

CCTSI Colorado Pilot Grant Program (CO-Pilots)
CCTSI Child Maternity Health Pilot Grant Program (CMH-Pilots)
CCTSI Translational Methods Pilot Grant Program (TM-Pilots)
CCTSI Community Engagement Pilot Grant Program (CE-Pilots)

What Are The “Translational Science Roadblocks”?

It should be noted that in most small clinical research projects there are specific barriers, so-called “translational science roadblocks,” that need to be overcome:

- improved study design by improving rigor and transparency in major generalizable areas of translational discovery
- technical execution of complex mechanistic studies in humans or animal models
- challenges to data acquisition, integrity, and analysis
- translational barrier from animal models to human trials; or between adult and pediatric patient populations
- timely participant recruitment and retention
- enhanced recruitments and engagement of underserved populations

In the application, the PI must state clearly what is your “translational science roadblock” that you will be addressing in your proposal. The CCTSI Pilot Grant team is available to assist you in designating a translational science roadblock in your study.

Some Examples of Translational Science Pilot Focus

Establishing Molecular Mechanisms of Polymorphism of Cytochrome P450: This study will be performed in vitro using Tg and KO epithelial and hepatic cells using novel immunosuppressive drug (CU AMC Drug Discovery Core). CYP450 polymorphism is a very generalized problem, and its understanding will help to establish pharmacokinetic properties of over 75% of existing therapeutic agents (CSU Drug Discovery Core). The pilot addresses the barrier of rigor and transparency in major generalizable areas of translational discovery.

Designing High-Throughput Screening of Novel Small-Molecule Inhibitors of mTOR pathway: Designing multiple tyrosine kinase/ mTOR inhibitors using in vitro and in vivo animal models of ovarian cancer will allow for future development of toxicity profiles and a compound library (CU AMC Drug Discovery Core/ OLAR) for pathway-based molecular inhibitors of mTOR, a major onco- and immunosuppressive pathway in human pharmacology. This project addresses challenges to data acquisition, integrity, and analysis.

Establishing Molecular Mechanisms of Pulmonary Fibrosis using Omics Technologies: Animal Models and human biopsies will be used to perform an expanded genomics (CU AMC Genomics Core) and metabolomics (CU SOP MS Metabolomics Core) in pulmonary hypertension. The data can be expanded to other lung diseases in the future and cross-validated with hepatic and renal fibrosis. This project addresses the barriers in technical execution of complex mechanistic studies in humans or animal models.

Developing Accelerated Contrast-Free MRI Protocol in Patient-Derived Mouse Models of Pediatric Brain Tumors: MRI is a gold-standard translational neuroimaging technique where shorted image times without the need of intravenous contrast are desired. Orthotopic mouse models will be used to

establish faithful animal models of pediatric malignancies. A novel multiparametric MRI protocol with advanced MR sequences will be developed using a 9.4 Tesla MRI scanner (CU AMC Animal Imaging Core). This project addresses the barriers in technical execution of complex mechanistic studies in humans or animal models AND translational barrier from animal models to human trials.

Advanced Bulimia Treatment in Adolescent Girls: Efforts will be made to enroll young female participants from diverse geo-economic and racial background to address eating and behavioral disorders. fMRI at a 3 Tesla MRI (CU AMC Brain Imaging Core) will provide pharmacodynamics readouts. This project addresses enhanced recruitments and engagement of underserved populations.

Creating Systems Biology of Early Atopy (SunBEAM): Will develop recruitment and enrollment strategies for community mothers including underserved clinics and Spanish only speaking mothers for long term birth cohort study. The recruitment methods overcome the translational barrier of involved underserved communities in research.

Establishing Skin Profiling of Atopic Dermatitis and Food Allergy: The project will develop a new skin tape epidermal sampling technique that allows multi-omics profiling from both adults and children and samples can be sent to other institutions for -omics analysis. This pilot addresses the barrier of rigor and reproducibility in clinical studies and translation of data between pediatric and adult populations due to methodological differences.

Validating Natural Animal Translational Disease Models: Many diseases of dogs, cats, horses, and other animals are more similar to diseases in people than induced diseases in traditional rodent models. For example, osteosarcoma in dogs is genetically similar to the same tumor in people and responds to similar therapies. Inflammatory bowel disease in cats has been increasingly diagnosed in feline companion animals with many of the same features as human disease. Idiopathic epilepsy in dogs has many symptoms that mimic childhood epilepsies. Musculoskeletal conditions of the equine athlete are identical to similar syndromes in humans, and stem cell and biological therapies are potential therapeutic modalities that can be rigorously assessed in the horse to inform human protocols. Accordingly, validating the molecular, diagnostic, and therapeutic features of these diseases in veterinary clinical trials (so called "T0.5") is a mechanism for improving translational science, addressing translational barrier from animal models to human trials. For more information, see <https://onehealth.colostate.edu/natural-animal-models/> <https://onehealth.colostate.edu/research-success-stories/>

Retrospective Analysis on Multi-Institutional CU-CSU Omics Data: These pilots could leverage the pilot to address the issue of performing team science across institutions and data harmonization and transfer between institutions, etc. The pilot addresses challenges in data acquisition, integrity, and analysis.