

**Center for Transformative Research in Metabolism
External Advisory Committee In-Person and Virtual Meeting
August 8-12, 2022**

Virtual Options, August 8, 9:00 a.m. to 1:45 p.m.; Thursday, August 11, 9:00 – 11:00 a.m.; 1:00 – 1:30 p.m.; and 3:45 to 4:15 p.m.; & Friday, August 12, 1:00 p.m. to 4:30 p.m.

EAC Meeting Agenda

Meeting Objectives:

1. Research Project Leaders and Pilot Project Investigators receive valued guidance from EAC members through one-on-one meetings. Investigators prepared to provide information regarding project updates and plans for moving forward to EAC members.
2. UAF and UAA Tours of Core Facilities and RPL labs
3. EAC meetings with UA administrators
4. Discuss plans for moving forward with applications to SuRE First (Sept 27, 2022), NSF (December 2022), NIA PO1 (Jan 25, 2023), SuRE (May 26, 2023) & the COBRE renewal (May 30, 2023).

Meeting Desired Output:

1. Professional development for TRiM's RPLs and Pilot Investigators based on EAC and mentor guidance.
2. UAF & UAA administrator support for the COBRE renewal application.

Monday, August 8: Meet at the Akasofu Building, Upper West Ridge campus, at 2160 Koyukuk Drive, Room 401 (In-person and [virtual](#) options available)

9:00 a.m. *Welcome and overview of the EAC August meeting goals and activities.*

Dr. Kelly Drew, Director, Center for TRiM

Breakfast snacks, coffee/tea and water provided

9:15 a.m. *Summer School in Environmental Physiology of Mammalian Hibernation*

Dr. Brian Barnes, Director, Alaska INBRE

10:00 a.m. *Break*

10:15 a.m. *Research Project Pitch, COBRE Renewal Application (30 minutes /pitch)*

- Oivind Toien, PhD, *Adaptations of Sleep and Cardiac Rhythms in the Hypometabolic State of a Human Sized Hibernator*
- Anya Goropashnaya, PhD, *Molecular changes in a hibernator's skeletal muscles during winter as a pathway to peripheral artery disease intervention.*
- Kriya Dunlap, PhD, *Vitamin D and Healthy Aging: Establishing the Sled Dog Sentinel for the Circumpolar North*
- Jack Chen, PhD, *Blood Biomarkers Associated with the Hibernating Arctic Ground Squirrel*

August 8, 2022 (continued)

- Mario Muscarella, PhD, *The Role of the Gut Microbiome in Host Response to Toxin Consumption*

12:45 p.m. Lunch Break – No host catered Lunch (Akasofu, Room 401)

1:30 p.m. Overview of the ASET Lab & Metabolomics – Dr. Patrick Tomco, UAA ([virtual](#) 15-minute presentation)

2:00 p.m. EAC Meeting with UAF Administrators. Meet in Chancellor’s Conference Room, Signer’s Hall – Room 330 (in-person only and [virtual](#) for EAC).

- Chancellor Dan White (invited but unable to attend)
- Nettie La Belle-Hamer, PhD, Vice Chancellor for Research
- Diane O’Brien, PhD, Interim Director, Institute of Arctic Biology
- Karsten Hueffer, PhD, Interim Dean, College of Natural Science and Mathematics
- Brian Barnes, PhD, Alaska INBRE Principal Investigator/Director
- Anupma Prakash, PhD, Provost and Executive Vice Chancellor
- Kristin O’Brien, PhD, Professor of Biology and Wildlife

3:15 p.m. UAF Tours of Research Labs & Facilities (in-person and [virtual](#))

- BiRD Facility (Biological Research and Diagnostics Facility), 1033 Sheenjek Drive (near the Murie building), Rooms 035 and 039 (15 minutes) (Note: Enter BiRD using the Murie tunnel. Masks, lab coat, and shoe covers are required and will be provided. Visitors will also be required to read the Visitor Procedures SOP and sign the visitor log.)
- HaMR Core, Lower Level Murie, led by Carl Murphy, PhD, Core Leader (10 minutes)
- Research Labs: Fedorov Project 1, Goropashnaya Pilot Project, and Dunlap Pilot Project, are all located in the West Ridge Research Building (WRRB) 2nd floor labs (10 minutes/lab visit)

4:30 p.m. Dr. Fedorov meets with the EAC - *State of the Lab Address* (in-person only and [virtual](#) for EAC), 252 WRRB

Recess to Thursday, August 12, 2022, Meet on the UAA Campus (in-person and virtual options available).

6:00 p.m. No Host Dinner – Meet at Chena Alaskan Grill outdoor deck, River’s Edge Resort, 4200 Boat Street *or* The Greens Bar & Grill, 1735 Farmers Loop Rd.

Tuesday, August 9, 2022 – Transportation by rail, Fairbanks to Anchorage

7:15 a.m. Meet at Alaska Railroad Fairbanks Train Depot, 1031 Alaska Railroad Depot Road. UAF TRiM staff will provide transportation for those staying in hotel. Check-in at 7:20 a.m. Train leaves @ 8:20 a.m. and arrives in Denali Park at 12:10 p.m. Food is available on the rail for purchase.

This observational tour will focus on the hibernation theme of the Center, by observing TRiM's model species, the Arctic Ground Squirrel and black bear, in the wild. We will also dedicate time to faculty professional development and grantsmanship strategies for TRiM's continued funding and investigator research. We will meet for a no-host dinner at 49th State Brewery.

Wednesday, August 10, 2022 – Transportation by rail, Denali Park to Anchorage

8:00 a.m. No-host continental breakfast will be served at Denali Grizzly Lodge from 8:00 to 8:45 a.m. Ground transportation will be provided by UAF TRiM personnel leaving from the Lodge to Denali train station at 11:15 a.m. Train leaves @ 12:30 p.m. from Denali Train Depot and arrives in Anchorage @ 8:00 p.m.

- Continued focus on professional development and grantsmanship strategies with TRiM investigators, mentors, and EAC members in small group discussions.
- Check-in at hotel and no host dinner.

Thursday, August 11, 2022 – UAA Campus. Meet in UAA Chancellor's Conference Room, ADM 204

9:00 a.m. *Welcome to UAA: The UA Center for TRiM Partnership, A Focus on UAA Resources and General Orientation (in-person and [virtual](#))*
Khrys Duddleston, PhD, Professor and Director, Department of Biological Sciences. PI, *Microbial provision of essential amino acids: Protein conservation in hibernation, Project 2*, and Chair of the Internal Steering Committee
Breakfast snacks and water/coffee/tea provided.

9:15 a.m. *UAA Tour of TRiM Research Labs & Facilities (in-person and [virtual](#))*
Conoco Phillips Integrated Science Building (CPISB, building next door)

- Advanced Instrumentation in Microbiome Studies Core (AIMS), 3rd floor
Brandon Briggs, PhD, Core Leader, Eric Henderson, B.S. Lab Manager, and Kirstin Grond, PhD, Bioinformatician
- Briggs Lab Tour, AIMS Core Leader, 3rd floor
- Duddleston Lab Tour, Project 2, 3rd floor
- ASET and Metabolomics Lab, Zac Redman, PhD, 3rd floor
- Physiology and Cell/Molecular Research Wings, 2nd floor
- Animal Vivarium, 1st Floor, led by Khrys Duddleston

- 11:00 a.m. EAC meeting with UAA Provost Denise Runge – Chancellor’s Conference Room, ADM 204 (in-person and [virtual](#) for EAC only). TRiM’s EAC members, Khrys Duddleston, PhD, Brandon Briggs, PhD, Kelly Drew, PhD, and Denise Daniello are invited to attend representing TRiM.
- 11:00 a.m. Lunch Break – All others. No host catered lunch in CPISB Lobby/Atrium (CPISB 100L1)
- 1:00 p.m. Overview of AGS Breeding Program - Chris Terzi, UAF Animal Resource Center ([virtual presentation](#)). (Chancellor’s Conference Room, ADM 204)

Thursday, August 11 (continued)

- 1:35 p.m. Dr. Duddleston meets with EAC - *State of the Lab Address* (in-person and [virtual](#) for EAC), ADM 204.
- 2:30 p.m. EAC meeting with UAA Administrators – Chancellor’s Conference Room, ADM 204 (in-person and [virtual](#) for EAC only)
- EAC members and TRiM key personnel to meet with VCR Aaron Dotson and Dean Jenny McNulty. Khrys Duddleston, PhD, Brandon Briggs, PhD, AIMS Core Leader, Kelly Drew, PhD, and Denise Daniello are invited to attend representing TRiM.
- 3:45 p.m. EAC meeting wrap-up, set upcoming meeting dates, and concluding remarks. ADM 204. ([Virtual option](#))
- 4:15 p.m. Adjourn
- 7:00 p.m. No host dinner at TBD location.

Friday, August 12, 2022

- 10:30 a.m. AIMS Working Group meeting. Meet in CPISB Room 105A. Khrys Duddleston, Brandon Briggs, Jason Burkhead, Kelly Drew, and Denise Daniello are invited to attend.
- 1:00 p.m. *Mock Study Section of Research Project Applications* - All who have responded to TRiM’s call for Project Proposals (August 1st) for inclusion in the COBRE renewal, as well as other applications submitted or being proposed with a future deadline. This session is for those who are available to attend, in-person and [virtual](#). Meet in CPISB Room 105A.

Center for Transformative Research in Metabolism (TRiM)

External Advisory Committee (EAC) May 2022 Meeting Notes



**Thursday, May 12, 9:00 a.m. to 1:00 p.m. and Friday, May 13, 2022, 9:00 a.m. to 12:45 p.m.,
Virtual Meeting**

Thursday, May 12, 2022, Day 1

Call to order: Dr. Kelly Drew welcomed all at 9:00 a.m. on Thursday, May 12, 2022, and provided a summary of the purpose of the EAC meeting which is to provide updates on research and pilot projects and the cores by the project and core leaders.

Attendance: EAC members included Chair Tom Kilduff, PhD; Detlev Boison, PhD; and David Lathrop, PhD. Margaret Rice, PhD, will attend the second day.

Others present representing UAF were Kelly Drew, PhD (Center Director); Vadim Fedorov, PhD (PI Project 1); Carl Murphy, PhD (HaMR Core Leader); Øivind Tøien, PhD (HaMR Core and Pilot Project 1); Diane O'Brien, PhD (IAB Interim Director); Brian Barnes, PhD (director of Alaska INBRE); Kristin O'Brien, PhD (possible PI for grant renewal); Anya Goropashnaya, PhD (Pilot Project 2); Hoshi Sugiura (Veterinary Technician, Admin Core); Pat Rivera (Research Technician); Jack Chen, PhD (screen pathogen-free animals for hepatitis); Denise Daniello (Admin Core); and Sarah Zieschang (Admin Core).

UAA representatives present included Brandon Briggs, PhD (AIMS Core Leader) and later joined by Pat Tomco, PhD (ASET Leader).

Daniel Promislow (Univ of Washington, mentor of Kriya Dunlap). Loren Buck, PhD (Arizona University, mentor for Khrys Duddleston)

Jen Danielson, External Evaluator with the Goldstream Group, also joined the meeting.

Welcome – Setting the Stage for the May 2022 EAC Meeting: Recent updates on TRiM Kelly Drew, PhD, Director of the Center for TRiM

Kelly asked each participant to introduce themselves. Kelly acknowledged the contribution of Phil Shenk to the HaMR Core, MRI trainer, who passed away May 4, 2022.

Kelly noted the goal for TRiM is to focus on the COBRE renewal as we begin the fourth year of five years of funding. Our aim is to submit a first draft, get reviewer comments, revise and resubmit in a more critical year.

Brief background: We are moving forward for renewal. We are in our fourth year and need to submit the first draft by September 27, 2022. Then, we will resubmit it next year (2023). We have challenges in clinical trial research as the medical community is overwhelmed with patient care and providers have

Limited time for research. In addition, Trey Coker, PI for Project 3 has moved on from UAF. We are also planning to improve our connections with the community through the Admin Core.



Two new areas for growth for TRiM moving forward include 1) a dog aging intervention model using the research dedicated MRI and 2) enhancing connection with the community through education and interaction with people connected to the aging community. We will continue to maintain a focus on hibernation and translation research. The new focus on community connection will help our investigators to understand the needs of the community and the community to understand the research. Kelly Drew sees a capacity for regenerative medicine and mechanisms that would enhance that research aim.

The organizational structure of TRiM was shared. The Administrative Core includes Kelly Drew as the PI with Denise Daniello, as Program Coordinator, and Sarah Zieschang, as Admin Assistant. The Admin Core will focus on enhancing our connections with the community. TRiM has the following committees: External Advisory Committee (EAC), Translational Advisory Committee, and the Strategic Advisory Committee (SAC). The EAC is provides overall scientific guidance and leadership for TRiM and our investigators. The SAC consists of all the UA administrators to help stay connected with what their needs are and our needs. The TAC is undergoing revision, with the loss of Trey Coker, PI for Project 3 and his clinical trial project. One of the recommendations is to include one of the clinician scientists from the dog aging project that Dr. Promislow from University of Washington leads.

COBRE Renewal:

For COBRE, the PI needs to have an active research project grant in order to be eligible for the grant to be reviewed. Kelly has a small one and three in review, but she is unsure if she will have an eligible active grant in September when the renewal is submitted. Therefore, Kristin O'Brien will come on to take the role of PI as she already has NSF funding, and Kelly would be the Deputy Director. Kelly sent a link to the overall specific aims to review.

Summer School in Hibernation:

There are talks of a hibernation summer school in 2023 for 20-30 people. Brian will be a leader for this focusing on environmental physiology of ground squirrels. There will be sections on the ongoing applied translational efforts. We will off this with CME credit through WWAMI along with a 3-day field trip through Denali Park. Nothing is official yet, but there is positive feedback for it. Loren may also be able to help. Carry forward funds will help support the program.

Tom Kilduff asked about advertising. Brian noted that participants will consist of graduate students, post-docs, and senior undergraduates. Participants will stay in the campus dorms. Twenty to thirty people are anticipated. Loren Buck suggested reaching out to NSF for supplemental funds. NSF would be excited about the themes in physiological ecology, arctic, and translational research. Daniel Promislow mentioned Ron Kolanski and submitting an R13. It's primarily for meetings, but it might be able to fund the summer school. He is willing to help out with making sure the boxes are checked correctly. David Lathrop mentioned that the R13 would be appropriate and to look at NIH Reporter to see funding.

If there's a strong aging component for the course, other sources of smaller funds include American Federation of Aging Research and the Glenn Medical Foundation.



There was discussion for including time on the May EAC meeting agenda, Day 2, to allow 15 minutes to discuss the draft specific aims shared by Kelly.

Health and Metabolism Research Core (HaMR), UAF – Carl Murphy, PhD presentation

Carl Murphy is Leader of the HAMR Core. Through a power point presentation, Carl shared the organizational chart. Two new facilities are being developed, microscopy and histology, with Jim Janoso as the manager with Pat Rivera helping out. Hoshi will manage animal support and continue to provide vet tech support. The Molecular Imaging Facility has 300MHz Varian and 6000 MHz Bruker NMRs. NMR usage is starting to see bounce back with end of Covid regulations and is expected to increase with hiring of new faculty. Imaging Suite contains the 1.5 Tesla MRI and GE Lunar iDXA.

Veterinary patients are steadily increasing. Adapting to changes in needs. Vet Diagnostic Imaging was not charging enough, and hiring more support to assist with animal MRIs to assist with others being overworked.

Rates increased to cover shortage; partly increased rates and part instrument starting to see a small decrease; see the future; without Coker, the human research for MRI will probably decrease more so. Saw an overall decrease in this year. Looking forward, MRI for human usage likely not to continue, but open to the opportunity.

iDXA scans are expecting a decrease in research use. Wanting to offer body composition scans for the general public. Further maintaining use of iDXA and a couple of other studies, maybe not human, that can use it.

Microscopy facility currently houses the Olympus Fluoview FV10i Confocal, Nikon Eclipse TE2000-U, Nikon Eclipse 80i, and NX50 Cryostat. There are needs for them available and usage however, equipment needs to be maintained. If maintained, then working on it. Overall approach for it.

Animal Support includes surgical implantation services and training in surgical techniques for students. Oivind helps maintain the animal instrumentation, which includes three Biotelemetry systems and multiple types of telemetry and data logger implants.

HaMR Core fiscal activity looking good for this year, and things are looking up for a positive balance next fiscal year.

Carl presented proposed updated rate to the instrument use. The only thing changing would be the charge for the radiologist for the veterinary diagnostic work. The other rates were used for the previous year. The new service rates would include \$200 for a Walk-in Body Composition Scan. HaMR Core has merit service awards to use university subsidy for people getting started with research proposals that can leverage extramural grant funds.

The HaMR Core specific aims for Phase 1 included supporting the Molecular Imaging Facility, supporting animal instrumentation, and implementing a long-term sustainable operation for the core.



The specific aims for Phase 2 include developing current capacities and expand those capacities to meet the needs of the users of HaMR core, supporting PIs, other COBRE investigators, and Pilot Projects; and continue to refine business plan for long-term sustainable core operation through the recharge service model.

Kelly Drew posed the question: What is the role of institutional support in the HaMR Core's long-term sustainability? If there is no university support, and insufficient revenue generated, the HaMR Core would not be able to provide merit service awards for pilot projects and new researchers.

Tom Kilduff asked how are we handling service contracts? Carl responded that those contracts are now directly supported by COBRE funding and another service contract covered by re-charge funds.

Kilduff was concerned that there was no direct support for the equipment that presumably the state purchased originally? Diane O'Brien answered that the Chancellor is supporting the Core with \$100k/year.

Service contracts that are part of the core part of the charge structure or will there be some support by the University? Service contract rates include facility service fees if there is enough use of the facility.

It was noted that there is a need to budget for depreciation; especially at UAA to support recharge centers. Increasing institutional support has been an ongoing goal.

Tom Kilduff is interested to hear how well PIs are being supported.

Advanced Instrumentation in Microbiome Studies (AIMS) Core Facility, UAA- Brandon Briggs, PhD, AIMS Core Leader and Pat Tomco, PhD, ASET Leader presentations

Sequencing is exponentially more than expected partly because of Khrys Duddleston's sequencing and the MiSeq at UAF is down and taking some of their sequencing to keep it going.

The original specific aims included 1) Provide and maintain state of the art technologies, 2) bringing on Kirsten Grond to develop pipelines, and 3) support and grow microbiome research through consultation and engaging in outreach events with COBRE and general public. UAA's STEM day is in October.

Kirsten has been able to provide consultation for UAA and UAF as well as branch campuses and has provided support for classes and independent study designs.

The Molecular services have seen more use than organismal analysis or bioinformatics.

Almost daily wastewater testing for Anchorage has moved things to more sustainability.

Metabolomics:



Pat Tomco is core lead for the ASET Recharge Center, and Brandon has been working with Pat to possibly create a new recharge center for AIMS that would include ASET resources. AIMS has had barriers in establishing a recharge center, which are being addressed.

Brandon noted that Pat Tomco has been working on LC-MS Orbitrap for metabolomics for microbial and model organisms. This service would help COBRE investigators and expand potential user base. It is set in the ASET recharge center now because they don't want to add in another core facility to support.

For the COBRE renewal, Brandon noted that discussions are underway to incorporate the LC-MS into a newly branded AIMS Core. Brandon proposed two models that would incorporate it best. Advanced Instrumentation in Microbiome and Metabolomic Studies (AIMMS). The new core would include resources from both AIMS and ASET. In this way, the new Core would have a broader base of expertise and equipment for research and the expertise. The other option is a conglomerate core that includes both the AIMS and ASET, which is the direction they would like to take. That way, technicians can transfer between AIMS and ASET. Pat with ASET, Brandon with AIMS and technicians transfer between the two.

Preliminary draft specific aims for the AIMS Core:

- support microbial and metabolomic research with state-of-the-art technologies
- develop and implement new protocols and techniques (wastewater, etc., as noted on the metabolomics side)
- educate and train mentees and other investigators
- implement and continually refine business plan for long-term sustainable operation of core

Looking at how to increase user base and be more sustainable. Who is going to pay for the service contracts and the people to do the work?

Focus on maintaining the people that maintain the expertise and the equipment. Personnel is a top priority for Brandon.

A significant challenge noted by Kelly is that the COBRE has no budget for taking on what metabolomics deserve. Use institutional support or share with INBRE, but that is tricky with grantsmanship.

Metabolomics will be able to generate uses and generate fees as long as we have paying users.

Brian: INBREs do have cores and has run a Genomics core in Fairbanks, but they are not planning to establish new cores. Most of the cores are dedicated to training and research and professional development. INBRE could help provide support, but not as a core within INBRE. Service contracts could have support from INBRE, but not permanently and be dependent on INBRE support.

Pat Tomco responded by stating that equipment can be paid for by grants; depreciation costs can be used to cover the cost of maintenance or the recovery costs. We want to maintain flexibility of running



samples as needed to support users and as a result, increase the number of users because services are responsive to their research needs.

AIMS/ASET needs the subsidy to cover the depreciation costs. The NMR and an older LC-MS are on the recharge, because they have depreciated. The Orbitrap needs factors ironed out before placing on the recharge.

An estimated time scale of 2-3 years is needed to develop a comprehensive recharge facility. Right now, focus on technique development, user base buildout. Demonstrating the capacities and generating publications with the Orbitrap.

People are asking about the cost of running samples. We need a full time employee to run the samples in order to implement a long-range plan.

COBRE Phase III expects a transition for all research cores to use a recharge model and become self-sustaining, AIMS/ASET is ahead of the game. Need conversation with UAA with what they are willing to provide in institutional support.

Pat Tomco delivered the rest of the presentation after having missed the scheduled timeslot due to a miscommunication.

The LC-Orbitrap, the first high resolution system in the state of Alaska, is popular in metabolomics, however, it is not an easy service to just plug in play. Tomco and his colleagues had methods training in Anschutz with Julie Haines and Trevecca Wilkerson with instruction on sample prep, extraction, instrumental methods, data curation, and reporting.

In June there will be a 3-day course from Thermo Scientific compound discover for metabolomics workflows.

There was discussion on the number of compounds that could be measured and the types of material extractions that could be conducted.

Others asked how long it took to train up a technician who is comfortable with every step of the process.

Admin Core, UAF – Denise Daniello, Program Coordinator, presentation

Denise Daniello presented information about the administrative core. The talk covered the goals and specific aims for the Admin Core, COBRE Phase 2 renewal application planning, and NIH reporting. Both the RPRR and SIRS reports were submitted on time with the RPRR submitted slightly early.

Denise noted the extensive planning in progress for the August EAC meeting, which will be discussed at tomorrow's meeting.

The long-term goal of the Admin Core is to provide leadership, vision and effort to strengthen, expand, and sustain the research projects and cores along with providing user friendly services. The Admin Core is here to provide day to day support as well as long-term support to our investigators and cores.



The first draft specific aim of the Admin Core is to provide scientific leadership, admin coordination, and fiscal management to sustainably the continued strengthening and expansion of the center, its research projects, and cores. Implement the EAC action plan and provide editing services.

The second draft Specific Aim is to provide investigator support by mentoring faculty and supporting the development of Junior Investigators to become competitive, successful investigators able to compete successfully for extramural funding.

The third draft specific aim is related to Technical Core support by directing early capacity building activities to establish new infrastructure in the Admin Core that once established will transition into one of the research technical cores. The goal is to leverage institutional support, grow user base, and implementing/maintaining a recharge center model for all service to achieve core self-sufficiency over the long-term

The fourth draft specific aim, which was not in the original application, is to promote community engagement and support through outreach and education in order to increase public awareness; improve communication; inform development, participation, and outcomes of TRiM’s research projects; and to build stakeholder support to sustain the Center.

Kelly added that everyone should watch the recorded webinar about [COBRE Phase 2](#) that is scheduled for today, May 12. Russ Mitchell will be available to help with graphics design and Sue Mitchell for editing TRiM’s COBRE renewal application.

Center for TRiM Evaluation: GY03 Outcomes and plans for COBRE Renewal - Jen Danielson, Goldstream Group, presentation.

Jen Danielson presented the TRiM program evaluation, Goldstream Group. The survey included 22 people. They focused on what factors make TRiM effective. They found that most of the personnel learned professional skills through mentoring with everyone needing the Admin Core. 2022 saw growth of networks and a strong core with lots of people. TRiM strengths are mentoring, useful facilities and expertise, and a growing network.

Jen will provide a written report at the beginning of June with continuing interviews in the next few weeks.

Tom Kilduff noted the increasing concern about aging as a theme emerging within TRiM and its appropriateness with NIGMS. Perhaps we should also be looking at NIA as a funding source. Kelly noted that Vadim and Anya will be working with Kelly, the HaMR Core, and the Admin Core to submit a P01 Center grant with NIA early next year.



EAC Meeting, Friday, May 13, 2022, Day 2

Attendees on May 13, 2022: Tom Kilduff, Margaret Rice, Detlev Boison, David Lathrop, Kelly Drew, Vadim Fedorov, Khrys Duddleston, Carl Murphy, Brandon Briggs, Oivind Toien, Anya Goropashnaya, Kriya Dunlap, Diane O'Brien, Daniel Promislow, Loren Buck, Jack Chen, Hoshi Sugiura, Pat Rivera, Jen Danielson, Sarah Zieschang, and Denise Daniello.

Welcome back and debrief of Day 1 – Kelly Drew, PhD, Director of the Center for TRiM

An overview from yesterday was presented by Kelly, which included cores and projects. She also said that cores are important to TRiM as they focus to support investigator needs.

David Lathrop brought up that the change in PI is a concern. Kelly has a small grant from ITHS, but there is a need for more senior person. Tom Kilduff mentioned that succession is expected in institutions as a natural evolution.

Margaret Rice would like to see a positive spin on the change in PI. Detlev suggested that the transition could be viewed as a restructuring of TRiM, and Kristin O'Brien comes in as a natural transition in a structural re-organization. Kelly would also stay lead of the Admin Core, which is the organizational structure that keeps it going.

Daniel Promislow said that being upfront regarding the transition and the program's future should be viewed in a positive way by reviewers.

Post-Transcriptional Mechanisms of Muscle Atrophy Prevention in Hibernating Mammals, Vadim Fedorov, PhD, Project 1 PI, UAF, presentation

Vadim will submit an R01 on June 5, 2022, with the title "Significance of post transcriptional gene regulation for muscle preservation during immobility of hibernation" to the NIH National Institute of Arthritis and Musculoskeletal and Skin Diseases.

The overall objective of the proposed research is to identify micro-expressions and the ribosome profiling candidate micro RNAs and signaling pathways that underlie the ability to reduce muscle atrophy in humans.

The rationale of the proposed research is that once the candidate micro RNAs and proteins are identified, then it will form the necessary foundation for mechanistic studies of molecular pathways on the lines of the ability to preserve muscle mass and possible to be used for improved treatments for muscle atrophy.

Vadim noted that the program officer found this proposal appropriate for the muscle development and physiology, under NIAMS, as well as the skeletal muscle exercise physiology study section.

In follow-up to Vadim's presentation, Tom Kilduff mentioned that aims starting with "analyze" would be better than ones that start with "test the hypothesis that...". David and Detlev also agreed with this suggestion to modify the aims statements.



Tom Kilduff also noted that Vadim could tie the proposed research to the broader biomedical community. The proposal has a unique angle that could be appropriate for a four- or five-year grant if the comparisons also included a standard mouse model.

Vadim said he will try to make changes to the way specific aims are stated prior to submitting the proposal June 5, 2022.

Margaret Rice also mentioned that having the main points summarized upfront will be beneficial for the review committee. Tom Kilduff added that a schematic would be a useful way to highlight the main points for reviewers. Kelly added that Russ Mitchell is available to generate schematics.

Tom Kilduff mentioned that pursuing a potential research collaboration with Sue Bodin, who is well established in the field, would go a long way as well to obtain positive reviews.

Microbial Provision of Essential Amino Acids: Protein Conservation in Hibernation, Khrys Duddleston, PhD, PI Project 2, UAA presentation

Khrys Duddleston presented summaries of her three recent proposal submissions. She mentioned the benefits of hibernation research related to spaceflight and obtaining a state of synthetic torpor by transplanting the gut microbiome of the AGS into a non-hibernate gut microbiome to minimize health impacts during space travel. Her proposal titled “Harnessing the hibernator gut microbiota: An innovative and feasible approach to reduce risk and improve health outcomes during and following synthetic torpor,” submitted to NASA TRiSH-BRASH on January 26, 2022, aims to address this research question.

Another proposal discussed was “Toward microbial intervention for muscle mass loss: The role of the gut microbiome in essential amino acid synthesis.” This R01 application was submitted to NIH-NIDDK on February 7, 2022.

The last proposal Khrys discussed was “Microbiota and inflammation in adiposity: The ground squirrel model” an R15 AREA Award submitted to NIH-NIGMS- February 25, 2022.

The EAC members were pleased with the progress of Khrys’s research.

Adaptations of Sleep and Cardiac Rhythms in the Hypometabolic State of a Human Sized Hibernator – Øivind Tøien, PhD, UAF, presentation

The goal of Oivind’s research is to use bears as a model of a human sized hibernator. The purpose is to find a way to reduce metabolic rate and oxygen demand, which could be applied to situations of cardiac arrest and trauma in humans.

Oivind developed sleep scoring for large hibernators as not much is known about sleep in bears. During hibernation, data shows that metabolic rate is reduced along with reduced oxygen demands, but not at the same levels as smaller hibernators such as the AGS.

Oivind is planning to submit a R01 proposal to the NIH Heart, Lung and Blood Institute on June 5, 2022, which will build on his pilot project research.

Molecular mechanisms underlying skeletal muscle temporal dynamics in a hibernating mammal as a pathway to peripheral artery disease intervention, Pilot Project – Anya Goropashnaya, PhD UAF, presentation

Anya called attention to the lack of effective treatments for patients suffering from Peripheral Artery Disease (PAD) that underscores the urgent need to understand the underlying molecular mechanisms leading to PAD abnormalities.

Anya will submit an R01 on June 5, 2022, entitled, “Molecular mechanisms underlying skeletal muscle temporal dynamics in a hibernating mammal as a pathway to peripheral artery disease intervention” to the NIH Heart, Lung and Blood Institute. The proposed animal model is the arctic ground squirrel.

Anya received training from her mentor, Esther Dupont, PhD, University of Kentucky, in her lab to establish protocol for staining muscle fiber types for comparing summer active and hibernating ground squirrels. She will submit a R01 proposal to NIH Heart, Lung, and Blood Institute on June 5, 2022. The program officer is Dr. Diane Reid.

Margaret Rice raised a concern that there is more than 3 years of work proposed. She asked if it would be possible to submit a 5-year R01 and add Vadim as a Co-Investigator as there is potential synergism between Vadim and Anya’s project. The aims on the COBRE renewal and R01 can be exactly the same, however, if both applications are approved, then the investigator must select one research project over the other.

Anya mentioned that RNAseq is easy, fast, and less expensive as compared to Riboseq analysis, which is conducted in Belgium and very expensive. The goal of RNAseq is to do 4-5 time points to identify pathways and look at differential protein levels.

Vitamin D and Healthy Aging: Establishing the Sled Dog Sentinel for the Circumpolar North, Pilot Project – Kriya Dunlap, PhD, UAF presentation

Kriya presented nutritional background about Vitamin D and the role salmon plays in the lives of Alaskan Native subsistence diets. Alaska has limited amounts of sunshine during the winter and Vitamin D levels in salmon are high which helps to supplement for deficiencies during winter. In modern times, Vitamin D levels have been reduced due to the transition to western diets.

Kriya presented here research on sled dogs and vitamin D levels. The specific aims are 1) Correlate markers of Vit D in animal model of circumpolar north and 2) determine effects of increased Vitamin D from wild Alaska salmon on biomarkers of insulin signaling and metabolic health in an animal model of the circumpolar north.

Kriya presented her research proposal to her research committee, Lawrence Brewer, PhD and Nada Porter, PhD on 02/10/2022.

Kriya is planning to submit a R03 to NIH National Institute on Aging on June 16th, 2022. She is on target for meeting her deadline.



Kriya welcomed suggestions from others for new project titles other than “Vitamin D and aging in the dog model.”

Low salmon runs may pose barriers for the proposed canine-salmon study, however, Kriya offered alternate ideas, such as the use of a salmon nutritional supplement for the dogs.

There was discussion about the safety of the dogs involved in the research, but because the dogs are personally owned, an IACUC waiver was obtained. Safety risks are minimized for the MRI imaging as UAF’s MRI imaging is IACUC approved and the procedure is conducted by a veterinarian. The dogs undergo a pre-screening health check prior to MRI and a blood screening.

Margaret Rice was concerned that an R03 is short in duration. She suggested using a timeline to show how and when research tasks are to be completed.

There was confirmation that this would be a good fit for NIA. There was also discussion about the serum plasma bank of 1000 dogs as a correlation study.

Daniel Promislow noted a study about canine cognitive dysfunction using companion dogs and shared this link: <https://pubmed.ncbi.nlm.nih.gov/20005753/>.

EAC August 8-11, 2022 Meeting – Kelly Drew and Sarah Zieschang, Admin Assistant

The purpose of the August 2022 meeting is similar to the May meeting, with the inclusion of a mock study section and in-person tours of facilities.

Sarah presented the logistic details of the EAC meeting in August. The meeting will be held August 8-11, 2022. The meeting on August 8, 2022, will be at UAF. Then, there will be a train ride August 9, 2022, to Denali and continue to Anchorage on August 10. The formal meeting will resume on August 11, 2022, at UAA.

There will be a van from UAF for transportation in Denali as this was more affordable than using local options. Denise Irish, with the UAF travel office, has been working on travel arrangements regarding hotels and flights for the August EAC meeting.

The EAC meeting adjourned and the EAC went into private session to discuss the EAC report.

TRiM Program Evaluation Summary - Project Year 3, Goldstream Group, External Evaluator

The Mammalian Hibernation Research: A Path Towards a Center for Transformative Research in Metabolism (TRiM) has made significant gains towards establishing a multidisciplinary research center at the University of Alaska. TRiM supports infrastructure cores and five pilot research projects to study hibernation and metabolism, with the long-term goal of developing therapies and treatments for metabolic diseases such as cardiovascular disease, diabetes, and obesity. The current research projects include 1) the study of post transcriptional mechanisms of muscle atrophy prevention in hibernating mammals; 2) microbial provision of essential amino acids and protein conservation in hibernation; 3) a study of skeletal muscle temporal dynamics in a hibernating mammal as a pathway to peripheral artery disease intervention; 4) a study of sleep and cardiac rhythms in large hibernators; and 5) a study of vitamin D and healthy aging in sled dogs.

The purpose of the evaluation is to assess how the program activities interacted to 1) support researchers, 2) encourage collaborations, and 3) enhance core facilities and resources to support multi-disciplinary research in hibernation and metabolic health and translation of therapies for human health.

The evaluation found that the center is effectively supporting researchers and facilities as seen by the following outcomes.

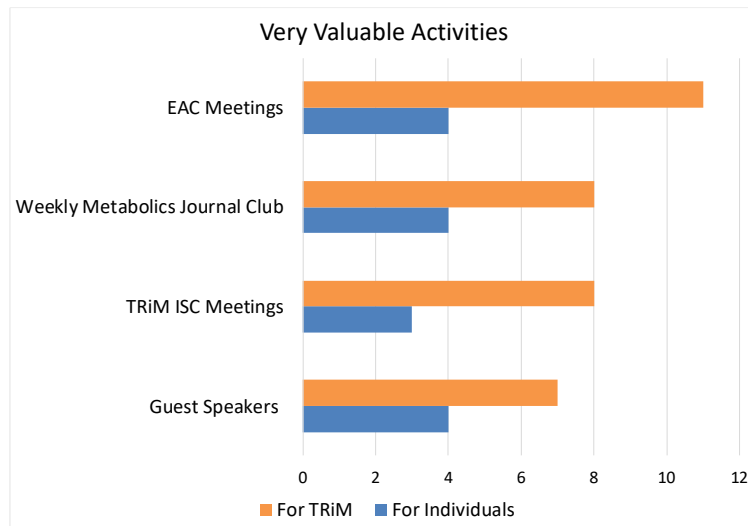
- More than half of researchers and support staff involved with TRiM report improving their professional skills in research, leadership, and analytical methods. They report that mentorship is the most common means of learning those skills.

*Figure 1. Spring Survey 2022 Results.
Question: What professional skills have you improved while working with TRiM?
Respondents could choose as many as they wanted of 4 responses: unchanged, improved through experience, improved through mentorship, or improved through training. (n=22).*



- Members of the TRiM team attend journal club meetings, internal steering committee meetings (ISC), external advisor board meetings (EAC), and an annual retreat. Team members reported in interviews that these meetings provided opportunities for collaboration and mentorship. More than half of survey respondents considered the EAC meetings very valuable to the center.

Figure 2. Spring Survey 2022 Results. Questions: A) How valuable are these activities to your own work? B) How valuable are these activities to the success of TRiM? Responses: Not at all valuable, a little valuable, somewhat valuable, very valuable.



- The facilities and expertise that the center supports such as the AIMS Core and the HAMR Core are being used to further the research projects. Team members report that the services provided are necessary to their projects, and all facilities are being used by several team members.

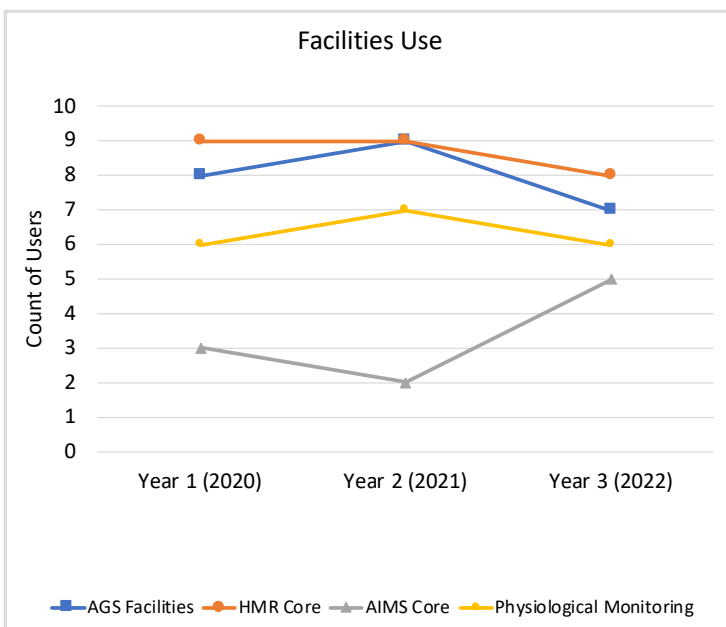
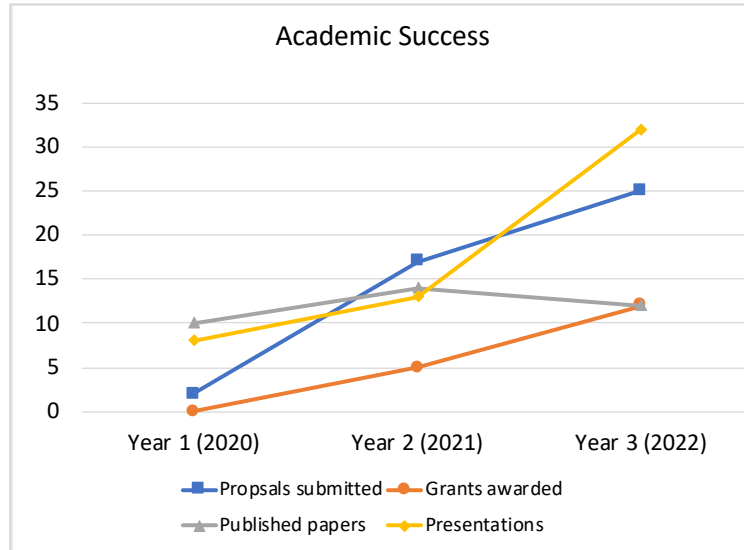


Figure 3. Facility Use Scores. (Individual's interview transcripts were scored based on the resources they reported using. Sums of the scores are charted here. Greater numbers equal more users but does not address questions of how often or how many different services were used.)

- The academic outcomes of numbers of presentations, proposals submitted and grants awarded have all increased.

Figure 4. Academic Success Scores (Counts of publications, proposals and presentations. Data collected by the Admin Core)



- Social network analysis indicates that the number of individuals involved in the center is growing and the number of individuals working on papers and proposals together is increasing.

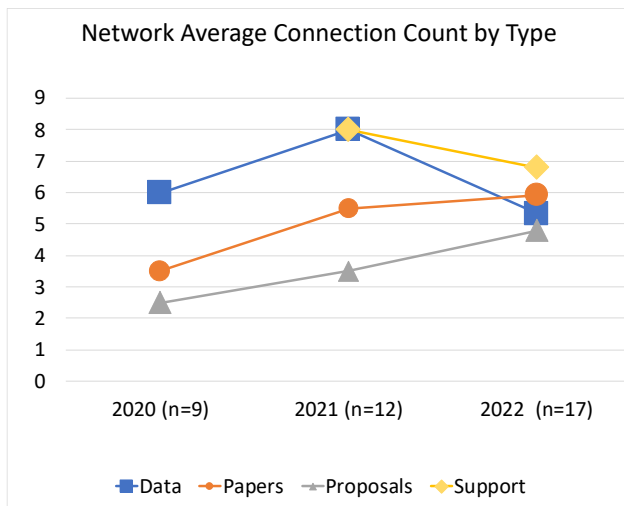
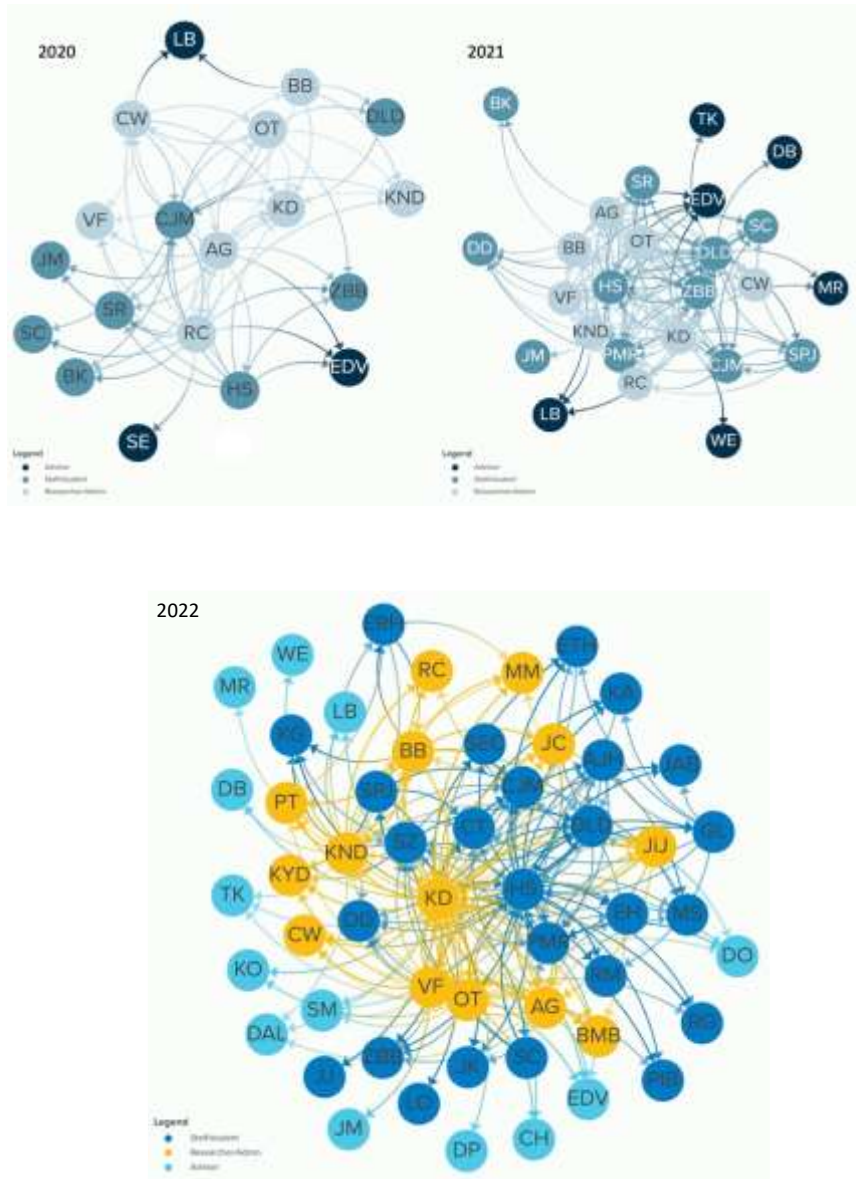


Figure 5 Social network connection counts by type of interaction reported. Individuals could choose how they worked with their colleagues: 1) shared data, 2) shared ideas for a paper or journal article, 3) shared ideas for a proposal, or 4) helped with animal care or administrative support.

Figure 6. Social Network Diagrams (More collaboration is indicated by more and shorter connections between individuals. Created at Kumu.io)



In conclusion, the evaluation indicates that at the end of Program Year 3, The Mammalian Hibernation Research: A Path Towards a Center for Transformative Research in Metabolism (TRiM) project is making progress towards its goals and is poised for continued success. For more details, please see the complete Year 3 Evaluation Report.

REPORT OF THE EXTERNAL ADVISORY COMMITTEE

1P20GM130443 “Mammalian Hibernation Research- A Path Towards a Center for Translational Research in Metabolism” – Kelly Drew, Ph.D., Principal Investigator
June, 2022

On May 12-13, 2022, the External Advisory Committee (EAC) met to evaluate progress toward the goals of this COBRE grant. EAC members were impressed with the science and overall quality of the presentations. Strengths of the program evident during this virtual meeting included a very strong mentorship capacity (mentor/mentee ratio: 2:1) which resulted in successful pilot studies and multiple grant submissions, as well as exciting new research directions including the potential to grow metabolomics in the AIMS Core (at UAA) through the Orbitrap mass spectrometry system.

The EAC makes the following recommendations to the TRiM PI and UAF Administration:

- While faculty presentations were on a high level scientifically, there is room for improvement of the presentation style. Investigators would benefit from practicing their presentations beforehand to obtain critiques, especially for new research directions. Investigators should only present to EAC members as opposed to the whole group to provide more opportunities for honest and constructive feedback. This could be achieved by adding extra time to EAC meetings to allow for more direct conversation between the EAC and investigators.
- Support of TRiM’s community engagement efforts by creation of a community engagement committee that will provide an interactive feedback loop for educating and receiving guidance from community members to inform TRiM’s research activities. The community engagement committee should be unique to TRiM and should not overlap with existing community engagement efforts at UAF.
- Include proposed Summer School in Environmental Physiology as part of community outreach activities to increase outreach to students/teachers, improve mentorship, and enhance visibility for UAF. UAF is recommended to co-sponsor this activity in partnership with TRiM.
- Increase engagement with WWAMI and health care providers, which can be initiated by offering CME credit for TRiM trainings. This will help to attract clinicians and graduate students. Collaborative efforts should be explored with Providence Alaska Medical Center to grow community engagement.
- Extend outreach to veterinary community by adding a member on the Translational Advisory Committee who is a physician familiar with the canine model in order to maintain focus on improving human health as long-term goal by using animal models, and to identify mechanisms that can be translated. Reach out to NIH Branch Chiefs to ask for their recommendations regarding use of canine trials.
- Support new faculty hires, including support for research faculty. This is important, because UA has lost faculty due to budget cuts and has not hired many new assistant professors as replacement.
- Increase institutional support of the TRiM cores as this is important for the grant renewal and TRiM’s long-term success.
- For the TRiM grant renewal application, name Prof. Kristen O’Brien as the new Center Director and appoint Prof. Drew as Deputy Director. Dr. O’Brien is an established scientist who can provide senior leadership to replace the departure of Dr. Robert Coker. Dr. Drew’s continued involvement as head of the Administrative Core will provide leadership continuity from TRiM in training its next generation of leaders.



Respectfully submitted:

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Margaret Rice, Ph.D., Professor and Vice Chair for Research, Dept. of Neuroscience and Physiology, NYU Grossman School of Medicine.