

UA Center for Transformative Research in Metabolism Translational Advisory Committee, Draft Agenda

Join Zoom Meeting

Date/ Time: Monday, January 17, 2022 (10:30 – 11:30 a.m. AST; 11:30 a.m. – 12:30 p.m. PST; 1:30 – 2:30 p.m. CST)

If you have any problems, please email Denise at: <u>dldaniello@alaska.edu</u> or Robert at: <u>rcoker@alaska.edu</u>

Participants	Attend	Invitees	Attend	Upcoming Meeting Dates
Robert Coker				
Denise Daniello				
Nicolaas Deutz				
Stacy Rasmus				
Katherine Tuttle				
Kelly Drew				

Торіс	Desired Outcome	Lead	
January 2021 Meeting Review	• Recap developments since January 2021 meeting. What has been done and work in progress. (Please see attached updates)	Robert and Denise	
Transitions	 Announcement and recommendations for how to move forward with building TRiM's translational capacity. Ideas for future partnering involving TRiM. 	Robert and All	
Prioritizing	 Discussion: Do the EAC recommendations line up (or not) with TAC's directives? (Please see attached EAC Recommendations & table of TAC meeting discussions as reference.) 	Robert and All	
Action Steps	 What action steps, if any, does the TAC want to take with respect to any of the EAC recommendations? EAC interim meeting is scheduled Feb. 7-8. What items do we want to include in the TAC report to the EAC? 	Robert and All	
External Partnerships	• How do we increase collaborations with providers during the pandemic? Should we change our focus?	All	
 A virtual EAC Interim Meeting is scheduled for February 7-8. All TAC members are welcomed to attend (9:00 a.m. to 12:30 p.m., <u>AST Day</u> Updates <u>1</u>, 2.7.2022 and 9:00 a.m. to 1:15 p.m. (<u>AST Day 2</u>, 2.8.2022). TAC and other TRiM committee reports are scheduled for Feb. 8 at noon. TAC member updates 		Kelly, Robert and All	
Junior/New Faculty Participation	• Engaging new investigators with TAC such as TRiM Pilot Project RPLs?	All	
	Schedule next meeting. Agenda items to discuss? Adjourn All		

Translational Advisory Committee, Draft Meeting Notes January 19, 2021

Members Present: TAC Chair Dr. Robert Coker, Dr. Kelly Drew, Dr. Stacy Rasmus, Dr. Katherine Tuttle, Dr. Nicholas Deutz, and Denise Daniello, MA (ex officio)

<u>Meeting Purpose</u>: Develop an action plan to enhance clinical research partnerships with health care providers.

Discussion Points:

- Recapped upcoming AI-AN CTRP Clinical Trial Training virtual series that will run every Friday afternoon from January 22 thru February 19, 2021. Marketing strategies include targeted outreach to Alaska INBRE, Alaska Native Tribal Health Consortium (ANTHC), Fairbanks Memorial Hospital, Chief Andrew Isaac Health Center, and Providence Hospital. Topics to be presented include an introduction to clinical trials and resources available (ITHS); PI presentations about clinical trial investigations being conducted (UAF, UAA, and ANTHC); IRB policies and regulations (UAF and MSU); and Tribal approval and data sharing agreements (ANTHC).
- Use the CTT series to set the stage for bringing together biomedical investigators with health care providers to share translational research being conducted at UA and for investigators to learn about unmet patient health care needs from the providers' perspective. Networking can lead to finding common ground and seed opportunities for collaborative clinical trial research.
- Discussed strategies to engage clinicians in research Assign a faculty title (but may be problematic on the types of titles that can be offered, due to union constraints), pay a meaningful consulting fee, and/or conduct research at the point of care so that clinicians can participate in research conducted within the clinical setting, without having to take time off from their job.
- Successful NIH proposals must be directed towards solving a compelling human health problem. Engage provider collaborators with experience in clinical trials and expertise in the population under study. Keep doors open to local and remote collaborations. Research outcomes that show "improved functioning" and "feeling better" due to an intervention are meaningful, especially in small clinical trials, and should be discussed in journal articles as they contribute to overall patient survival.
- Discussed strategies to support the CTR renewal (building on CTR's established network with rural communities and their providers) and ways to address NIH's critique of Dr. Coker's nutritional supplement clinical trial research. One potential area to explore is the intersection between metabolic health and behavioral health nutritional supplements that can help people with addictions to feel better with improved functioning and survival, without having to take a pill. This intervention type may be more acceptable to the patient and could build on the work of CTRP's focus on behavioral health and TRiM's metabolic perspective.
- Provided a quick update about TRiM's pilot project program including how many proposals were received (n=6), amount of funding available (\$80,000/year for two years, pending EAC approval), and reviews being conducted. Kelly noted that some of the pilot proposals requested funding for technique development, which could be potentially funded with carryover funds.
- Agreement that having open-ended TAC discussions are productive and will help to define our path forward to expand translational clinical research capacity for UAF and TRiM.

Proposed Action Steps:

- Engage clinicians: Plan an in-person "listening session" in the fall (pending it's safe to do so) to highlight examples of biomedical clinical research being conducted at UAF (AK INBRE, CTRP, and TRiM) and invite local clinicians. Investigators would provide brief presentations (5 minutes or so) that would highlight the basic science and how their research could be used as a tool in patient care. Develop a one-slide abstract for each presentation that would show as a backdrop to engage the audience. Emphasize how the work could translate into improved patient care (including a bottom-line statement in the slide backdrop) and request feedback from practitioners. Chances for a successful collaboration depend on being able to identify a clinical problem of high concern to providers and offering a translational solution at the point of care. Recognize that developing clinician relationships takes time. "Be patient and maintain the course" (Dr. Nicholas Deutz).
- Schedule next TAC meeting in late April or early May.



Center for Transformative Research in Metabolism (TRiM) Key Personnel Contributions: Grant Submissions, Publications, and Presentations in GY03 (6.1.2021 – 12.31.2021) for COBRE and non-COBRE effort

Proposals	Grants	Funding	Funding	Manuscripts	Manuscripts	Approved	Invited
Submitted	Awarded	Requested	Approved	Submitted	Accepted/Published	Abstracts	Presentations
17	7	\$7,780,721	\$3,443,644	26	21	3	19

The Center's Snapshot, GY03 (to date)

Note: All grant applications and manuscripts reported in GY03 were submitted by TRiM Key Personnel.

Robert Coker, PhD: PI Nutritional strategies for metabolic health in aging (Project 3); Chair, TRiM Translational Advisory Committee; Professor of Biology, Clinical Nutrition and Exercise Physiology, Institute of Arctic Biology, UAF

Research Support/Grants Awarded or Proposals Pending (not specifically related to COBRE)

- Department of Defense, United States Air Force Research Laboratory, Predictors of Physiological Resilience during Physical and Environmental Stress, \$550,000 awarded, 10.1.2021 – 9.30.2024. This project is a threeyear multi-site consortium between UAF (Site PI Robert Coker), University of Montana (Site PI Brent Ruby), and the University of Nebraska (Site PI Dustin Slivka).
- NIH/NCATS (National Institutes of Health/National Center for Advancing Translational Sciences, 5UL1TR002319-03), *Institute of Translational Health Sciences renewal application*, PI Nora Disis, Site PI Robert Coker. This five-year renewal to the UW-led ITHS was recently <u>awarded</u> (September 2021). There is a \$230,000 subaward specifically directed towards Dr. Coker's role as a Co-I on the Integrating Special Populations Core and his involvement in Translational Workforce Development
- NIH/National Institute of Diabetes and Digestive and Kidney Diseases), Northwest Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), PI Katherine Tuttle, Site **PI Robert Coker**, pending.
- NIH/National Cancer Institute R01, Early Detection of Genetic Risk (EDGER) in Rural Settings (PI: Deb Bowen; Site PI: **Robert Coker**) The proposed study will conduct a randomized controlled trial of point of care versus direct patient engagement to identify the best practices for genetic testing of cancer risk in rural communities, \$550K subaward to UAF, pending.
- NIH/National Institute on Aging U01, Improving Dementia Detection in Primary Care (PI: Elizabeth Phelan; Site PI: **Robert Coker**), \$1.2M subaward to UAF, pending.

Publications/Manuscripts

- Coker MS, Ladd KR, Schutzler SE, Park SY, Williams RH, Deutz NEP, Wolfe RR, Coker RH. Equivalent servings of free-range reindeer promote greater net protein balance compared to commercial beef, Int J Circum Health, 2021 80 1. doi: 10.1080/2243982.2021.1897222.
- Coker MS, Ladd KR, Murphy CJ, Ruby BC, Shriver TC, Schoeller DA, Newcomer BR, Taber KR, Bartlett L, **Coker RH**. *Alaska backcountry expeditionary hunting promotes rapid improvements in metabolic health in males and females*, Physiol Rep, 2021 9(1): e14682. doi:10.14814/phy2.14682.
- Rice SA, Ten Have GAM, Reisz JA, Gehrke S, Stefanoni D, D'Alessandro A, **Coker RH**, Deutz NEP, Drew KL. *Nitrogen recycling buffers against ammonia toxicity from skeletal muscle breakdown in hibernation*.

Nat Metab, 2020 2: 1459-1471. doi:10.1038/s42255-020-00312-4.

- Coker MS, Ladd KR, Clark F, Murphy CJ, Newcomer BR, Wolfe RR, **Coker RH**. *Essential amino acid enriched nutritional supplement promotes reductions in intrahepatic lipid in individuals with alcohol use disorder*, Nutrients, 2020 Jan 19, 12, 25. doi: 10.3390/nu12010254.
- Hassell L, Gregor C, Melvin A, Goss C, **Coker RH**, Laukes C, Albritton S, Brant J, Amoroso P, Whitener N, Tuttle KR. *Feasibility of connecting regional research programs to national studies by the CTSA Trial Innovation Network*. J Clin Trans Sci 2020 4 (2): 75-80. https://doi.org/10.1017/cts2019.437.
- Rosales AM, Dodds PS, Hailes WS, Sol J, **Coker RH**, Quindry J, Ruby BC, *Deterioration of lipid metabolism despite fitness improvements in wildland firefighters*, Med Sci Sports Exerc, Submitted July 1, 2021.
- Ruby BC, **Coker RH**, Sol J, Quindry J. *Physiology of the Wildland Firefighter, Environmental and Occupational Perspectives: Invited Review*. Comp Physiol, Revised and resubmitted.
- Kienast C, Biere K, **Coker RH**, Genov N, Joerres M, Maggioni MA, Mascarell-Maricic, Schalt A, Wypukol M, Gunga H-C, Steinach M. *Key Predictors to Successfully Cope with the Yukon Arctic Ultra: The Longest and Coldest Ultramarathon*. Front Physiol. Revised and resubmitted.
- Steinach M, Biere K, **Coker RH**, Gaul AL, Hoerl M, Jorres M, Kienast C, Mascarell-Maricic L, Schalt A, Gunga H-C, Chouker A, Rehm M. *Shedding of Glycocalyx during an Ultramarathon in a Subarctic Climate*, Med Sci Sports Exer. Revised and resubmitted.
- Coker MS, Barati Z, Murphy CJ, Bateman T, Newcomer BR, Wolfe RR, **Coker RH**, *Essential amino acids enriched meal replacement improves body composition and physical function in older, obese adults: a randomized controlled trial.* Clin Nutr, Submitted Sep 02, 2021.

Invited Presentations

- **Coker RH,** Ruby BC, Quindry J. Invited Symposium: *Friends and Enemies of Physiological Resilience*. American College of Sports Medicine Annual Meeting. June 5, 2021.
- Coker MS and **RH Coker**, *Nutrient Strategies for Metabolic Health in Aging*. Foundation Health Partners and Interior Public Health Partners, July 20, 2021
- **Coker RH**, *Early Detection of Genetic Risk in Rural Settings*. Alaska Native Tribal Health Consortium Brown Bag Series, July 21, 2021.
- Daniello D, Ground K, Drew K, **Coker RH**, Fedorov V, Duddleston K. *Translating hibernation research to promote healthy aging across the lifespan.* 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 3, 2021.
- **Coker RH**, Nutritional Strategies for Metabolic Health in Aging, Foundation Health Partners, Fairbanks, AK, October 6, 2021.
- Coker MS and **Coker RH**, Skeletal Muscle Function with Aging, Osher Life Long Learning Institute, October 11 and 13, 2021.

Professional Service

- Chair, Steering Committee, Northwest Participant Clinical Interactions Network, University of Washington led ITHS
- Appointed Member, NIH CTSA Diversity, Equity and Inclusion Task Force
- Appointed Member, Operations Support Team for COVID mitigation, UAF
- Regular Member, NIH NIDDK B Study Section
- Regular Member, UW ITHS Scientific Success Committee
- Chair, Translational Advisory Committee, TRiM, UAF
- Reviewer, UW-led Multidisciplinary Clinical Research Career Development program
- Reviewer, Alaska INBRE Grant Review Committee, UA System

• Innovation and Commercialization. Co-Owner and Lead Scientist of Essential Blends, LLC, a company focused on the development of medical nutrition products targeting obesity, sarcopenia, heart failure, and liver disease. The company has also developed a meal replacement formula designed to protect muscle loss during aging that will be tested using a clinical trial as part of the Center's research.

Kelly Drew, PhD, Director, Center for Translational Research in Metabolism and Professor, Institute of Arctic Biology, Department of Chemistry and Biochemistry, UAF

Research Support/Proposals Submitted:

- Alaska NASA EPSCoR Space Emergency Medicine: Drug Development at an Inflection Point, **\$30,092** awarded.
- Seed Fund Support, Center for Innovation, Commercialization and Entrepreneurship, UAF, **\$16,394** awarded.
- *Pharmacodynamic and Prototype Refinement of BCP-191.* Submitted to ITHS in the amount of **\$100,00** awarded.
- NASA (BRASH 20101), TRiSH Biomedical Research Advances for Space Health, \$995,995 (not approved)
- Alaska INBRE Carryover Request, MOD 21, "Develop and validate method to quantify small molecular weight compounds in brain tissue using LC-MS, \$14,500 requested (pending).
- Alaska INBRE Carryover Request, MOD 21, "Upgrade and replace malfunctioning equipment required for small animal surgery," \$25,608 requested (pending).
- NASA EPSCOR, preproposal, Drew K (PI), Fedorov V (Co-PI), Toien Oivind, Laughlin Bernard, and Goropashnaya Anya. *Translating Hibernation for Space Torpor and Remote Emergency Medicine*, \$750,000 (submitted on 11.8.2021, pending).
- Centers of Biomedical Research Excellence (COBRE) (P20) Mammalian Hibernation Research: A Path Towards a Center for Transformative Research in Metabolism \$11,810,112 (a 5-year NIH grant awarded July 16, 2019 thru June 30, 2023)

Publications/Manuscripts

- Frare C, **Drew KL**. Seasonal changes in adenosine kinase in tanycytes of the arctic ground squirrel (urocitellus parryii). J Chem Neuroanat. 2021;113:101920
- Rice SA, Mikes M, Bibus D, Berdyshev E, Reisz JC, Gehrke S, Bronova I, D'Alessandro A, **Drew KL**. *Omega 3 fatty acids stimulate thermogenesis during torpor in the Arctic Ground Squirrel*. Sci Rep. 2021: 11(1): 1340. PMCID PMC7809411
- Rice, SA; Ten Have, GAM4; Reisz, JA; Gehrke, S; Stefanoni, D; D'Alessandro, A; Deutz, NEP; **Drew, KL** *Metabolic tracing in vivo shows nitrogen recycling and myofibrillar breakdown in hibernation*. In Revision for Nature Metabolism
- Zanetti Fiammetta, Baker Hailey, Chen Chao-Yin, **Drew Kelly**, Sugiura Hoshi, and Barati Zeinab, *Characterization and seasonal modulation of adenosine A1 receptors in the arctic ground squirrel brain*. Hibernation and Daily Torpor (International Hibernation Symposium, Special Publication), (pending).

Invited Presentations

- **Drew, Kelly**, Understanding and Translating Hibernation for Neurocritical Care and Space Travel. One Health Seminar, October 11, 2021.
- **Drew, Kelly** L., Carlson, ZA, Frare, C, Rice, SA, Reisz, JA, D'Allessandro, A. *An Adenosine Model of Hibernation*. 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 4, 2021.

- Drew, Kelly L. *Transformative Research in Metabolism- A Center of Excellence in Hibernation Science*, Autophagy, Inflammation and Metabolism in disease Center of Biomedical Research Excellence (the AIM Center), April 6, 2021.
- Daniello D, Ground K, **Drew K**, Coker RH, Fedorov V, Duddleston K. *Translating hibernation research to promote healthy aging across the lifespan.* 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 3, 2021.

Approved Abstracts for 2022 Invited Presentations

- **Drew K** and D. Daniello. *The Fruits of Hibernation*. Osher Life Long Learning Institute, March 9, 2022 (abstract approved for invited presentation).
- Daniello D. and **Drew K**. *Translating Hibernation Research to Promote Healthy Aging*. American Society on Aging, April 13, 2022 (abstract approved for poster presentation)

Other Service and Appointments

- Founder and Chief Science Officer (CSO) of BeCool Pharmaceutics, LLC, a small molecule drug development company, focused on creating therapeutics to modulate metabolism and body temperature by mimicking mechanisms used in hibernation to provide emergency care for patients suffering cardiac arrest, neonatal hypoxic ischemic encephalopathy (HIE), spinal cord injury and stroke.
- Appointed, Director of Center for Transformative Research in Metabolism, 2019-present.
- Appointed, Chair TRiM Strategic Advisory Committee, 2019-present.
- Search committee, Attending Veterinarian, UAF, 2019-present.
- Biomedical Planning Committee, 2021-present.
- Coordinator, Biochemistry and Neuroscience Graduate Program, 2015-present.
- Appointed Coordinator for Biochemistry and Molecular Biology graduate program (renamed to Biochemistry and Neuroscience in 2014), 2011 to present.
- Scientific Program Committee for the 14th International Conference on Brain Energy Metabolism (ICBEM) Energy substrates and microbiome govern brain bioenergetics and cognitive function with aging Rescheduled for Oct 24-27, 2022, Santa Fe, NM.

Vadim Fedorov, PhD, PI, Post transcriptional mechanisms of muscle atrophy prevention in hibernating mammals (Project 1); Research Associate Professor, Institute of Arctic Biology, UAF. <u>Proposal Submission</u>

 NASA EPSCOR, preproposal, Drew K (PI), Fedorov V (Co-PI), Toien Oivind, Laughlin Bernard, Goropashnaya Anya. *Translating Hibernation for Space Torpor and Remote Emergency Medicine*, \$750,000 (submitted on 11.8.2021, pending).

Invited Presentation

• Fedorov, V. Post Transcriptional Mechanisms of Muscle Atrophy Prevention in Hibernating Mammals. Metabolomics Journal Club, October 22, 2021

Publications/Abstracts

 Edana Lord, Aurelio Marangoni, Mateusz Baca, Danijela Popović, Anna V. Goropashnaya, John R. Stewart, Meitje Germonpré, Elodie-Laure Jimenez, Natalia I. Abramson, Sergey Vartanyan, Stefan Prost, Nickolay G. Smirnov, Elena A. Kuzmina, Remi-André Olsen, Vadim B. Fedorov, Love Dalén. *Population dynamics and demographic history of Eurasian collared lemmings*. Ecology and Evolution (submitted, under review).

- Vadim B. Fedorov, Emiliano Trucchi, Anna V. Goropashnaya, Nils Chr. Stenseth. *Conflicting nuclear and mitogenome phylogenies reveal ancient mitochondrial replacement between two North American species of collared lemmings (Dicrostonyx groenlandicus, D. hudsonius)*. Molecular Phylogenetics and Evolution (submitted, under second review).
- Michelle Johannsen, Anna V. Goropashnaya, Stephanie Byrum, Oivind Toen, Brian M. Barnes, **Vadim B. Fedorov**. *American black bears (Ursus americanus) regulate metabolic and skeletal muscle homeostasis pathways during hibernation*. (Manuscript to be submitted in December 2021).

Khrys Duddleston, PhD, Pl Microbial provision of essential amino acids: protein conservation in hibernation (Project 2); Professor and Director of Biological Sciences, UAA.

Research Support/Grants Submitted

- NIH/National Institute of Diabetes and Digestive and Kidney Disease (NIDD), *Toward Microbial intervention for lean mass loss: the role of the gut microbiome in essential amino acid synthesis* (working title), R01 (to be submitted by 2.5.2022).
- NIH/National Institute of General Medical Sciences (NIGMS), Microbiota and inflammation in adiposity: The ground squirrel model, R15 (to be submitted by 2.25.2022).

Publications/Manuscripts

- Grond, Kirsten, Courtney C. Kurtz, Jasmine Hatton, Michelle M. Sonsalla, and Khrystyne N. Duddleston. Gut microbiome is affected by gut region but robust to host physiological changes in captive activeseason ground squirrels. Animal Microbiome, 3(56), published August 13, 2021, <u>https://doi.org/10.1186/s42523-021-00117-0.</u>
- Sonsalla, Michelle, Santidra Love, Lauren Summers, Hannah Follett, Aminata Bojang, Khrystyne N.
 Duddleston, and Courtney C. Kurtz. *Development of metabolomic inflammation during pre-hibernation fattening in thirteen-lined ground squirrels (Ictidomys tridecemlineatus)*. Journal of Comparative Physiology B, 191 (941-953), published June 24, 2021, <u>https://doi.org/10.1007/s00360-021-01384-8</u>.
- Rouse, Natalie, Katrina Counihan, Deborah Boege-Tobin, Caroline Goertz, and **Khrystyne Duddleston**. *Habitat associations between Streptococcus lutetiensis and Streptococcus phoacae in the marine environment*. Marine Ecology (Accepted with minor revision).
- Tomco, Patrick L., **Khrystyne N. Duddleston**, Adrienne K. Driskill, Jasmine Hatton, Kirsten Grond, Toshia L. Wrenn, Matthew A. Tarr, David C. Podorski, Phoebe A. Zito. *Dissolved organic matter production from herder application and in-situ burning of crude oil at high latitudes: Bioavailable molecular composition patterns and microbial community diversity effects.* Journal of Hazardous Materials, *In Press*.

Brandon Briggs, PhD, Advanced Instrumentation for Microbiome Studies (AIMS) Core Lead and Associate Professor, Department of Biological Sciences, UAA.

Research Support/Grant Submissions

- National Science Foundation Polar Programs, ANT LIA: Collaborative Research: Genetic Underpinnings of Microbial Interactions in Chemically Stratified Antarctic Lakes; 8.1.2020-5.31.2023 funding timeline; Role PI, **\$1,017,158 awarded**.
- DOE National Energy Technology Laboratory (NETL), *Bringing Alaska's CORE-CM potential into perspective*, 8.1.2021-7.30.2023 funding timeline; Role Senior Personnel; **awarded \$1,500,000**.
- Critical Materials Institute, *Novel non-acidic REE bio-recovery process from diverse minerals*, 1.1.2022 6.30.2023; Role Co-PI; request \$1,500,000, in review.

Manuscripts/Publications

- Eichelberger L, Subhabrata D, Howe T, Barnes DL, Bortz E, Briggs B, Cochran P, Dotson A, Drown D, Hahn M, Mattos K, Aggarwal S. *Implications of inadequate water and sanitation infrastructure for community spread of COVID-19 in remote Alaskan communities*. Science of the Total Environment, volume 776, July 1, 2021, https://doi.org/10.1016/j.scitotenv.2021.145842.
- Couture, J.M., Z.C. Redman, J. Bozzini, R. Massengill, K. Dunker, **B.R. Briggs**, P.L. Tomco (2022) *Field and laboratory characterization of rotenone attenuation in eight lakes of the Kenai Peninsula*, Alaska. Chemosphere: 288:132478

Invited Presentations

- Briggs, B. and Henderson, E. AIMS Core Overview. Metabolomics Journal Club, October 8, 2021.
- **Briggs, B.R**. *Geomicrobiomes of extreme environments and their biotechnological applications*. Miami University Microbiology Seminar Series (October, 2021)

Anna (Anya) Goropashnaya, PhD, Research Assistant Professor and TRiM Pilot Project RPL, IAB UAF Research Support / Proposals Submitted

- Alaska INBRE Carryover Request, MOD 21, *Conofocal and Fluorescence Microscopy at UAF*, \$80,974 requested 12.1.2021 (pending).
- NASA EPSCOR, preproposal, Drew K (PI), Fedorov V (Co-PI), Toien Oivind, Laughlin Bernard, Goropashnaya Anya. Translating Hibernation for Space Torpor and Remote Emergency Medicine, \$750,000 (submitted on 11.8.2021, pending).
- NIH NIGMS, *The Molecular Mechanisms Underlying Skeletal Muscle Temporal Dynamics in a Hibernating Mammal as a Pathway to Peripheral Artery Disease Intervention*. Approved \$40,000 as a pilot project awarded February 2021. (Note: This pilot project award was not counted in the overall award counts for June 1-December 31, 2021, but is included here as one of three TRiM pilot projects awarded since the last TAC meeting.)

Manuscripts/Publications

- Edana Lord, Aurelio Marangoni, Mateusz Baca, Danijela Popović, Anna V. Goropashnaya, John R. Stewart, Meitje Germonpré, Elodie-Laure Jimenez, Natalia I. Abramson, Sergey Vartanyan, Stefan Prost, Nickolay G. Smirnov, Elena A. Kuzmina, Remi-André Olsen, Vadim B. Fedorov, Love Dalén. *Population dynamics and demographic history of Eurasian collared lemmings*. Ecology and Evolution (submitted, under review).
- Vadim B. Fedorov, Emiliano Trucchi, **Anna V. Goropashnaya**, Nils Chr. Stenseth. *Conflicting nuclear and mitogenome phylogenies reveal ancient mitochondrial replacement between two North American species of collared lemmings (Dicrostonyx groenlandicus, D. hudsonius)*. Molecular Phylogenetics and Evolution (submitted, under second review).
- Michelle Johannsen, **Anna V. Goropashnaya**, Stephanie Byrum, Oivind Toen, Brian M. Barnes, Vadim B. Fedorov. *American black bears (Ursus americanus) regulate metabolic and skeletal muscle homeostasis pathways during hibernation*. (Manuscript to be submitted in December 2021).

Presentations

• Goropashnaya, AV. *Pilot Project Update, Peripheral Artery Disease*. Metabolomics Journal Club, December 10, 2021.

• **Goropashnaya, AV**. Genetic diversity and functional genomics of Northern species, Institute of Arctic Biology, June 18, 2021. (Dr. Goropashnaya presented this talk as a candidate for the Research Assistant Professor position to IAB.)

Oivind Tøien, PhD, Research Assistant Professor, TRiM Pilot Project RPL, and Manager of Animal Instrumentation, Health and Metabolism (HaMR) Core, IAB UAF

Research Support / Proposals Submitted

- NASA EPSCOR, preproposal, Drew K (PI), Fedorov V (Co-PI), Toien Oivind, Laughlin Bernard, Goropashnaya Anya. *Translating Hibernation for Space Torpor and Remote Emergency Medicine*, \$750,000 (submitted on 11.8.2021, pending).
- NIH NIGMS, Adaptations of Sleep and Cardiac Rhythms in the Hypometabolic State of a Human Sized Hibernator (Center for TRiM Pilot Project), approved \$71,089, February 2021. (Note: This pilot project award was not counted in the overall award counts for June 1-December 31, 2021, but is included here as one of three TRiM pilot projects awarded since the last TAC meeting.)

Presentations

- **Toien, Oivind** and Brian Barnes. *Absence of Circadian Activity Rhythms in Hibernating Black Bears Kept in Dark Dens*. 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 3, 2021.
- Zeinab Barati., Sugiura H., Wong A., Vitkovitsky, C., **Toien, O**., Pourrezaei, K. *Peripheral and Central Blood Flow Monitoring During Arousal from Torpor in Arctic Ground Squirrels*. 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 4, 2021.
- Barnes, Brian M., Wilbur Sarah, **Toien Oivind**, Buck C. Loren, Williams Cory T. *Circannual and Annual Rhythms in Captive and Free-Living Hibernating Ground Squirrels*. 16th Annual International Hibernation Symposium, Groningen, Netherlands, August 3, 2021.
- **Toien, Oivind**, *Hibernating black bears as a biomedical research model*, Institute of Arctic Biology, June 17, 2021. (Dr. Toien presented this talk as a candidate for Research Assistant Professor to IAB.)

Kriya Dunlap, PhD, Associate Professor of Biochemistry and TRiM Pilot Project RPL, IAB UAF Research Support /Grants Submitted

• NIH NIGMS, Vitamin D and Healthy Aging: Establishing the Sled Dog Sentinel for the Circumpolar North, (Center for TRiM Pilot Project), approved \$49,998, February 2021. (Note: This pilot project award was not counted in the overall award counts for June 1-December 31, 2021, but note is included here as one of three TRiM pilot projects awarded since the last TAC meeting.)

Publications/Manuscripts

- Witkop JJ, Vertigan T, Reynolds A, Duffy L, Barati B, Jerome S, Dunlap K. Sled dogs as a model for PM2.5 exposure from wildfires in Alaska. Environment International, volume 156, 10767, November 2021, <u>https://doi.org/10.1016/j.envint.2021.106767.</u>
- Chauhan, S, Dunlap K, Duffy L. Effects of Methylmercury and Theaflavin Digallate on Adipokines in Mature 3T3-L1 Adipocytes: A Recent Study. Current Advances in Chemistry and Biochemistry Vol. 6, 28 May 2021, pp 18-35, <u>https://doi.org/10.9734/bpi/cacb/v6/8134D</u>
- Dunlap K (author chapter 3), Dreher JD, Armando V, Freitas P, Ouideau S. (book editors of <u>Answering</u> <u>the Call of the Wild</u>). *Polyphenols in Traditional Therapeutic Practice*, 4.28.2021, <u>https://doi.org/10.1002/9781119545958.ch3</u>.

REPORT OF THE EXTERNAL ADVISORY COMMITTEE

1P20GM130443 "Mammalian Hibernation Research- A Path Towards a Center for Transformative Research in Metabolism" – Kelly Drew, Ph.D., Principal Investigator

June, 2021

On June 1-2, 2021, the External Advisory Committee (EAC) met to evaluate progress toward the goals of this COBRE grant since June, 2020. EAC members found progress over the past 12 months to be beyond adequate. Strengths of the program evident during this on-site visit included enthusiasm of the participants; the commitment and expertise of the administrative team; the facilities including office and laboratory space; the recently-approved pilot projects on sled dogs, bears, and the squirrel model of peripheral arterial disease; and the new Arctic Ground Squirrel (AGS) breeding facility. A significant step in the past year was the designation of the Center for Transformative Research in Metabolism (TRiM) as an official UAF Center.

Nonetheless, multiple challenges were identified. The EAC makes the following recommendations to the TRIM PI and UAF Administration:

- Initiate regular contact with the NIGMS Program Officer to assess whether the COBRE is meeting goals with a trajectory for continued funding.
- Educate UA administrators about needs and goals of the Center, how to balance compliance (e.g., teaching, IACUC) vs. productivity, and the short- and long-term value of a larger indirect cost recovery stream from research activities for the UA system.
- Work cooperatively to expand and utilize the current animal resource center needed by COBRE investigators to develop pre-clinical animal models to facilitate translation of their findings.
- The UAF Veterinarian Search Committee should actively seek candidates credentialed as Diplomates of the American College of Laboratory Animal Medicine, who would be likely to understand the research needs of the UAF TRiM Center.
- Consider teaching buyout for NIH Study Section service.
- Respond to recent faculty loss and budget cuts as an opportunity to recruit and groom additional research faculty.
- Increase productivity through more collaborations, both internally and externally.
- Utilize the Multi-PI mechanism for collaborative partnerships with established NIH investigators.
- To develop a pipeline of researchers for future development of UA system, UA should exploit its unique geographic, climatological and research resources as an asset to attract researchers at all levels from undergraduate to established researchers for short-term visits that may result in recruitments and create more external collaborations.
- Consider creation of nationally/internationally-advertised week- to month-long courses on Arcticoriented research to attract both students and external faculty.
- Consider sponsorship of conferences in collaboration with organizations such as the Gordon Research Conference, Keystone Symposia, etc. or with professional societies with interest in day-length or environmental factors affecting human biology.
- Implement the President's Professorships that were proposed as part of the TRiM application.
- Utilize "red team"/virtual study sections to pre-review proposals prior to submission.
- Send Specific Aims to EAC members for their feedback at least one month prior to proposal submission; follow up by sharing critiques.
- Potential synergism between Drs. Coker and Fedorov on muscle in AGS, bears, and humans remains to be exploited. A multi-PI basic science R01 proposal should be considered.
- Monthly or bimonthly check-up on career development plans for all project leaders.
- Regularly discuss productivity and publication obstacles with all project leaders.

- Monthly Zoom meetings between Drs. Drew, Duddleston, and Buck to help the project catch up after the challenges of the past year.
- Cost structure for the AIMS Core should be communicated to Dr. Drew and Ms. Daniello and be transparent to all.
- Request additional two months of salary for the manager of the Advanced instrumentation and Microbiome Studies (AIMS) Core.
- Continue to partner with Alaska INBRE to develop technical cores, such as an immunohistochemistry and microscopy core that leverages existing equipment to support ongoing projects.

Respectfully submitted,

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EAC 2021 Recommendations and Translational Advisory Committee Meeting Discussions

Categorized Groups of EAC recommendations discussed during the TRiM retreat:

EAC Recommendations, Session 1 (10.1.2021):

- a) Method of informing UA Administrators (EAC Recommendation #2)
- b) Expand and utilize animal resource center (EAC Recommendation #3)
- c) Recruit and groom research faculty and increase short-term visits to increase external collaborations (EAC Recommendations #6, #8)

EAC Recommendations, Session 2 (10.2.2021):

- d) Encourage use of multi-PI mechanism (EAC Recommendation #8)
- e) Arctic-oriented workshops, conference sponsorship with related organizations (Gordon, Keystone) (EAC Recommendations #10, #11)
- f) Increase successful grant submission (Red team) study sections (EAC Recommendation #13)

To be addressed by the administrative group:

• EAC recommendations 1, 4, 5, 11, 13, 17, 18, & 19

To be addressed during a future journal club:

- Individual Development Plans (IDP) (#15 EAC recommendation)
- Productivity/Publication Obstacles (#16 EAC recommendation)

External Advisory Committee (EAC)Purpose: As the scientific advisory board for the
Center, the EAC reviews program process,
critiques scientific progress of the Center, advises
the Center's Director on scientific and policy
matters, and works with the Director to facilitate
development of a sustainable, collaborative
research environment to support competitive
R01 proposals and research programs.Purpose:
Purpose:
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Translational Advisory Committee (TAC) Purpose: Advises the Center's Director regarding strategies to increase translational and clinical research capacity for TRiM and in Alaska.

EAC #1 - Initiate regular contact with the NIGMS Program Officer to assess whether COBRE is meeting goals with a trajectory for continued funding.	Not discussed by TAC
EAC #2 - Educate UA administrators about needs and goals of the Center, how to balance compliance to teaching, IACUC vs. productivity, the short- and long-term value of a larger indirect cost recovery stream from research activities for the UA system.	TAC Meeting Notes , <u>11.10.2020</u> Growth of clinical research is stymied by a lack of infrastructure and partnerships with local health care facilities/clinicians that must be filled in order to promote translational research at UA and in Alaska ("Identified Barrier").
	Inform administrators and providers about the benefits of doctors engaging in clinical research that can both benefit the institution (by supporting recruitment, training, and retention strategies) and benefit the patient by offering access to improved quality care through participation in clinical trials (Proposed "Action Step").
EAC #3 - Work cooperatively to expand and utilize the current animal resource center needed by COBRE investigators to develop pre- clinical animal models to facilitate translation of their findings.	Not discussed by TAC
EAC #4 - The UAF Veterinarian Search Committee should actively seek candidates credentialed as Diplomates of the American College of Laboratory Animal Medicine, who would be likely to understand the research needs of the UAF TRIM Center.	Not discussed by TAC
EAC #5 - Consider teaching buyout for NIH Study Section Service.	Not discussed by TAC
EAC #6 - Respond to recent faculty loss and	TAC Meeting Notes 1 19 2021
budget cuts as an opportunity to recruit and	Discussed strategies to engage clinicians in research –
budget cuts as an opportunity to recruit and	Discussed strategies to engage clinicians in research –
groom research jacany.	of titles that can be offered, due to union constraints), pay a meaningful consulting fee, and/or conduct research at
	the point of care so that clinicians can participate in research conducted within the clinical setting, without having to take time off from their job.
	 TAC Meeting Notes, <u>11.10.2020</u> Limited existing faculty and ability to hire new faculty due to budget constraints (Identified "Barrier"). Hire a research health care clinician to build clinical research capacity (Long-Term Goal). Difficult to engage local clinicians to do investigative clinical research because of increasing patient loads (rising senior population with complex medical needs) and workforce capacity (number of ratiring providers avecads number of setimes and setimate the set of the

	 new providers going into practice) (Identified "Barrier"). Build relationships with WWAMI in order to promote awareness and interest among medical students in clinical translational research (Proposed "Action Step"). Establish clinician partnerships locally to grow our pipeline of exploration for new faculty and to increase clinical trial capacity at UAF. Clinicians are our primary customers who serve their patients (our secondary customers). (Take-home meeting message)
collaborations, both internally and externally.	See relevant notes below under EAC #8.
EAC #8 - Utilize Multi-PI mechanism for	TAC Meeting Notes, <u>1</u> .19.2021
collaborative partnerships with established NIH	Discussed strategies to support the CTR renewal (building
investigators.	on CTR's established network with rural communities and their providers) and ways to address NIH's critique of Dr. Coker's nutritional supplement clinical trial research. One potential area to explore is the intersection between metabolic health and behavioral health – nutritional supplements that can help people with addictions to feel better with improved functioning and survival, without having to take a pill. This intervention type may be more acceptable to the patient and could build on the work of CTRP's focus on behavioral health and TRiM's metabolic perspective.
	TAC Meeting Notes, <u>11.10.2020</u>
	Explore possible connections between metabolism and
	cognition; subsistence and mental health. Are there
	(brain health) and mental health?
EAC #9 - To develop a pipeline of researchers for	TAC Meeting Notes, <u>1.19.2021</u>
future development of UA system, UA should	Engage clinicians: Plan an in-person "listening session" in
exploit its unique geographic, climatological,	the fall (pending it's safe to do so) to highlight examples of
and research resources as an asset to attract	biomedical clinical research being conducted at UAF (AK
researcners at all levels – from undergraduate	INBRE, CIRP, and IRIVI) and INVITE local clinicians.
that may result in recruitments and	or so) that would highlight the basic science and how their
importantly, create more external	research could be used as a tool in patient care. Develop a
collaborations.	one-slide abstract for each presentation that would show
	as a backdrop to engage the audience. Emphasize how the
	work could translate into improved patient care (including
	a bottom-line statement in the slide backdrop) and request
	collaboration depend on being able to identify a clinical
	problem of high concern to providers and offering a
	translational solution at the point of care. Recognize that
	developing clinician relationships takes time. "Be patient

	and maintain the course" (Dr. Nicholas Deutz) (Proposed
	Action step).
	 TAC Meeting Notes, <u>11.10.2020</u> TRiM and CTRP work together to develop partnerships and collaboration with Providence clinicians. Providence has a medical research program. Dr. Tuttle may be able to help us connect with Providence clinicians. Organize an opportunity for input from clinicians to understand their interests and priorities for research. Potentially coordinate with INBRE and CTRP to organize an event to get feedback and discussion from potential Alaskan clinical partners. Based on a recommendation from our EAC member Dr. Lathrop, TRiM is planning to host a seminar in May highlighting the work of our research targeting clinicians to provide us with feedback about this work particularly how well this work addresses health issues they observe in the community and how we can build strong working relationships going forward. TRiM to continue making stakeholder presentations. An upcoming presentation is being developed for Fairbanks Memorial Hospital (February 2021) and one statewide presentation has been conducted for Alzheimer's Resource Agency (November 2020). Difficult to engage local clinicians to do investigative clinical research because of increasing patient loads (rising senior population with complex medical needs) and workforce capacity (number of retiring providers exceeds number of new providers going into practice) (Identified Barrier). Limited relations with providers including Southcentral Foundation, Chief Andrew Isaac and Providence to support clinical trial research (Identified Barrier). Lack of partnerships with local medical providers and heath care institutions, particularly those with clinical research argeiry (Identified Barrier). Talk with clinicians ("our customer") to learn about health problems they see in the community. Clinicians are the voice of their patients.
EAC #11 - Consider sponsorship of conferences in collaboration with organizations such as the	Not discussed by TAC
Gordon Research Conference, Keystone	,

Symposia, etc. or with professional societies	
with interest in day-length or environmental	
factors affecting human biology.	
EAC #12 – Implement the President's	Not discussed by TAC
Professorships that were proposed as part of	
the TRiM application.	
EAC #13 - Utilize "red team"/virtual study	TAC Meeting Notes, 1.19.2021 TAC identified strategies to
sections to pre-review proposals prior to	increase successful grant submissions were:
submission.	 Direct the research towards "solving a compelling human health problem." Engage provider collaborators with experience in clinical trials and expertise in the population under study. Keep doors open to local and remote collaborations. Research outcomes that show "improved functioning" and "feeling better" due to an intervention are meaningful, especially in small clinical trials, and should be discussed in journal articles as they contribute to overall patient survival. TAC Meeting Notes, <u>11.10.2020</u> Work to address study section bias against support for clinical trials outside of large urban centers. Robert Coker's recent experience with his R01 submission was offered as a case in point.
EAC #14 Sand Specific Aims to EAC members	EAC recommendations #14 #21 wars not discussed by the
EAC #14 - Send Specific Anns to EAC members	EAC recommendations #14-#21 were not discussed by the
proposal submission; follow up by sharing critiques.	TAC, based of a review of the meeting notes.
EAC #15 – Potential synergism between Drs. Coker and Fedorov on muscle in AGS, bears, and humans remain to be exploited. A multi-PI basic science R01 proposal should be considered.	
EAC #16 – Monthly or bimonthly check-up on career development plans for all project leaders.	
EAC #17 – Regularly discuss productivity and publication obstacles with all project leaders.	
EAC #18 – Monthly zoom meetings between Drs. Drew, Duddleston and Buck to help the project catch-up after the challenges of the past year.	

EAC #19 – Cost structure for the AIMS Core should be communicated to Dr. Drew and Ms. Daniello and be transparent to all	
EAC #20 – Request additional two months of salary for the manager of the Advanced Instrumentation and Microbiome Studies (AIMS) Core	
EAC #21 – Continue to partner with Alaska INBRE to develop technical cores, such as an immunohistochemistry and microscopy core that leverages existing equipment to support ongoing projects.	