Spring 2021 Grant Awards

Spring 2021 AB Nexus Grant Awards

New Collaboration ($50,000)

Acute intermittent hypoxia in persons with spinal cord injury: studying corticospinal drive and motor adaptation

Andrew Smith (CU Anschutz; Department of Physical Medicine and Rehabilitation, Physical Therapy Program, School of Medicine)
Andrew Q Tan (CU Boulder; Department of Integrative Physiology, CU Boulder Center for Neuroscience)

Spinal cord injury (SCI) disrupts sensory and motor pathways, resulting in lifelong mobility impairments and loss of functional independence. This proposal will characterize how breathing modest bouts of low oxygen (acute intermittent hypoxia; AIH) may enhance the excitability of spared pathways to the lower limb as well as augment motor adaptation in humans with SCI.

Chronic Inflammation and ECM Degeneration as Key Mediators of Pelvic Organ Prolapse

Chronic Inflammation and ECM Degeneration as Key Mediators of Pelvic Organ Prolapse (POP)

Injection of Lipopolysaccharide (LPS) to model metabolic endotoxemia in a mouse that exhibits spontaneous POP

Fibulin-5 Knockout mouse  Pelvic support structure ECM

1. Characterize LPS accumulation and inflammatory cell content in the urogenital ligament (USL) and vaginal wall; evaluate ECM changes at the time of POP onset.

2. Evaluate biomechanical properties of USL and vaginal wall at time points after exposure to LPS. Test hypothesis that LPS endotoxemia model favors pelvic floor support degeneration.

Chronic Inflammation and ECM Degeneration as Key Mediators of Pelvic Organ Prolapse
Pelvic organ prolapse is a costly, and debilitating disorder that impacts millions of women, yet the underlying mechanisms responsible for the compromise of the pelvic support tissues are poorly understood and few animal models to study prolapse exist. We have identified evidence of inflammation and metabolic endotoxemia (ME) in pelvic support tissues from women with prolapse, and our studies in this proposal will establish an ME mouse model that will define the impact of circulating lipopolysaccharide on inflammation, extracellular matrix content and biomechanical properties of critical pelvic support structures in order to create a practical animal model to further study the effects of ME on the pelvic floor, and ultimately develop early intervention strategies to prevent pelvic organ prolapse.

Combining simulations and experiments to determine protein/ligand-mediated microglial activation in Alzheimer's Disease
Kimberley Bruce (CU Anschutz; Division of Endocrinology, Metabolism and Diabetes, School of Medicine)
Kayla Sprenger (CU Boulder; Chemical and Biological Engineering Department)

This study aims to use a novel computational and experimental platform to unravel the molecular complexity of microglial activation, and to identify microglial phenotypes that may protect against Alzheimer's disease development and progression.

Integrated COVID Genomic Sampling, Sequencing, and Variant Tracking
David Pollock (CU Anschutz; Department of Biochemistry and Molecular Genetics, School of
The project aims to follow and assess risk variation associated with evolutionary change in genomic variants of SARS-CoV-2, the virus responsible for COVID-19 in humans. To do this, we will deploy fast and integrated Bayesian sequence and phylogenetic network analysis.

**Predicting the environmental distributions and pathogenicity of nontuberculous mycobacteria, an emerging group of bacterial pathogens**

Michael Strong (CU Anschutz; Division of Infectious Diseases, School of Medicine, and National Jewish Health)

Noah Fierer (CU Boulder; Department of Ecology and Evolutionary Biology, Cooperative Institute for Research in Environmental Sciences)

Nontuberculous mycobacteria (NTMs) are a diverse group of bacteria with some members of this group capable of causing environmentally acquired pulmonary disease, an emerging public health problem in the U.S. We seek to understand why NTMs vary in their pathogenicity and which particular environments are most likely to harbor pathogenic NTMs.

**Swimming through mucus: Anisotropy and other obstacles for bacteria**

Christopher M Evans (CU Anschutz; Division of Pulmonary Sciences and Critical Care Medicine)

Nuris Figueroa (CU Boulder; Department of Physics, College of Arts and Sciences)

This study focuses on physical properties of mouse colonic mucus that control bacterial trajectories, and how mucus composition determines those properties. It has to potential to
identify causes for chronic penetration of commensal bacteria through mucus in the digestive tract, which is relevant in diseases characterized by changes in the intestinal microbiome, and could lead to new avenues for treatments that will target mechanical properties of mucus.

Existing Collaboration ($125,000)

**Biomaterial and Small Molecule Targeting of Macrophage BRD4 to Prevent Pathological Cardiac Fibrosis**

Timothy McKinsey (CU Anschutz; Division of Cardiology, School of Medicine)
Kristi Anseth (CU Boulder; Department of Chemical and Biological Engineering and BioFrontiers Institute)

We aim to uncover novel mechanistic information about the pathological role of inflammatory cells on cells in the heart and the progression of cardiac fibrosis. Specifically, we will study how macrophages control fibroblast activity through cellular, biomechanical and epigenetic cues with the goal of identifying new therapeutic innovations for patients suffering from end-stage cardiac and valvular fibrotic diseases.

**Molecular targeting Phase-Change Ultrasound Contrast agents for Early Diagnosis and Guided Treatment of Type 1 Diabetes**

Richard KP Benninger (CU Anschutz; Department of Bioengineering and Department of Pediatrics)
Mark A Borden (CU Boulder; Department of Mechanical Engineering)

Type1 diabetes follows the immune-mediated destruction of insulin-producing beta cells, requiring life-long insulin therapy and increasing the risk of diabetic complications. We will
develop novel molecularly-targeted phase-change ultrasound contrast agents to track the progression of insulitis and guide therapeutic treatments to prevent type 1 diabetes.

Groups audience: AB Nexus

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