TRiM Translational Advisory Committee (TAC) Meeting Notes
October 16, 2024

**Members Present**: Kelly Drew, PhD; Nicholaas Deutz, PhD, MD; Judith Kelleher-Andersson, PhD; Daniel Promislow, DPhil; Greg Pietsch, DVM; and Denise Daniello, MA (ex officio). Krya Dunlap was serving on a NIH study section and not available for this meeting.

**Meeting Purpose**: Discuss strategy to integrate the canine model in the COBRE renewal.

**Discussion**
Kelly Drew facilitated the meeting in the absence of TAC Chair Kriya Dunlap, who was serving on a NIH study section. .

1. Status of COBRE Renewal Application – Kelly provided an update on the COBRE renewal application, emphasizing the role of canine models in two ongoing research projects. One project, led by Kriya Dunlap, utilizes sled dogs as "human sentinels." Both humans and sled dogs share the same environment, diet, and have protective skin covering (fur for dogs and parkas for humans) that keeps them warm but also limits vitamin D synthesis from sun exposure. Due to their shorter lifespans, shared environment, and similar biochemical pathways, dogs are viewed as an important biomedical research model for studying brain aging.

Kriya's successfully secured an NIA R03 grant using preliminary data gathered from a TRiM pilot project and is now preparing an R01 application. Her research investigates how vitamin D levels and dietary intake of wild Alaskan salmon affect aging biomarkers in sled dogs, specifically looking at brain changes and insulin signaling. Kriya's main hypothesis is that vitamin D will improve metabolic and brain health. Kriya is using the HaMR Core's MRI to assess brain changes, including hippocampal volume and morphology, in the study's canines, comparing young and older animals before and after being fed a salmon diet. Kelly noted her interest in involving Scott Jerome in the HaMR Core as a research navigator to support both canine projects, if the COBRE is renewed. Scott, who already collaborates with Kriya on her sled dog research, holds a PhD from UAF and has a background in human performance research with athletes. Kelly and Scott have been invited to a Department of Defense DEVCOM meeting next week. DEVCOM focuses on research to enhance soldiers' cognitive and physical performance.

2. Canine Cognitive Dysfunction (CCD) Study - Greg Pietsch, DVM, UAF Assistant Professor of Veterinary Medicine, is the lead on the Canine Cognitive Dysfunction (CCD) study. This project is funded with a $10,000 research grant from NeuroNascent. Inc., a biopharmaceutical company developing therapies for neurodegenerative disorders like Alzheimer's and Parkinson's disease. Judy Kelleher-Andersson, PhD, NeuroNascent's CEO, noted that CCD is a natural model for Alzheimer's disease (AD) due to similar symptoms (anosmia and behavioral changes) and brain volume loss in the hippocampus. This CCD study has two main goals: (1) Establish CCD as a testing platform for testing new treatments for AD and other dementias in dogs with potential for human application, and (2) investigate CCD incidence in interior Alaskan dogs and track symptom progression over three months. This includes monitoring behavioral changes (using CADES), anosmia test results, and hippocampal volume changes via MRI (pre- and post-study). The study will also examine brain plasma P-tau levels as a potential biomarker. While not yet proven in dogs, P-tau is a promising early validation biomarker for AD in humans. Validating the same biomarkers in both canine and human populations would help to advance Alzheimer's research.

To date, two dogs have been studied, but the team plans to include more. Referrals come from veterinarians, or owners can refer their pets. Despite interest in the study, many dogs do not qualify because they do not meet eligibility requirements (for age and size), while others have pre-existing medical conditions, such as cancer, which could skew the results. The initial age range (8-11 years) for study dogs was considered too

young for CCD development to be evident. Greg and the CCD team worked with IACUC to extend the age range. Standardizing blood sampling also remains a challenge.

Greg noted his interest in working more closely with Kriya Dunlap and Scott Jerome on their dog aging research. Kelly suggested that Kriya's R01 work might look at canine biomarkers for CCD that could translate to Alzheimer's. Greg added that his study, aiming to recruit older dogs with possible CCD and a larger dataset, may be valuable to Kriya's work.

3. Additional Updates - Kelly followed up with Daniel Promislow's referrals regarding canine MRI imaging at the University of Colorado. Daniel added that Stephanie McGrath, University of Colorado, is collaborating with physician-scientist Martin Davas (University of Washington). Dr. Davas is developing assays for Aβ42 (Amyloid Beta 42) as well as P Tau to detect CCD and has shown some success.

Daniel shared an interesting finding from research conducted by Marina Watowich (University of Washington, now Arizona State postdoc) under Snyder-Mackler's lab. While larger dogs generally have accelerated life trajectories (grow faster, die younger), this study found that cognitive development and aging follow the same trajectory across all dog breeds, regardless of size, lifespan, or breed (early life development, late life decline).

The TAC inquired about the milestones COBRE Phase 1 needed to achieve for Phase 2 consideration. Kelly clarified that Phase 1 focused on Center development, while Phase 2 aims to strengthen initial efforts.

Kelly further explained that a key challenge is having the capacity to conduct human subjects research; however, that expertise was lost with Trey Coker's leaving, and Fairbanks lacks physician oversight for human subjects research. Research direction is guided by faculty expertise. Kelly added that while finding someone to conduct human subjects research is a challenge, UAF is recruiting for a new biochemistry faculty member who may bring expertise in both biochemistry and human subjects research. The Center has concentrated on unique Alaskan niches for translational research, such as hibernation. This niche was expanded to include two sled dog projects. Kriya's research involves dietary interventions, and Greg's CCD project will use a mechanistic perspective. The Center also has unique access to an MRI for animal research.

Judy asked about the possibility of a shared faculty where UAF could contract with a researcher from another university for specific expertise. Kelly responded that collaborations will be expanded through planned summer technical workshops in Phase 2 (pending funding), acknowledging the challenges of distance collaboration. The Center strives to broaden its network of collaborators.

4. Funding Options for CCD Projects – Daniel offered additional guidance on funding CCD research, noting that translational research does not always have to involve human subjects. He clarified that as long as the research translates from model systems (like cells or animals) for potential human application, it can still be considered translational.

Daniel offered the following funding suggestions:

- Supportive NIA contacts – Manuel Moro, Program Officer (morom@mail.nih.gov), Luigi Ferruci, Scientific Director (ferrucciLu@mail.nih.gov), and Jen Fox, Research Administrator, Program and Project Manager (Program Officer, Translational Research Branch and Programs (jennifer.fox@nih.gov). Daniel suggested starting with Manual Moro or Luigi Ferruci. He also suggested finding a receptive study section. NIA has a "geriatrics study section." The NIA recently funded the rapamycin project for the Dog Aging Project.
- Other potential funders - Morris Animal Foundation and the American Kennel Club Canine Health Foundation, both of which fund dog research; however, grants are small. Daniel added that the

American Kennel Club may have a call this spring or winter for grants specifically targeting aging and dogs. They offer two general grants – the “Acorn” (grants from $10K to $20K) and the “Oak” ($50K to $70K) that can fund preliminary data for NIH grant pursuits.

The meeting adjourned at 1:00 p.m. (AK time).