| PI | Department | Title | Co-Investigators | Department/School/College | Project Summary |
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| Olga Baker | Otolaryngology | Building a better saliva substitute | Robert Zitsch<br>Tabith Galloway | Otolaryngology<br>Otolaryngology | Chronic dry mouth is directly associated with radiation therapy administered every year to approximately 60,000 head and neck cancer patients in the USalone, a condition that contributes directlyto oral infections and severely impairs daily life activities. Although a host of products have attempted to address dry mouth, all to date lack the critical properties of saliva and thus fail to provide the desired relief. Our projectaims to create a plant-based saliva substitute spray consisting of mucoadhesive, lubricating and digestive salivary proteinssimilar to those found in natural saliva at a high degree of purity and low cost. |
| Jonathan Bath | Surgery | Computational Fluid Dynamics Modeling in Asymptomatic and Symptomatic Carotid Disease | Binbin Wang | Engineering | Carotid artery narrowing (stenosis) can lead to stroke, which is the 4thleading cause of death in the US. There are still no reliable methods for determining which individual with carotid stenosis will develop a stroke. Computational fluid dynamics (CFD) is a computer-modeling process that generates flow characteristic data. Our multidisciplinary research team will use CFD, based upon CT scan images of individuals with carotid stenosis, to find out which flow characteristics may be linked with stroke. This work could help avoid unnecessary and risky operations in individuals with carotid stenosis, who have a low risk for stroke. |
| Lisa Beamer | Biochemistry | Unified view of inherited metabolic diseases: enzyme dysfunction phenotypes | John Tanner | Agriculture, Food, and Natural Resources | Treatment of inherited metabolic diseases is a new frontier in precision medicine.  Understanding how genetic mutations associated with these disordersimpact enzyme function is essential fordevelopingindividualized patient treatments.This proposal willleverage the biophysical expertise of the investigators on disease-related mutationstodevelop a combined approach, using both experimental and computational methods, to efficiently characterize missense variants associated with disease.  Our goal is to harnessthe power of biochemistry, structural biology, and bioinformatics tofacilitateclinical efforts to improve patient treatmentand prognosisfor inborn errors of metabolism. |
| David Beversdorf | Radiology, Neurology, Psychological Sciences | Development of a multimodal imaging platform for precision medicine targeting in autism spectrum disorders | Carlos Leiva Salinas<br>Amolak Singh<br>Carmen Cirstea<br>Benjamin Black<br>Brett Froeliger<br>Brad Ferguson<br>Jeff Johnson<br>Shawn Christ<br>Robert Thomen | Radiology<br>Radiology<br>Physical Medicine and Rehabilitation<br>Child Health<br>Psychiatry; Arts and Science<br>Radiology; Health Professions<br>Arts and Science<br>Arts and Science<br>Radiology | Our purposeis to develop a multimodalimaging platformforprecision medicine in autism spectrum disorder(ASD). We previously showedthe relationship between connections across brain regions and neurotransmitterconcentrations in ASD, and used these to predict responses to selected drugs. Now we willharness this expertise to examine a broader rangeof neurotransmitters, first to understandrelationships between this full range of neurotransmitters and ASD behaviors as well as connections between brain regions, and then to predict responses to a full range of drugs. This will help to understand why only some patients with ASD respond to particular drugs. |
| Amy Braddock<br>Richelle Koopman | Family and Community Medicine<br>Family and Community Medicine | Development of CommitFit App to Facilitate Health Behavior Change among Clinic Adolescents | Aneesh Tosh<br>Rachel Proffitt | Pediatric Adolescent Medicine<br>Health Professions | 35% of adolescents have overweight or obesity.Mobile health (mHealth)apps have potential to improve health behaviors and weight. We will utilize auser-centered design process with focus groupsand interviews of adolescents and caregivers to develop and iterate a "CommitFit app"electronic prototype, which will use gamification to motivate behavior change. We will also use focus groups of physiciansto design an electronic health record visualization of CommitFit data, to expand the current model of patient/provider health behavior co-management. This cutting-edge technology will empower adolescents to set and achieve health behavior goals and discuss these goals with their physician. |
| Shiyou Chen<br>Xiaobang Cui | Surgery<br>Surgery | Targeting response gene to complement 32 to alleviate pulmonary arterial hypertension |  |  | Pulmonaryarterial hypertension is a progressive andcurrentlyincurable disease characterized by lung artery thickening which consequentlyleads toright heart enlargementand failure.Since pharmacotherapeuticefforts fail to reverse thediseasedevelopment, and the prognosis of remains poor,identifying novel therapeutic targets is clinically urgent.The proposal is aimed to studyhow response gene to complement 32 (a protein)accelerates the disease progression and test if blocking the function of this protein using a small peptide hinders or reserves the disease developmentusing animal models.Thestudy could lead to a therapeutic invention for treating pulmonary arterial hypertension. |
| Carmen Cirstea | Physical Medicine and Rehabilitation | Multimodal biomarker of neurodegenerative diseases affecting motor system - an integrative neuroimaging and behavioral study | Raghav Govindarajan<br>David Beversdorf<br>Bradley Ferguson<br>Syed Shah<br>Trent Guess<br>Scott Frey<br>Greg Petroski | Neurology<br>Radiology; Neurology; Arts and Science<br>Radiology; Health Professions<br>Neurology<br>Physical Therapy, Orthopaedic Surgery<br>Physical Medicine and Rehabilitation<br>Health Management and Informatics | Precision medicine, which emphasizes leveraging all available data about an individual to improve health, is in its nascence in amyotrophic lateral sclerosis (ALS)andParkinson's disease (PD). These diseases have in common irreversible motor deteriorationand a unfortunately lack of effective treatments.Shedding light on underlying neural mechanisms may provide new ways to approach therapy development by developing sensitive, reliable biomarkers. We propose a prospective cohort study of patients with ALS orPD utilizing advanced neuroimaging and behavioral techniques to methodicallytestwhether biology of the motor system at diagnosis is a robust biomarker oftreatment response and disease progression. |

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| Gary Clark<br>Danny Schust | Obstetrics, Gynecology, and Women's Health<br>Obstetrics, Gynecology, and Women's Health | Development of an Early Diagnostic Test for Preeclampsia | | | Preeclampsia is a condition that affects about 8% of all pregnancies in the United States, with an economic impact estimated to be $2.18 billion in 2017. Major symptoms include hypertension, proteinuria, severe headaches and nausea. Without intervention, preeclampsia progresses to eclampsia, resulting in seizures and death. Eclampsia is the cause of 15% of all maternal deaths in the United States. Preeclampsia is thought to be the result of abnormal placentation. This study is focused on the development of an early diagnostic test for preeclampsia that will enable subsequent medical interventions that minimize harm to the mother and her fetus. |
| Brett Crist | Orthopaedic Surgery | Biologic Hip Restoration in Young Active Patients using an Optimized Allograft Transplantation Strategy | James Cook<br>Trent Guess<br>Aaron Stoker<br>Chantelle Bozynski<br>Cristi Cooke | Orthopaedic Surgery<br>Orthopaedic Surgery; Health Professions<br>Orthopaedic Surgery<br>Orthopaedic Surgery<br>Orthopaedic Surgery | Young active patients can have debilitating hip disorders that detrimentally affect their lives, but they are not optimal artificial total hip replacement (THR) candidates based on the need for lifelong activity restrictions and likelihood of revision surgeries. Our ultimate goal is to provide a safe and effective biologic total hip restoration (BTHR) strategy using osteochondral allografts that consistently improves these patients' pain and function without activity limitations. This study will allow progress towards that goal through computational simulations, biomechanical testing, and preclinical animal modeling that will result in optimizing BTHR such that its functional outcomes are consistently superior to THR. |
| Ashley Curtis | Psychiatry | Cognitive Training in Mild Cognitive Impairment: Effects on Sleep, Cognition, and Arousal | Christina McCrae<br>David Beversdorf<br>Nelson Cowan | Psychiatry<br>Radiology<br>Arts and Science | Insomnia and mild cognitive impairment are associated with increased risk of developing Alzheimer's Disease. Current sleep medicationsare associated with unpleasant side effects, and there are currently no medicationsto improve cognition. This TRIUMPH study will be completely remote and will examinethe effects of 8-weeksof cognitive training (online Cognifit) relative to an active control program (online Trivia Training) for improving mental abilities/cognition, sleep, and arousal inolder adults with mild cognitive impairmentand insomnia. Findings will increase knowledge regarding sleep/wake associations in this population and provide new information aboutmechanisms underlying response to cognitive interventions. |
| Timothy Domeier | Medical Pharmacology and Physiology | AAV micro-dystrophin gene therapy for aging-associated atrial fibrillation | Dongsheng Duan | MMI | Atrial Fibrillation (AF) is the most common sustained arrhythmia, and greater than 2.7 million people are living with AF in the United States. Lower levels of the critical muscle structural protein dystrophin have been observed in AF patients. This research project will use a gene therapy approach to increase levels of a micro-dystrophin protein in hearts of aged animal models with AF. The goal of this pre-clinical project is to provide mechanistic proof-of-concept that micro-dystrophin gene therapy improves aging-associated AF, and accelerate clinical translation to human patients with AF. |
| William Durante | Medical Pharmacology and Physiology | Targeting Glutamine in Diabetes-Associated Vascular Disease | | | Vascular disease is the primary cause of mortality in patients with diabetes. While its etiology is multifactorial, endothelial dysfunction is a seminal feature of diabetes-associated vascular disease. This proposal will examine the ability of glutamine and its metabolites to counteract the negative effects of high glucose concentrations on human endothelial cell function, and determine if oral administration of glutamine or its metabolites improves endothelial dysfunction in diabetic animals. This work may identify glutamine as a new therapeutic target in preventing endothelial dysfunction in diabetes and may inform future clinical studies employing novel dietary regimens to treat vascular disease in diabetes. |
| David Gozal | Child Health | Melanoma surface markers for precision phenotyping of hypoxia-induced tumor aggressiveness | Donald Burke | MMI | This is a collaborative project between the Gozal and Burke labs that is based on previous observations that intermittent hypoxia (as occurs in sleep apnea and many other respiratory conditions) is strongly predictive of adverse cutaneous melanoma aggressiveness and outcomes. Since it is currently impossible to identify when such aggressive melanoma is present, molecular probes are needed. This projects aim to develop molecular probes called 'aptamers' using a refined and productive workflow that has already been preliminarily tested and has confirmed a priori feasibility. As such, we will conduct unbiased screens to uniquely identify aptamers that differentiate among human melanoma lines that respond in very different ways to intermittent hypoxia, and then identify the molecular targets that are recognized by those aptamers. Successful completion of this work will provide the tools that should guide patient-specific melanoma diagnostics and personalized treatment. |
| Bumsuk Hahm*<br>*Award declined due to overlap with anticipated NIH R01 Award | Surgery, Molecular Microbiology and Immunology | Regulation of T cell dysfunction and viral persistence by sphingosine kinase | Ravi Nistala | Medicine | n/a |
| Mark Hannink | Biochemistry | Molecular Mechanisms of Drug Resistance in Head and Neck Squamous Cell Carcinoma | Gary Weisman | Biochemistry | Cancers that arise in the oral cavity and pharynx, also known as head and neck cancers, have a 5-year survival rate of less than 50%. Although targeted therapies for head and neck cancer have been developed, the outgrowth of treatment-resistant tumor cellsfollowing treatment is a major clinical problem.This proposal will examine the role of extracellular nucleotides and oxidative stress in the development of resistance to targeted therapies in head and neck cancers. One outcome of our proposed experimentswill be to identify biomarkers that predict if a patient's tumor has developed resistance to targeted therapies. The proposed experiments may also lead to new therapeutic approaches to prevent the outgrowth of treatment-resistant tumors. |

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| Xiao Heng | Biochemistry | A novel platform for peptide design with applications to targeting antibiotics resistance | Xiaoqin Zou<br>Hongmin Sun | Dalton Cardiovascular Research Center<br>Medicine | The overarching goal of this project is to establish a novel platform for rapid and reliable design of effective peptides targeting a given protein, by integrating efforts from bioinformatics and computational biology, structural biology and protein biophysics/biochemistry, microbiology, and peptide synthesis and modification. Potent peptide inhibitors targeting TEM β-lactamases have been identified in preliminary studies. Successful development of peptide inhibitors in the project will set the stage for future development of a new class of therapeutics to combat antibiotic resistance. |
| Raghuraman Kannan | Radiology | MU-CN29 | A Novel Nanoparticle Platform for Treatment of Drug-Resistant NSCLC | Anandhi Upendran<br>Richard Hammer | Institute for Clinical and Translational Science<br>Pathology and Anatomical Sciences | Lung cancer is the leading cause of cancer mortality. The 5-year survival rate remains a dismal 16% for the past 40 years. The emergence of drug resistance is the key obstacle to achieving long-term patient survival. Our team has identified the critical molecular determinants of drug resistance. Subsequently, we have developed MU-CN29, a nanotechnology-based therapeutic agent, to inhibit the resistance-driving genes and overcome the resistance. In this project, we will evaluate the therapeutic efficacy of MU-CN29 in clinically relevant patient-derived xenografts. The data will validate the MU-CN29 nanoparticle platform as a promising strategy to combat drug resistance and catalyze clinical trials in the future. |
| Teresa Lever | Otolaryngology | Establishing neurophysiology-based biomarkers for early detection and monitoring of chemoradiation-induced dysphagia in head and neck cancer patients | Gregory Biedermann<br>Laura Dooley | Radiology<br>Otolaryngology | Dysphagia (swallowing impairment) is a common side effect of chemoradiation therapy (CRT) in head and neck squamous cell carcinoma (HNSCC)patients, leading to weight loss/malnutrition, aspiration pneumonia, feeding tube dependence, and depression/social isolation. To understand how CRTcausesdysphagia, our team has been developingclinical toolsfor earlier detection of dysphagia and identification of correspondingly damaged neuroanatomical structures(brain, cranial nerves, muscles).These tools will be used to test40 HNSCC patients and 20 healthycontrols.The ultimate goal is to accelerate the discovery of precision medicine-based strategies to preserve swallowing function in tandem with extending survival in HNSCC patients. |
| Zhenguo Liu | Medicine | Ambient fine particulate matter exposure impairs cognitive function | Ronald J. Korthuis<br>Zezong Gu | Medical Pharmacology and Physiology<br>Pathology & Anatomical Sciences | Ambient fine particulate matter (PM) is the key components for air pollution, and PM exposure increases the risk for cardiovascular diseases. PM exposure also increases the risk for cognitive dysfunction and dementia with the mechanisms largely undefined. It is known that small cerebrovascular diseases havebeen identified as an important contributor to vascular-related cognitive impairment and dementia. Theproject was to test thehypothesisthat "PM exposure impairs cognitive function through oxidative stress-induced small cerebrovascular dysfunction". The data will provide evidence to support the conceptthat PM exposure significantly impairs small cerebrovascular function andcognitive function through oxidative stress. |
| Christine McCrae | Psychiatry | Impact of Improving Sleep and Reducing Opioid use in individuals with chronic pain on central pain processing. | Ashley Curtis<br>Mary Beth Miller<br>Chelsea Deroche<br>Chokkalingham Siva<br>Ouwole Popoola<br>Jason Craggs<br>Neetu Nair | Psychiatry; Arts and Science<br>Psychiatry<br>Health Management & Informatics<br>Medicine - Rheumatology<br>Psychiatry<br>Health Professions; Arts and Science<br>Psychiatry | Patients who experience chronic pain also experience insomnia. While opioid therapy is commonly prescribed for these patients, its long term efficacy is questionable and side effects can be severe. Withdrawing from opioids is difficult, and poor sleep and ongoing pain can make it more difficult. This study will examine whether improving insomnia through cognitive behavioral therapy for insomnia (CBT-I) improves pain and subsequently helps reduce opioid use. This study will improve understanding of sleep's potential to improve pain and support opioid withdraw and has important implications for the millions of individuals living with chronic pain, their families, communities, and healthcare. |
| Ravi Nistala | Medicine | Unbiased identification of intervenable genetic and metabolic programs that lead to progression of Chronic Kidney Disease | Naveen Pokala<br>Trupti Joshi<br>Katie Murray | Surgery<br>Health Management & Informatics<br>Surgery | With the increasing prevalence of overweight/obesity in the US population, there is increasing risk for chronic kidney disease (CKD) from obesity related kidney disease (ORKD), a recently recognized entity. There's now evidence from National Surveys thatobesity when combined with metabolic syndrome leads to progression of CKD, independent from diabetes or hypertension, the other major causes of End Stage Renal Disease/dialysis in the US. The goal of our project is to perform an unbiased (no prespecified target) examination of the genetic and metabolic programs that are altered and identify novel targets to prevent CKD progression to ESRD in overweight/obese individuals |
| Elizabeth Parks<br>Yezaz Ghouri | Nutrition and Exercise Physiology<br>Medicine | Variability in Microbial Response to Dietary Fiber | Katherene Anguah<br>Aaron Ericsson | Human and Environmental Sciences<br>Veterinary Medicine | This TRIUMPH grant is a collaboration between the Departments of Medicine, Nutrition and Exercise Physiology, and Veterinary Pathobiology to determine how different people respond to high-fiber diets differently, to determine individual patient factors (sex, body weight) that influence how microbes populate the colon. Patients who are scheduled to complete a health-screening (~50 year old) colonoscopy must undergo a standardized preparation before their medical procedure to reduce the microbes in their colon. After the procedure, these patients are fed a 2-week, high-fiber diet and fecal samples are taken, along with blood samples to measure health biomarkers. |

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| Alan Parrish | Medical Pharmacology and Physiology | Lead Induces Renal Cell Carcinoma Epithelial-to-Mesenchymal Transition | Ayman Gaballah<br>Kevin Staveley-O'Carroll | Radiology<br>Surgery | Lead is an established toxicant, however, its role in kidney cancer is not clear. Our laboratory demonstrated that challenge of kidney cancer cells with lead induces molecular – loss of E-cadherin expression, increased matrix metalloproteinase-9 expression – and phenotypic changes – increased cell growth, loss of cell-cell adhesion, increased wound healing - consistent with cancer metastasis. In these studies, we will focus on i) direct effects of lead on tumor cells and ii) indirect effects of lead on the kidney that promote tumor progression in vivo. |
| Thomas Quinn | Biochemistry | Novel use of P2X7 receptor antagonists to protect salivary glands in PSMA-617 targeted radiotherapy for prostate cancer. | Timothy Hoffman<br>Gary Weisman<br>Thomas Dresser | Medicine<br>Biochemistry<br>Radiology | A novel prostate cancer radiotherapeutic gaining considerable attention is radiolabeled PSMA-617, which targets prostate specific membrane antigen present on prostate cancer tumors. Dramatic reductions in disease were reported in metastatic prostate cancer patients. Unfortunately, toxicities associated with salivary gland uptake have been reported. The goal of this project is to reduce radiolabeled PSMA-617 induced salivary gland toxicity by co-administration of salivary gland avid anti-inflammatory agents, attenuating tissue damage. Results from these studies will determine the protective properties of salivary gland avid anti-inflammatory agents during radiotherapy, with the goal of being translated into the clinic to improve radiolabeled PSMA-617 treatment. |
| Lixing Reneker | Ophthalmology | The estrogen's role in age-related dry eye disease (DED) | Dennis Lubahn<br>Frederick Fraunfelder | Biochemistry<br>Ophthalmology | Dry eye disease (DED) is a common complaint in daily ophthalmic practice, affecting 1 in 5 people and the number is expected to increase with aging. The existing therapies for DED are merely palliative and often provide inadequate relief of symptoms. The focus of the research program is to understand how decline or deficiency of the sex hormone, estrogen, affects the function of tear-producing glands in genetically engineered mouse models. Our goal is to develop targeted therapies to prevent and treat age-related tear gland dysfunction and to improve the quality of life in the aging population. |
| Laura Schulz | Obstetrics, Gynecology, and Women's Health | Effect of Gestational Diabetes on Placental Development | Danny Schust<br>Kathleen Pennington<br>Geetu Tuteja<br>Omonse Talson | Obstetrics, Gynecology, and Women's Health<br>Baylor College of Medicine<br>Iowa State University<br>Avila University | Gestational diabetes is the most common complication of pregnancy, with long-term consequences for both maternal and infant health. The goal of this project is to understand how disruptions in placental function and placenta-islet communication contribute to the pathophysiology of the disease. A novel mouse model of gestational diabetes will be used to determine how factors released by the placenta and their receptors in the pancreas change over time in pregnancy, while non—invasive imaging will be used to study whether gestational diabetes alters placental function in early pregnancy in women. |
| Richard Sherwood<br>Dana Duren | Pathology and Anatomical Sciences<br>Orthopaedic Surgery | Maturation-based prediction of craniofacial growth | Kevin Middleton | Pathology & Anatomical Sciences | The goal of this study is to improve evidence-based pediatric treatment for craniofacial abnormalities through expanded understanding of growth expectations in the absence of intervention. Proper treatment planning in adolescents demands accurate assessment of a patient's current growth status and prediction of future growth. The overall impact of this research will be a shift in the clinical management of pediatric patients with craniofacial perturbations. Leveraging the substantial longitudinal resources on craniofacial growth assembled by MPI Sherwood (NIH R01DE024732) the project will add detailed assessments of skeletal maturity (the work of MPI Duren; NIH R01AR055927) allowing us to develop precise individualized predictive models of patient growth. |
| Emily Smith | Dermatology<br>Health Management and Informatics | Using deep learning to triage dermoscopic images of skin lesions to aid in early detection of skin cancer | Mirna Becevic<br>Praveen Rao<br>Eduard Simoes | Dermatology<br>Health Management & Informatics<br>Health Management & Informatics | Skin cancer is the most common type of cancer in the world; when detected and treated early, it is highly curable. As many Missourians do not have ready access to a dermatologist, concerning skin lesions are often evaluated by other healthcare providers with less experience in the diagnosis of skin cancer. We will harness the power of deep learning to develop a Missouri-specific smart-device application that can be used by non-dermatologists to classify photographs of skin lesions as benign or malignant. Such triage will prompt timely referral, facilitate early diagnosis, and decrease skin cancer mortality in the state of Missouri. |
| Todd Vogel | Surgery | Using Information Technology to Improve Transitions of Care after Vascular Surgery | Robin Kruse<br>Dong Xu<br>Lori Popejoy | Surgery, Family and Community Medicine<br>Engineering<br>Sinclair School of Nursing | Improving surgical care and lowering hospital readmission after surgery requires adopting evidence-based practices, improving personalized care, and reducing variation in care. We will identify factors associated with outpatient complications and readmission after lower extremity vascular surgeries using the Re-Engineered Discharge (RED) framework to create vascular RED (vRED), create a patient-centric VAscular Surgery Discharge Application (VASDA) leveraging IT technology, and conduct an implementation study to determine the effectiveness of vRED and VASDA. A successful study will offer improved patient-centric outcomes, tailored transition plans to patient needs, lower readmission, and hold promise to customize care for other high-risk populations. |
| Andrew Wheeler | Surgery | Biometabolic Outcomes After Weight Loss Surgery: An Individualized Approach | Scott Rector | Nutrition and Exercise Physiology | Gastric bypass surgery is highly effective for treating obesity, but mechanisms of effectiveness are poorly understood. We will use a clinical trial, randomizing gastric bypass patients to variable lengths of bypassed intestine to determine if technical modifications can lead to improved clinical outcomes while investigating biologic mechanisms that lead to improved metabolic health. Changes in the gut microbiome, circulating miRNA, and circulating gut hormones will be examined. This translational research will investigate both clinical outcomes and basic science research to understand how the gastric bypass can better treat obesity and its comorbidities while providing information to direct precision obesity treatment. |

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| Rebecca Whiting | Ophthalmology | Identification of disease progression biomarkers in the protein profile of tear fluid and blood plasma in a canine model of CLN2 neuronal ceroid lipofuscinosis | | | Our goal is to identify changes in the protein profile of serial biological samples which correlate with disease progression in a canine model of CLN2 Batten disease, an inherited neurodegenerative disorder with pediatric onset. The study will facilitate the development of effective treatments for CLN2 disease by establishing a panel of protein biomarkers that can be used to monitor disease progression non-invasively and to potentially gauge therapeutic efficacy throughout preclinical studies. This panel would significantly aid in obtaining sponsorship to conduct preclinical trials, particularly if biomarkers are translatable from the canine model to human patients. |