolic enzymes and metabolites, blood metabolomics and gut development in LBW neonatal piglets for 3 weeks. The approach is innovative because for the first time, using a unique piglet model of SGA, the engagement of hepatic mTOR/IGF-I signaling and large intestine microbiota in regulation of bone growth by altering dietary Ile and Val will be assessed. The proposed project is expected to provide novel information on our understanding of how nutrition of Ile and Val can improve the postnatal life in SGA infants. This knowledge will lead us to optimize the nutritional needs of LBW infants. LBW has been a growing threat in Oklahoma and the results of this project will have a potential to significantly improve the health care for Oklahoma citizens.
Research Area 1	Nutrition/Psychology/Public Health
Research Area 2	Physiology/Pharmacology
Research Area 3	Chemistry & Biochemistry

PI: Franklin R. Champlin	**Project Title: Characterization of Genes Associated with Resistance to Hydrophobic Antibacterial Agents and Biofilm Formation in Nosocomial Species of the Genus Serratia**
HR21-133	**Organization:** Oklahoma State University Center for Health Sciences
Rank: 100	**Year 1:** $45,000 **Year 2:** $45,000 **Year 3:** $0 **Total:** $90,000
Research	Certain members of the gram-negative genus Serratia are capable of causing opportunistic infections, hence are particularly important pathogens in nosocomial settings. While a considerable amount of research has been focused on Serratia marcescens, an overall paucity of work has been published regarding the cellular and molecular mechanisms which underlie the major virulence factors of members of this genus. Work in our laboratory has emphasized investigations of the physiological interactions between their cell envelopes and hydrophobic substances. We have determined that many of these opportunistic pathogens are resistant to the hydrophobic biocide triclosan, and the proposed research will examine expression profiles for selected genes affected by triclosan treatment. Solid surfaces are often hydrophobic, and this proposal also examines biofilm formation, which requires initial hydrophobic adhesion between the bacterial cell and solid substrate surfaces. While observations of biofilm formation have been published for S. marcescens and Serratia liquefaciens, very little basic research has been conducted which relates outer cell envelope properties to the ability to opportunistically infect host tissues. Nosocomial infections may be potentiated by biofilm formation which protects the bacteria from the deleterious effects of antibacterial agents and host immune system components. The purpose of the present research is to obtain a better understanding of how outer membrane impermeability for hydrophobic molecules, cell surface hydrophobicity properties, and the expression of targeted genes contribute to the pathogenicity of opportunistic Serratia species in susceptible human populations. The propensities of 10 disparate opportunistically infectious Serratia species to form in vitro biofilms will first be determined within the context of cell envelope properties affecting adhesion and maturation. Comparative genomic and transposon insertion analyses will be employed to identify target genes in order to better understand characteristics which contribute to cell surface association and adhesion properties for hydrophobic substances.
Research Area 1	Infectious Disease
Research Area 2	Cell/Molecular Biology
Research Area 3	Genomics & Gene Expression

PI: John E. Gustafson	Project Title: Novel Gram-negative antibiotic resistance mechanism			
HR21-014	**Organization:** Department of Biochemistry and Molecular Biology, Oklahoma State University			
Rank: 101	**Year 1:** $43,938	**Year 2:** $44,938	**Year 3:** $0	**Total:** $88,876
Research	The cell envelope of Gram-negative bacteria includes an outer membrane (OM) which forms a barrier that controls the uptake and efflux of antimicrobials. The diffusion of relatively large antibiotics (e.g. vancomycin) is prevented by the OM, making these drugs ineffective for the treatment of most Gram-negative infections. The Elizabethkingia are opportunistic Gram-negative pathogens that express an intrinsic multiple antibiotic resistance mechanism which has not been investigated. Compared to other Gram-negatives, the Elizabethkingia demonstrate relatively low vancomycin MICs and this drug has been used to treat Elizabethkingia infections. We isolated vancomycin-resistant (VR) mutants of Elizabethkingia anophelis which also demonstrated multidrug reduced-susceptibility. We revealed that this mechanism is due to a single mutation in a gene ("vancomycin susceptibility regulator" or vsr) that encodes a PadR DNA-binding protein, that leads to increased expression of the putative vsr-orf551 operon. orf551 encodes a 551 aa protein with 5 transmembrane regions and an internal phage shock protein C conserved module. The phage shock protein system is thought to detect and mitigate problems that alter inner membrane permeability. padR and phage shock protein C genes are widely distributed among Gram-negative pathogens, yet they have not been linked to antibiotic resistance until now. The overall goal of our research is to investigate the mechanism by which VR mutants express vancomycin resistance and multidrug reduced susceptibility. We intend to determine if the vsr-mutation leads to alterations in physiological parameters that can directly influence antibiotic susceptibility, such as: antimicrobial accumulation, outer membrane structure, cell surface hydrophobicity, and the proteome of membranes. We hypothesize that VR mutants will demonstrate a reduction in antimicrobial accumulation and altered membrane protein content that allows antibiotics to enter the cell and that pump antimicrobials out of the cell. We also hypothesize that we will find increased ORF551 concentrations in a membrane of VR mutants, which would indicate that this uncharacterized protein plays a role in cell membrane physiology. The research proposed will identify the physiological alterations that support a novel antibiotic resistance/reduced susceptibility mechanism based on two genes not previously associated with antibiotic resistance in Gram-negative organisms.			
Research Area 1	Infectious Disease			
Research Area 2	Genomics & Gene Expression			
Research Area 3	Chemistry & Biochemistry			

PI: Caio Martinelle Barbalho de França	Project Title: Genome Epidemiology of COVID-19 in Oklahoma			
HR21-181	**Organization:** Southern Nazarene University			
Rank: 102	**Year 1:** $45,000	**Year 2:** $45,000	**Year 3:** $45,000	**Total:** $135,000

Research	The state of Oklahoma has a large rural population (~34%), a strained healthcare system, and poor overall health. As of this writing there are only 394 sequences available via GISAID EpiCov (https://www.epicov.org/) corresponding to the state of Oklahoma. To increase sequence surveillance on the SARS-COV-2 virus within Oklahoma, and specifically in our underserved populations, we are proposing a large-scale effort entitled Genomic Epidemiological Surveillance of COVID-19 in Oklahoma (GESCO). In this proposal we leverage the testing capacity of two large established SARS-COV-2 surveillance programs to ascertain the presence of different viral variants within the population of Oklahoma. First, we will leverage our partnership with the Oklahoma Shared Clinical and Translational Resources (OSCTR), and their RADxUP initiative entitled Community Engaged Approaches to Testing in Community and Healthcare settings (CATCH-UP). This will enable us to perform sequencing surveillance in predominantly rural areas and in marginalized populations that are currently underserved in testing capacity. Second, our partnership with IMMYLabs will allow us to leverage the capacity of this large-scale testing provider to achieve greater sample sizes. These two partnerships will allow us to direct the majority of our funding to sequencing samples that have already been shown to be positive for SARS-COV-2 by an FDA approved test; we will not need to fund any testing for SARS-COV-2 from this grant. We plan to sequence 1200 viral genomes by the end of GESCO which will increase the sequences available from the state of Oklahoma by over three-fold.
Research Area 1	Infectious Disease
Research Area 2	Genomics & Gene Expression
Research Area 3	Chemistry & Biochemistry

OCAST Health Research Postdoctoral Fellowship Applications Approved for Funding Below the Funding Line

Rank	Application Number and Title	Organization & PI	Year 1 Request	Year 2 Request	Total Request
4	HF21-040: Role of FBW7 in Autosomal dominant polycystic kidney disease (ADPKD)	University of Oklahoma Health Science Center Leonidas Tsiokas			
			$75,000	$75,000	$150,000
5	HF21-032: Targeting immunometabolism to combat Clostridioides difficile gastrointestinal infection	University of Oklahoma Health Sciences Center Lauren A. Zenewicz			
			$75,000	$75,000	$150,000
6	HF21-039: Cerebrovascular mechanisms of long-term cognitive decline in breast cancer patients following chemotherapy	Oklahoma University College of Medicine, Department of Biochemistry & Molecular Biology Zoltan Ungvari			
			$74,278	$73,978	$148,256
7	HF21-011: Mechanisms of PROX1 in Heart Valve Disease	Oklahoma Medical Research Foundation Sathish Srinivasan			
			$75,000	$75,000	$150,000
	Totals		**$299,278**	**$298,978**	**$598,256**

2021 OCAST Health Research Postdoctoral Fellowship Applications Not Approved for Funding

Application No.	Organization	PI	Title
HF21-018	University of Oklahoma Health Sciences Center	Arlan Richardson	Role of necroptosis-induced neuroinflammation in Alzheimer's disease
HF21-037	University of Oklahoma Health Sciences Center	Martin-Paul Agbaga	Essential Role of Very Long Chain Saturated Fatty Acids in Synaptic Function
HF21-024	The University of Oklahoma Health Sciences Center	Michael Stout	Unraveling mechanisms by which estrogens and their receptors modulate liver fibrosis in male mammals
HF21-036	University of Oklahoma	Chenkai Dai	Investigating atraumatic effect of cochlear implant on the vestibular function
HF21-035	University of Oklahoma	Luca Fornelli	Elucidating the role of apolipoprotein E in cardiovascular and neurodegenerative diseases among Oklahoma's ethnic populations
HF21-022	Oklahoma Medical Research Foundation	Lijun Xia	Role of sialylation in maintaining mucus layer and protection from colitis
HF21-010	University of Oklahoma Health Sciences Center	Carol F. Webb	Functions of ARID3a in Naïve B Cells
HF21-013	Oklahoma Medical Research Foundation	Lorin Olson	Spatial and Temporal Mapping of Active PDGFR Signaling in vivo
HF21-007	Oklahoma Medical Research Foundation	Courtney Griffin	Paracrine and Autocrine Roles for Endothelial Chromatin Remodeling Enzymes in Promoting Lung Development
HF21-006	Oklahoma Medical Research Foundation	Chi Fung Lee	Role of mitochondrial dysfunction in the generation of cardiac arrhythmias
HF21-015	University of Oklahoma Health Sciences Center	Bethany Hannafon	Targeting DCLK1 in Platinum-Resistant Ovarian Cancer
HF21-033	Board of Regents of the University of Oklahoma Health Sciences Center	John Kimble Frazer	Correlating MYC-driven replication timing and transcriptional aberrations in ALL subtypes
HF21-005	University of Oklahoma Health Sciences Center	Blaine Mooers	Structure-based drug design targeting RNA editing substrates
HF21-008	Oklahoma State University	Matthew Cabeen	Critical steps in glycerol catabolism in Pseudomonas aeruginosa
HF21-020	Oklahoma State University Center for Health Sciences	Alicia Ford	Cognition and biomarker outcomes in treatment for opioid use disorder
HF21-030	Oklahoma State University Center for Health Sciences	Randall L. Davis	Transcriptional programming and behavioral signatures of maternal prenatal emotional stress

PI: Deepa Sathyaseelan	**Title:** Understanding the role of necroptosis in hepatocellular carcinoma
HF21-009	**Organization:** University of Oklahoma Health Sciences Center
Rank: 1	**Year 1:** $75,000 **Year 2:** $75,000 **Total:** $150,000
Research	Hepatocellular carcinoma (HCC), the major form of liver cancer, is the fourth leading cause of cancer-related deaths worldwide. In recent years, obesity has emerged as the major risk factor for HCC. HCC is predicted to be the third leading cause of cancer-related deaths in the United States by 2030 due to obesity epidemic. Obesity leads to fatty liver (nonalcoholic fatty liver disease, NAFLD) characterized by excess accumulation of fat in the liver. NAFLD that affects nearly 25% of the US population is a key driver of HCC in obese individuals. NAFLD eventually progresses to nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and ultimately to HCC in 2 to 13% of the individuals with NAFLD. Despite this strong association between obesity-induced chronic liver disease and HCC, the mechanism(s) that drive HCC development in obesity is not clearly understood. Studies have shown that inflammation is a major contributor to the development and progression of HCC in obesity. Necroptosis is a programmed cell death pathway that has been shown to play a major role in inflammation. In this application, we propose that inflammation due to necroptosis in liver cells (hepatocytes) is a major driver of NAFLD-HCC progression in obesity. Therefore, we will test the hypothesis that blocking/reducing necroptosis generally or specifically in hepatocytes will reduce inflammation and the progression of NAFLD to HCC. This hypothesis will be tested using genetic and pharmacologic approaches to inhibit necroptosis globally or in hepatocytes and assess its effect on inflammation and HCC progression in mice fed a western diet (WD) that is known to cause obesity and HCC. The proposed study will determine if inflammation induced by necroptosis is involved in obesity-mediated HCC and identify the role of hepatocyte necroptosis in NAFLD-HCC progression. If successful, the study is translationally relevant because pharmacological agents are currently available that inhibit necroptosis and could potentially be used to treat/prevent HCC progression in obesity.
Research Area	**Cancer Research**

PI: Benjamin F Miller	**Title:** Tapping into myonuclei for muscle regrowth after atrophy
HF21-023	**Organization:** Oklahoma Medical Research Foundation
Rank: 2	**Year 1:** $74,643 **Year 2:** $74,905 **Total:** $149,548
Research	The population of people 60 years and older in Oklahoma is projected to increase 27.6% by 2030, which is a growth rate almost 3x faster than the general population. A consequence of aging is the loss of muscle mass and function (sarcopenia), which increases morbidity and mortality. The gradual loss of muscle mass and function is accelerated by periods of disuse, such as extended bed rest or limb immobilization. Unfortunately, there are no effective therapies to help aged muscle completely regain mass/function after a period of disuse. Satellite cells (SCs), skeletal muscle stem cells, are necessary for postnatal growth and muscle regeneration, but their role in muscle regrowth following an atrophic stimulus remains unclear. It is thought that SCs fuse into myofibers to replace myonuclei lost via apoptosis during disuse atrophy to maintain the myonuclear domain. Myonuclei are believed to be post-mitotic, arrested in the G0 phase of the cell cycle, and thus unable to proliferate. However, several studies from our lab and others suggest that under certain conditions, myonuclei can replicate. This myonuclear replicative potential could represent an alternative to stem cell therapy, which has not been successful so far in atrophied muscle, to facilitate regrowth after disuse atrophy. The goal of the current proposal is to determine whether myonuclear replication occurs in the absence of SCs, thus becoming a target for treatment to support regrowth in older individuals. The central hypotheses are that: 1) the absence of SCs unmask the ability of resident myonuclei to replicate during reloading (RE) after a period of disuse atrophy, and that 2) SC ablation will not impede ribosomal biogenesis during RE after disuse atrophy. To address this question, we will use an innovative mouse model, the Pax7-DTA; HSA-GFP mouse. This mouse uses tamoxifen (TAM) treatment to ablate SCs (Pax7-DTA), and doxycycline (DOX) treatment for temporal labeling (Tet-ON) of myonuclei (HSA-GFP). When combined with our stable isotope (D2O) labeling of DNA, RNA, and ribosomal proteins, we can unambiguously determine myonuclear replication and ribosomal biogenesis. This highly innovative project will determine if myonuclear replication is a previously untargeted mechanism to facilitate regrowth after a period of disuse and form the basis for future studies targeting muscle regrowth in aged muscle.
Research Area	**Cell/Molecular Biology**

PI: Javier A. Jo	**Title:** Label-free morphological, metabolic and biochemical imaging system for surgical tumor margin assessment		
HF21-021	**Organization:** The University of Oklahoma		
Rank: 3	**Year 1:** $75,000	**Year 2:** $75,000	**Total:** $150,000
Research	The chances of dying from oral cancer are quite high in great part because it is extremely difficult to find and remove all the cancerous tissue during surgery. The surgeon is limited to visual inspection and palpation when attempting to detect all the cancer from the patient's oral cavity; thus, new technologies that would facilitate locating all the oral cancer during surgery are urgently needed. In this project, we will design, build and test new imaging tools that can be used inside the operating room to help the surgeon visualize, find and remove all the oral cancer from the patient.		
Research Area	**Biomedical Engineering**		

PI: Leonidas Tsiokas	**Title:** Role of FBW7 in Autosomal dominant polycystic kidney disease (ADPKD)
HF21-040	**Organization:** University of Oklahoma Health Science Center
Rank: 4	**Year 1:** $75,000 **Year 2:** $75,000 **Total:** $150,000
Research	Autosomal dominant polycystic kidney disease (ADPKD) is a common, life-threatening genetic disease that results from inactivating mutations mainly in the PKD1 or PKD2 genes. It is a leading cause of end-stage renal disease affecting ~1 in 500 to 1,000 individuals worldwide and in the US. Unfortunately, despite years of work, the disease is still incurable with a poor patient prognosis. Current therapeutic modalities, including tolvaptan and dialysis, have limited success and are associated with significant side effects. Striving to identify and develop new and more effective therapeutic approaches is of paramount importance in putting an end to this debilitating disease. Increasing evidence suggests that inactivating mutations in PKD1 or PKD2 genes lead to abnormally long primary cilia. Primary cilia have long been implicated in the pathophysiology of ADPKD, but the exact mechanisms are poorly understood. They are antenna-like organelles housing several signaling pathways. A unique feature of primary cilia is that they are dynamic organelles whose length is determined at any given time by the balance of cilia assembly and disassembly pathways. The Tsiokas lab has recently shown that genetic deletion of the Pkd1 gene in mice and cells results in longer cilia due to slower cilia disassembly rate. However, how the loss of PKD1 regulates ciliary disassembly still remains entirely unknown and is the focus of this proposal. My preliminary data suggest that loss of PKD1 upregulates FBW7, which in turn controls cilia length by regulating cilia disassembly factors PLK1 and HEF1. Consistently, genetic inactivation of FBW7 in mice normalizes cilia length, completely rescues kidney function, and ameliorates cyst progression in certain segments of the kidney in a clinically relevant animal model of ADPKD. Based on these data, I will test the hypothesis that FBW7 functions as a negative regulator of cilia disassembly, whose upregulation in PKD1-deficient cells leads to abnormally long cilia and contributes to ADPKD progression. This hypothesis will be tested in two separate aims: In Aim1, I will focus on the cellular mechanisms by which FBW7 controls ciliary disassembly. In Aim 2, I will identify the cell types in the kidney where these cellular mechanisms are important for ADPKD pathophysiology. Successful completion of the proposed studies will: 1) discover the underlying mechanism(s) causing slower cilia disassembly in ADPKD, 2) advance the understanding in the pathophysiology of ADPKD, and 3) identify unique, more specific, and effective therapeutic targets that can be exploited to improve patient outcomes.
Research Area	**Cell/Molecular Biology**

PI: Lauren A. Zenewicz	**Title:** Targeting immunometabolism to combat Clostridioides difficile gastrointestinal infection
HF21-032	**Organization:** University of Oklahoma Health Sciences Center
Rank: 5	**Year 1:** $75,000 **Year 2:** $75,000 **Total:** $150,000
Research	Clostridioides difficile, often referred to as “C diff”, is a bacterium that causes a hospital acquired infection, that can range from mild diarrhea to death, and is also the most common cause of diarrhea associated with antibiotic use. In 2017 in the US there were an estimated 223,900 cases and 12,800 deaths due to this pathogen. Oklahomans who are 65 or older, take antibiotics, who stay in hospitals or nursing homes for an extended period of time or people with weakened immune systems are especially susceptible. One you have had one C. difficile infection you are at higher risk for subsequent, more severe C. difficile infections. This suggests that our immune responses to the pathogen are not good enough to prevent re-infection. There is no FDA-approved vaccine and few treatments for patients. In this application, we present a project that will examine how a toxin produced by C. difficile dampens the immune response. We predict that the toxin changes the metabolism of immune cells so they fail to properly respond to the infection. We will test to see if changing the immune cell metabolism during infection can reduce disease severity or prevent re-infection in an animal model. The results of our study will have implications on the design of new therapeutics to treat or prevent C. difficile infections.
Research Area	**Immunology**

PI: Zoltan Ungvari	**Title:** Cerebrovascular mechanisms of long-term cognitive decline in breast cancer patients following chemotherapy
HF21-039	**Organization:** Oklahoma University College of Medicine, Department of Biochemistry & Molecular Biology
Rank: 6	**Year 1:** $74,278 **Year 2:** $73,978 **Total:** $148,256
Research	Advances in the treatment of cancer have greatly improved survival. However, side effects related to cancer treatment have gained increased attention. Cancer survivors often report a progressive loss of memory and attention. These side effects have a significant impact on quality of life. "Chemo brain" refers to these symptoms that can persist for months or years after treatment. Until relatively recently, "chemo brain" was largely unrecognized. Most of the symptoms were deemed to be related to primary cancer or emotional stresses. It is not known how chemotherapeutic agents affect neuronal function. It cannot be a direct effect because they do not cross the blood-brain barrier. In contrast, cancer drugs have a direct effect on the cells of blood vessels. Our hypothesis is that cancer drugs cause an age-related phenotypic change in the cells of brain blood vessels. We propose that this change results in worsening of the brain blood flow and leads to chemo brain symptoms. We will test our hypothesis in a cohort of patients diagnosed with breast cancer who are prescribed chemotherapy. We will perform evaluations before and after the chemotherapy.
Research Area	**Physiology/Pharmacology**

PI: Sathish Srinivasan	**Title:** Mechanisms of PROX1 in Heart Valve Disease
HF21-011	**Organization:** Oklahoma Medical Research Foundation
Rank: 7	**Year 1:** $75,000 **Year 2:** $75,000 **Total:** $150,000
Research	Heart valves open and close approximately 40 million times a year in a normal human being. When open, healthy heart valves permit blood flow without obstruction and when they close, they prevent backflow. Proper organization of cells and scaffolding proteins, known as extra cellular matrix (ECM), is important for heart valve function. Defects in the cells and ECM are frequently associated with heart valve disease that affects nearly 2.5% of the entire US population. Heart valves are made of two major cell types: valvular interstitial cells (VICs) and valvular endothelial cells (VECs). VICs are primarily responsible for producing ECM. However, VECs regulate the identity of VICs through incompletely understood mechanisms. We have determined that the transcription factor PROX1 is expressed in a subset of VECs. Furthermore, deletion of PROX1 from VECs results in abnormal ECM production and thickening of heart valves. In this proposal we will investigate the mechanisms by which PROX1 regulates ECM production. We will also determine if an FDA-approved drug could slow down the valve defects of mice lacking PROX1 in VECs.The valve defects of mice lacking PROX1 are characteristic of several valve disorders such as Marfan syndrome, non-syndromic progressive heart valve disease and degenerative heart valve disease. Thus, our work will have a positive impact on public health by shedding light on a disease that is associated with significant mortality and morbidity. Our studies might also lead to a non-invasive approach to treat heart valve defects.
Research Area	**Cell/Molecular Biology**