TRiM Translational Advisory Committee (TAC) Meeting Notes
November 1, 2022, 2:00 to 2:30 PM AST

Members Present: Kelly Drew, PhD; Nicholas Deutz, PhD, MD; Katherine Tuttle, MD, FASN, FACP, NKH; Stacy Rasmus, PhD; Judith Kelliher, PhD; Daniel Promislow, DPhil; and Denise Daniello, MA (ex officio)

Meeting Purpose: Introduce new TAC members, Drs. Judith Kelliher and Daniel Promislow, and provide updates regarding TRiM's canine intervention platform and the COBRE renewal application.

Discussion

Member Introductions - Kelly introduced current TAC members, Drs. Mick Deutz, Katherine Tuttle, and Stacy Rasmus noting their areas of expertise in health research, interests in translational research, and institutional affiliations. Dr. Deutz is Professor in Translational Research in Aging and Longevity at the Department of Health and Kinesiology, Texas A&M University. His research interests focus on clinical nutrition and metabolism research in animals and humans. Dr. Deutz is finishing up a study involving hibernating bears and will share the results of his study upon completion. Dr. Tuttle serves as the Executive Director for Research at Providence Health Care, Co-Principal Investigators of the Institute of Translational Health Sciences (ITHS), and Professor of Medicine at the University of Washington. Her major research interests are in clinical and translational science for diabetes and chronic kidney disease. Dr. Rasmus is the Director for the Center for Alaska Native Health Research and an Associate Research Professor at UAF. Her research focuses on the role of resilience and protective factors to reduce health disparities of American Indian/Alaska Native peoples. She has a broad background in medical anthropology with specific expertise in the translation of cultural knowledge and practice into health interventions.

Kelly introduced TAC's new members Drs. Daniel Promislow and Judith Kelliher, and their expertise in canine studies and translational research. Dr. Promislow, Co-PI on the Dog Aging project at the University of Washington funded by a U19 grant from NIA, is focused on a broad set of aging-related questions. This project has enrolled 41,000 dogs with about 10,000 having whole genome sequencing, and approximately 1,000 having biospecimens with CBC/Chem/UA, epigenome, metabolome, microbiome and FACS analysis completed. The goal of the Dog Aging Project is to understand how genes, lifestyle, and environment influence aging to increase health span and the period of life spent free from disease for both dogs and humans. Dr. Promislow is also involved with another canine brain health study funded by a R24 grant. This project will necropsy a handful of dogs to measure brain pathology to assess the prevalence of canine cognitive dysfunction (CCD). Dr. Promislow explained that CCD has been observed in dogs aged 11 years and older, but the condition is rare.

Dr. Judith Kelliher is founder and Chief Executive Officer for the biotechnology company, Neuronascent. Her company focuses on developing small-molecule, non-invasive therapeutics to treat people suffering from chronic neurodegenerative disorders, such as Alzheimer's disease and related dementias, that lack any disease-modifying therapeutic options. TRiM is working with Judy and Neuronascent using the sled dog/canine model as an intervention platform to test novel treatments to prevent or reverse brain

aging. Canine cognitive dysfunction has marked similarities to Alzheimer's disease and currently there are no treatments that can stop or reverse either disorder.

TAC Purpose - Kelly summarized TAC's purpose which is to keep TRiM on track with conducting translational research. The study of hibernation is broad, Kelly noted, and the metabolic adaptations have applied benefits for human health and aging, including neurogenerative properties such as preventing muscle atrophy and ischemic reperfusion injury, mechanisms found during re-warming of the hibernating Arctic Ground Squirrel (AGS). This research is important for Alaska and the health of older Alaskans. Per capita, Alaska has the fastest growing proportion of people age 65+ than any other state in the U.S. which has significance for rising health care costs and quality of life for older adults.

Kelly reiterated the guidance from Dr. Trey Coker, former TAC Chair, shared at the last TAC meeting. He observed that while UA lacks the clinical oversight for human clinical trials, we do have the capacity to conduct human observational research. UAF's Vet Med program provides veterinary oversight that makes it possible to conduct canine intervention research as UAF has both veterinarians on staff and veterinary diagnostic imaging.

COBRE P2 Renewal – Kelly said that she is not eligible to be the PI on the COBRE P2 application as her previous grants do not meet NIH qualifications for this COBRE grant. Dr. Loren Buck, a Professor of Biology at Northern Arizona University, is a UAF graduate and former student of Dr. Brian Barnes, a Professor specializing in hibernation and endocrinology. Loren has several research projects including a R01-funded project conducting a community-based participatory research (CBPR) study at St. Lawrence Island focused on environmental health.

<u>Possible Research Ideas and Take-Away Points Discussed</u>

- Engage in an observational comparative study of both dogs and humans to characterize the effects of exercise on muscle (function, volume, and mass) and brain in addition to gut microbiome diversity and brain health. Sled dogs are a viable model to test the effects of exercise since there are active and nonactive sled dogs.
- Look at research conducted by Dr. Bill Evans regarding osteoarthritis in dogs and humans. His research focused on muscle strength and health as prevention of osteoarthritis (or morbidity due to osteoarthritis). Note that Bill Evans' D3-creatinine would need to be validated in dogs in order to do this type of comparative research in dogs and humans. (See Evans et al., Pediatric Research, volume 89, pp 1508-1514, 2021).
- Track mild cognitive impairment in humans and dogs (potentially owners and companion dogs).
- Exercise ties together the health of muscle, brain, and gut. Exercise promotes anabolic sensitivity, plasticity, and the ability to regenerate new muscle and neurons. Exercise may also play a role in promoting mental health.
- Reach out to Arleigh Reynolds for input on TRiM's proposed One Health approach to increase our translational research capacity.

The meeting adjourned at 2:35 p.m.