

TRANSFORMATIVE RESEARCH IN METABOLISM

Annual Report, FY19-FY20

GY01 Year in Review

National Institutes of Health, Institutional Development Award

NIGMS of the NIH Grant Award Number P20GM130443



Dr. Kelly Drew, Principal Investigator

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TRiM is the first and only biomedical research center in the U.S. to adopt a model of natural adaptations as an approach to treat metabolic diseases and related conditions, based on the translation of basic knowledge gained from the study of mammalian hibernation to improve human health.



The Institute of Arctic Biology has a 60-year history of research in hibernation. The intellectual and physical infrastructure for hibernation and metabolic health research at UAF coupled with strong institutional commitment for growth of biomedical research capacity led to a successful NIH Center grant. The grant (P20GM130443) supports creation of an official Center of Biomedical Research Excellence named *The Center for Transformative Research in Metabolism*. We are currently seeking recognition of official center status by UAF administration. The NIH award supports three research projects, two research cores, and one administrative infrastructure core under the umbrella of the new Center. The NIH award also supports the establishment of an arctic ground squirrel breeding colony. The goal of the Center is to bring together existing research activities related to hibernation, metabolism and metabolic health through multi-PI teams. The synergy of collaborative, cross-disciplinary research, inspired by the unique metabolic adaptations of hibernating and other arctic species, is expected to vertically advance understanding of human metabolic health. We aim to grow and sustain the Center through multi-faceted revenue streams generated by successful PI- and multi-PI initiated research grants, industry partners and state-wide stakeholder support.

Here we share who we are, what we do and the steps we are taking. The story is shaped largely by the structure and activities of the grant that brought us together. I ask that you help us imagine a future where the P20 grant will describe only a small portion of this great community resource.

Kelly Drew

Kelly Drew, PhD, PI for the Center for Transformative Research in Metabolism

University of Alaska, Fairbanks
Institute of Arctic Biology

Translating Hibernation Research to Promote Healthy Aging Across the Life Span

The UA Transformative Research in Metabolism (TRiM) is working to establish an interdisciplinary biomedical research center at the University of Alaska. Funded through the National Institutes of Health (NIH) National Institutes of General Medical Sciences (NIGMS) using the Centers of Biomedical Research Excellence (COBRE) funding mechanism ([P20GM130443](#)), TRiM supports three pilot research projects and three infrastructure cores to study hibernation and metabolism with the long-term goal of developing therapies and diagnostics to treat metabolic diseases such as diabetes, obesity, and cardiovascular disease that impact older adults and other people at-risk. This five-year grant, approved on July 16, 2019 in the amount of \$11.8 million, is eligible for 2 five-year grant renewals (for a total of 15 years) and an additional \$17 million.

TRiM's purpose is two-fold: (1) Establish a self-sustaining, multidisciplinary biomedical research center that builds on UA's legacy of hibernation research, infrastructure, and long-term commitment to apply what has been learned about the underlying mechanisms in hibernation into treatments that advance human metabolic health; and (2) Support the research and career development of both new and experienced scientists in all stages of translational studies related to hibernation, metabolism, and microbiome research in Alaska.

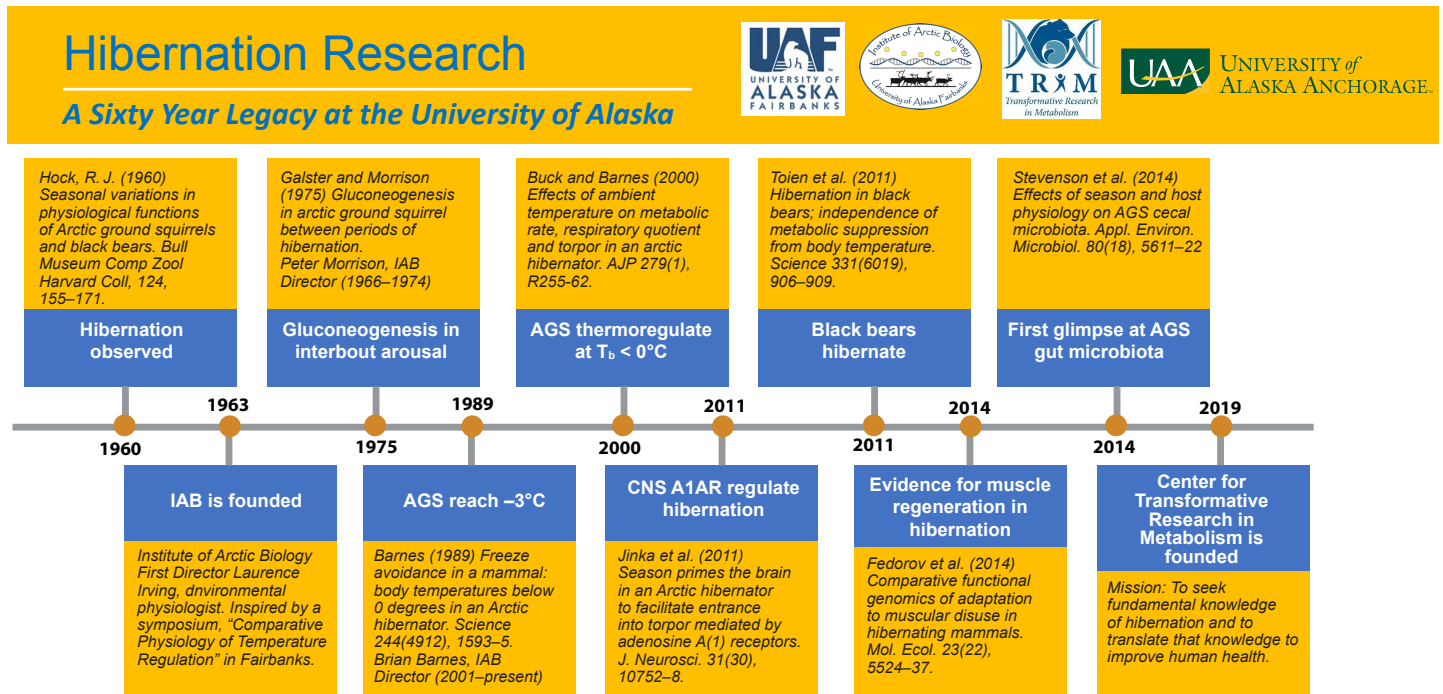
Overall, our specific aims are designed to build infrastructure and support research by UA investigators until it is competitive and successfully funded:

- SA1: Establish an organizational structure and research infrastructure comprised of an Administrative Core, a Microbiome Core (Advanced Investigations in Microbiome Sciences), and a Health and Metabolism Research Core that will support and promote a multidisciplinary framework that defines mechanisms of metabolic adaptations in hibernating mammals.
- SA2: Enhance the careers of experienced project leaders and new investigators leading pilot projects by using effective mentoring and collaboration plans involving established NIH-funded investigators that will allow new investigators to submit high quality, competitive proposals to NIH for their individual research grants.
- SA3: Support research and pilot projects to develop an understanding of hibernation mechanisms - physiological, genetic, and gut microbial - and define how these mechanisms may play a role in treating metabolic disease and muscle atrophy or sarcopenia.
- SA4: Support clinical research projects related to the theme of this Center.

TRiM utilizes the collaborative expertise and resources of research faculty and staff located at the University of Alaska Fairbanks (lead institution) and the University of Alaska Anchorage (partner institution).

What We Have Done

The University of Alaska is a world class leader in the field of hibernation research that has resulted in 60 years of scientific investigations and more than 100 publications authored by UAF investigators counted in Pub-Med alone. Research has focused on the physiologic, genetic, and microbiome mechanisms regulating hibernation that began in the 1960s.



What have we learned from this research?

Hibernation is a specialized adaptation that allows northern mammals to *comfortably* survive Alaska's long winters. Through research, we are learning that hibernating mammals reduce their metabolic rate to conserve energy and withstand prolonged periods of extreme cold and inadequate food availability.

Hibernators:

- Drop their body temperature below freezing,
- Preserve muscle mass and bone density despite not eating or moving for 8 months, and
- Switch from carbohydrate to fat metabolism during hibernation.

We have also discovered:

- Which genes turn on and off during hibernation, and
- How body chemicals change during hibernation.

Our research goals are to apply what has been learned about the mechanisms underlying the physiological changes in hibernation to address unresolved health issues relevant to metabolism and metabolic diseases such as disuse muscle atrophy, sarcopenia, obesity, Type 2 diabetes, and cardiovascular disease. Employing Arctic mammal models, such as arctic ground squirrels and black bears, has the potential to reveal fundamental mechanisms of mammalian metabolic regulation that may be not apparent in traditional laboratory species. In addition to basic research studying hibernation of northern mammals, our plan is to translate this knowledge into clinical trials utilizing human subjects in order to address metabolic disease and trauma.

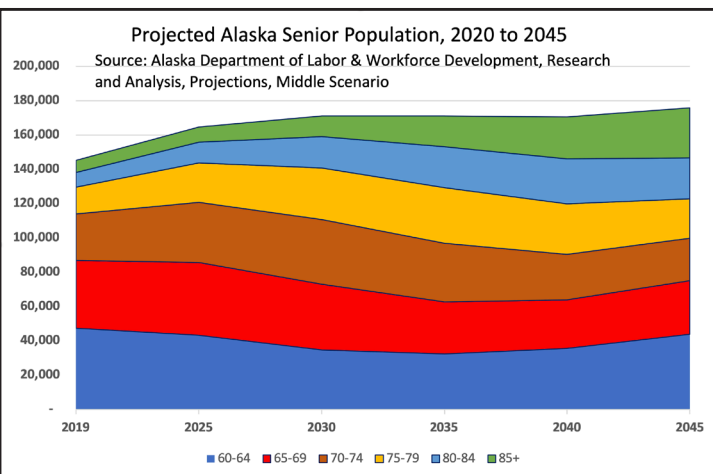
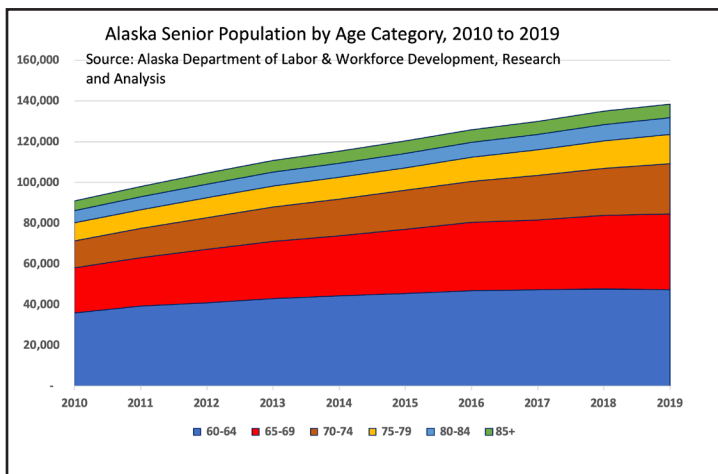
Why is the study of hibernation important to human health and Alaskan health?

Hibernation science has novel cues to treat metabolic disease and promote healthy aging across the life span. Type 2 diabetes, for example, the 6th leading cause of death among adults age 65+ in the U.S., is associated with other chronic health conditions related to metabolic disorders. Age increases risk for many diseases and frailty such as:



- Sarcopenia
- Disuse muscle atrophy
- Cachexia
- Anorexia
- Obesity
- Cerebral Ischemia and stroke
- Type 2 diabetes
- Osteoporosis
- Cardiac disease
- Fatty liver
- Fall Risk

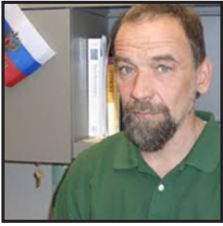
Alaska is the state with the fastest growing older adult population in the nation. Seniors are the fastest growing age segment in Alaska today with approximately 139,000 residents age 60+ (Alaska DOL-WD, Research and Analysis 2019). Looking forward to 2045, the senior population will continue to increase with those aged 85+ more than tripling in size based on current population estimates. Many older adults live with chronic metabolic health conditions, as age increases their risk, that may lead to disability, disease, and premature death. Moreover, Alaska is second in the U.S. with having the highest health care costs, behind the District of Columbia (Anchorage Economic Development Corporation 2016). Our goal is to translate hibernation science platforms into therapies and diagnostics to improve healthy aging across the life span and to turn the curve on the rising cost of health care in Alaska.



Who We Are: Research Projects and Cores

TRiM's central scientific focus is on the regulation of metabolic flexibility, anabolic sensitivity, and energy homeostasis and includes basic, translational, and clinical research informed by hibernation biology. Currently, TRiM has three research projects:

Post transcriptional mechanisms of muscle atrophy prevention in hibernating mammals, P.I. Vadim Fedorov, PhD.



PI Vadim Fedorov, PhD,
Genomics, UAF

Summary: Focuses on post-transcriptional regulation of genes involved in skeletal muscle metabolism during hibernation of arctic ground squirrels and black bears to identify targets for sustaining skeletal muscle mass and strength during prolonged disuse.

Microbial provision of essential amino acids, protein conservation hibernation, P.I. Khrys Duddleston, PhD.



PI Khrys Duddleston, PhD,
Microbiology, UAA

Summary: Determine the potential of the gut microbiota as a source of essential amino acids during prolonged fasting in hibernation.

Nutritional strategies for metabolic health in aging, PI Robert Coker, PhD.



PI Robert Coker, PhD,
Clinical Nutrition and
Exercise Physiology, UAF

Summary: Using a small clinical trial, this project aims to define how an experimental meal replacement containing an optimized blend of essential amino acids promotes skeletal muscle growth, improves indices of metabolic health, and modifies expression of anabolic genes in elderly, obese individuals.

Core Resources

The Administrative Core (UAF), Health and Metabolism Research Core (UAF), and the Advanced Investigations in Microbiome Sciences (UAA) comprise the organizational structure and research infrastructure that support the multidisciplinary framework to define mechanisms of metabolic adaptations in hibernating mammals.

Administrative (Admin) Core, Dr. Kelly Drew, PI and Core Leader:

The Admin Core provides oversight for TRiM's administrative and scientific functions. Dr. Drew leads the administrative components with scientific leadership and professional advising provided by members of the External Advisory Committee, Translational Advisory Committee, President's Professors, and other NIH-funded advisors to provide scientific mentoring enhancing the ability of TRiM's investigators to compete successfully for complementary NIH individual grants and other sources of support. The Admin Core oversees TRiM's cores as well as the Pilot Project Program to seed the growth of future new investigators and evaluate their progress.



Dr. Kelly Drew,
Admin Core Leader, UAF

Other key personnel include Anya Goropashnaya, Research Professional (UAF), Bahareh Barati, Biostatistician (UAF), Denise Daniello, Program Coordinator (UAF), and Brittany Wilhite, Fiscal Technician and Administrative Assistant (UAF).



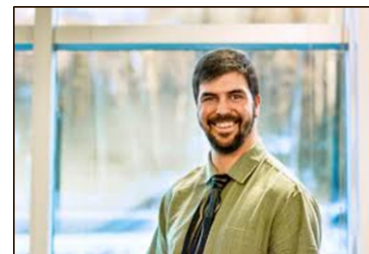
Dr. Cory Williams,
HaMR Core Leader, UAF

Health and Metabolism Research (HaMR) Core, Dr. Cory Williams, Core Leader:

The HaMR Core combines the existing Molecular Imaging Facility (MIF) at UAF with existing equipment and expertise in animal instrumentation. The goal of the Core is to co-locate basic research in hibernation with human subject's research to promote interdisciplinary collaborative and transformative discoveries and to adapt to TRiM's research needs. HaMR has evolved into a recharge center within the TRiM program utilizing user fees. Other key personnel include Dr. Carl Murphy, MIF Manager; Dr. Øivind Tøien, Manager of Instrumentation; and Scott Jerome, Research Navigator.

Advanced Instrumentation of Microbiome Sciences (AIMS), Dr. Brandon Briggs, Core Leader:

Characterization of microbial communities and isolates is a key element for TRiM's research projects. AIMS renovated facility, supported by the Alaska INBRE program, performs laboratory culturing, molecular analysis, and computer-based informatics in support of TRiM's Project 2, future pilot projects, production of Virtual Transport Medium (VTM) for Alaska's COVID-19 testing, and other users. This Core has incorporated 54 microbial species. AIMS is working to establish a recharge center to become self-supporting. Other key personnel include Eric Henderson, Lab Manager, and Tylor Fox, Lab Technician.



Dr. Brandon Briggs,
AIMS Core Leader, UAA

Core Resources of the Transformative Research in Metabolism: UAF and UAA

Admin Core



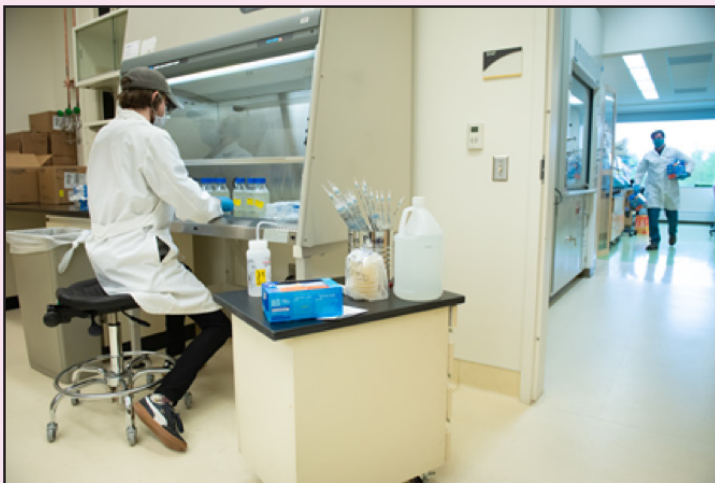
Professor Kelly Drew with her student measuring the core body temperature of a hibernating arctic ground squirrel.

Health and Metabolism Research (HaMR) Core



Dr. Carl Murphy, MIF Manager, with a hibernating black bear using the Toshiba Excelart/Vantage 1.5 Tesla MRI for diagnostic imaging at the Molecular Imaging Facility, UAF.

Advanced Instrumentation of Microbiome Sciences (AIMS) Core, UAA

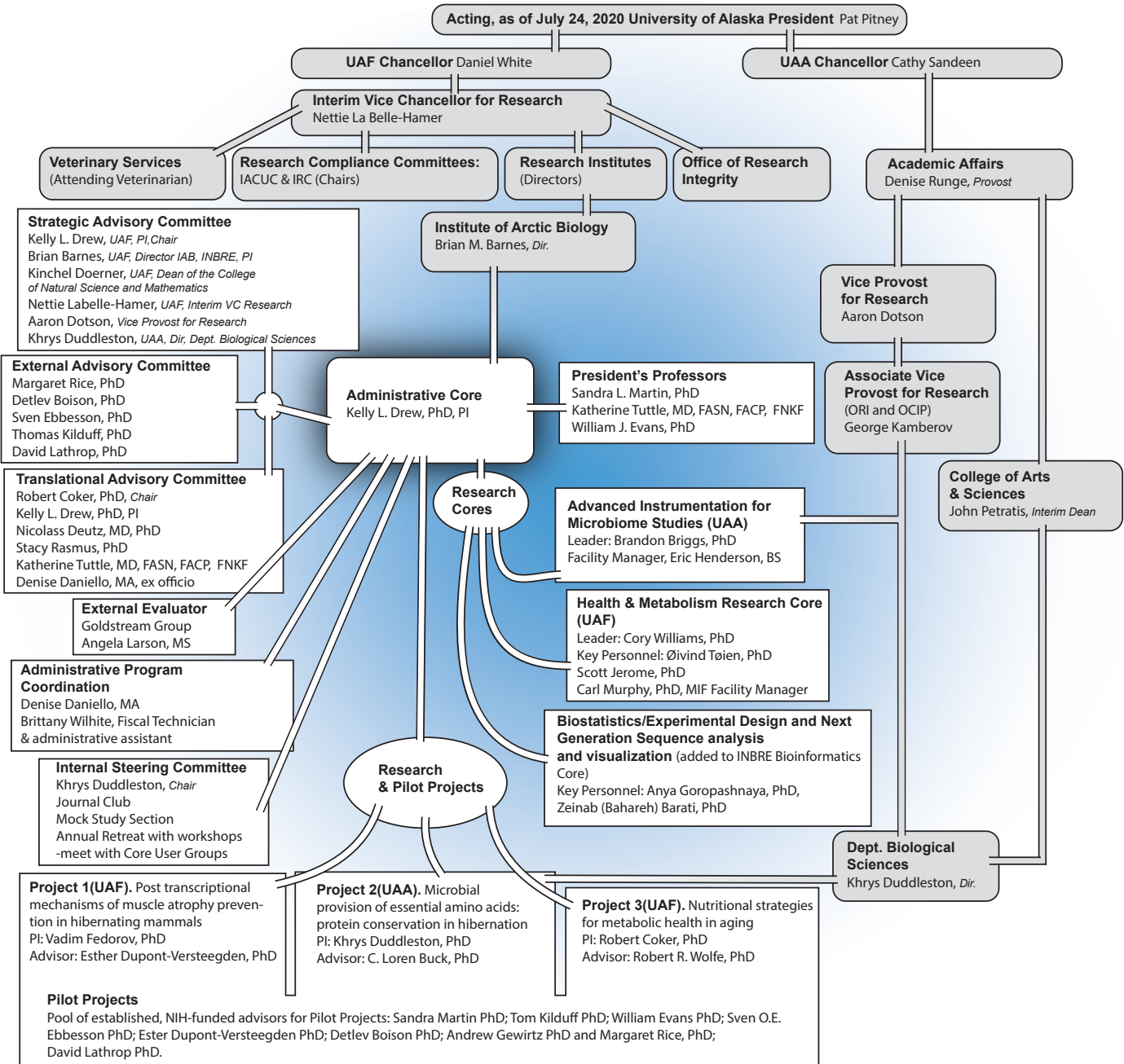


Tylor Fox, Lab Assistant (foreground) and Dr. Brandon Briggs (walking) conducting microbiome research at the AIMS Core lab.



The Anaerobic Chamber is used to grow microbes without oxygen.

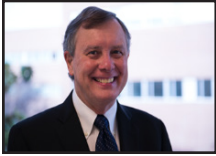
Transformative Research in Metabolism, Organizational Chart (as of 7.3.2020)



Committees—TRiM’s Committees, including the External Advisory Committee, President’s Professor Program, Translational Advisory Committee, and the Strategic Advisory Committee, are designed to provide scientific guidance and broaden professional networks to enhance opportunities with NIH-funded investigators. The Internal Steering Committee (ISC), with support from the Strategic Advisory Committee (SAC) and the External Advisory Committee (EAC), set direction for program research, adjust Core services to meet investigator needs, and promote the sustainability of the COBRE TRiM based on feedback, input, and their perspective. (Please see the Organizational Chart for members who serve on TRiM’s committees.)

External Advisory Committee (EAC):

The EAC is the main resource for NIH policy interpretation and guidance. The EAC reviews program process, critiques scientific progress of the COBRE TRiM, and advises the PI on scientific and policy matters. The EAC works with the PI to facilitate development of a sustainable, collaborative interdisciplinary research environment to support competitive R01 proposals and research programs. The PI consults with the EAC when developing and planning concepts and programs, identifying resources, evaluating development of the TRiM program, evaluating progress of individual research projects, and evaluating progress of TRiM's investigators toward acquiring independent status.



Dr. Thomas Kilduff, Director of the Center for Neuroscience at SRI International, serves as TRiM's EAC Chair.



Dr. Margaret E. Rice, Professor and Vice Chair for Research in the Dept. of Neuroscience and Physiology at the New York University Grossman School of Medicine.



Dr. Detlev Boison, Professor and Vice Chair of Research and Training at the Dept of Neurosurgery, Robert Wood Johnson Medical School and New Jersey Medical School, at Rutgers, The State University of New Jersey.



Dr. David A. Lathrop, Consulting Scientist and former Chief of the Heart Failure and Arrhythmias Branch in the Division of Cardiovascular Sciences at the National Heart, Lung, and Blood Institute of the National Institutes of Health.



Dr. Sven O. Ebbesson, Professor Emeritus, formerly served as a Professor at UAF in the areas of medical science, neuroscience, and marine science.

TRiM's Vision, Mission and Values

Vision: Translating hibernation research to improve human health

Mission: To seek fundamental knowledge about the nature and behavior of hibernating mammals and the translation of that knowledge to enhance human health, lengthen life, and reduce illness and disability.

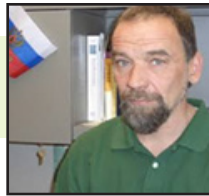
Value Statement: "TRiM"

- **T for Team Science:** Multiple, diverse perspectives and expertise empowers great and innovative science.
- **R for Respect:** Respecting each person for their unique perspective, expertise, and contribution to the overall effort.
- **I for Integrity:** Helping people to be the best at what they do best and keeping a high ethical standard.
- **M for Motivation:** Motivating oneself and others to do the job better than it has been done before in order to create a cycle of empowerment and accomplishment for both the scientific community and the Institute.

UAF and UAA faculty/staff working together to build a Center for Transformative Research in Metabolism



Kelly Drew, PhD
TRiM PI, UAF



Vadim Fedorov, PhD
Project 1 PI, UAF



Khrys Duddleston, PhD
Project 2 PI, UAA



Robert Coker, PhD
Project 3 PI, UAF



Cory Williams, PhD
HaMR Core Leader



Carl Murphy, PhD
MIF Facility Manager
HaMR Core, UAF



Oivind Toien, PhD
Manager, Animal
Instrumentation
HaMR Core, UAF



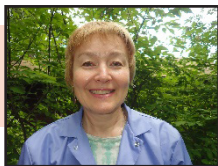
Scott Jerome, PhD
Research Navigator
HaMR Core



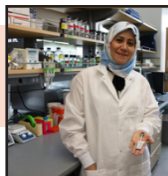
Brandon Briggs, PhD
AIMS Core Leader



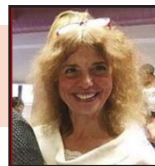
Eric Henderson BS
Lab Manager AIMS
Core, UAA



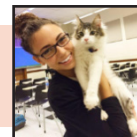
Anya Goropopashnaya,
PhD
Research Professional
Admin Core, UAF



Bahara Barati, PhD
Biostatistician Admin
Core, UAF



Denise Daniello, MA
Program Coordinator
Admin Core, UAF



Brittney Wilhite, MS
Fiscal Tech/Admin
Assistant Admin Core,
UAF



Hoshi Sugiura, BS, LVT
and Bernard Laughlin,
DO, PhD Candidate

What we are doing...

Alteration and Renovation: UAF LARS Arctic Ground Squirrel (AGS) Breeding Facility

The UA Transformative Research in Metabolism program utilizes hibernation as a natural adaptation model in metabolism to understand and develop treatments for metabolic diseases. UA has relied on wild, live-trapped arctic ground squirrels for laboratory investigations. However, this research is confounded by the prevalence of pathogens including Arctic Squirrel Hepatitis, which is endemic to Alaska's wild AGS population, as well as *Salmonella spp.*

Renovation of the UAF Large Animal Research Station (LARS) into the AGS Breeding Facility is being conducted with funding provided by the NIH COBRE grant. Dr. Jack Chen, Director of the Virology Unit of the Alaska State Public Health Laboratory, in collaboration with the UAF Animal Resource Center (ARC), will provide virus screening to identify hepatitis free founders as well as subsequent animals. ARC will provide animal care.

The AGS Breeding Facility will optimize 5,000 square feet of space to breed Hepatitis B free AGS in an open-air facility. Approximately 40 virus-free, live-trapped AGS from the Brooks Range will initiate the breeding facility. This facility will include six 500-sq. ft. pens used to house 30 pathogen-free wild AGS as founder animals. The expected completion date is August 1, 2020. The long-term goal is to provide pathogen-free AGS for UA researchers and their collaborators in a sustainable manner.

Preparing the site at the AGS Breeding Facility, UAF Large Animal Research Station (LARS)



1st Year Scientific Accomplishments

Grant Proposal Submissions by TRiM investigators:

- Two NIH RO1s submitted by PI Duddleston and PI Coker. Both received positive reviews. Resubmissions are on track for 7.6.2020.
- Administrative Supplement (PI Coker) to add sex as a variable to clinical trial – Pending
- M.J. Murdock Charitable Trust Commercialization grant (May 2020) (PI Coker) – Pending
- Dr. Cory Williams, HaMR Core Leader, submitted a proposal to NSF – Pending
- Hosted a virtual 2020 Hibernation Symposium featuring 13 presentations. Sixty-five participants attended the event and reported ‘high satisfaction,’ according to the participant evaluations.

Publications by TRiM investigators and core leads (7.16.2019-5.1.2020):

- 2 publications cited COBRE TRiM grant: Dr. Vadim Fedorov, PI
- 8 additional scientific publications authored by TRiM investigators: V. Fedorov, K. Duddleston, R. Coker, B. Briggs, C. Williams, C. Murphy and K. Drew
- 4 pending publications: V. Fedorov, A. Goropashnaya, R. Coker, B. Briggs, C. Murphy, and K. Drew

Presentations:

- 10 poster presentations
- 9 presentations: Invited speaker & stakeholder presentations

1st Year Infrastructure Accomplishments

- Established Core Resources: Admin Core, HaMR Core, and AIMS.
- Completed renovations plans for AGS Breeding Colony. Contractor is hired and work is underway.
- Completed renovation of the Microbiome AIMS facility (funded in part by the Alaska INBRE program).
- All new hires are now completed and TRiM’s cores and research projects are fully staffed.
- Provided outreach materials for legislative tour and other stakeholder events.
- Conducted videoconference meetings of the External Advisory Committee, Internal Steering Committee, Strategic Advisory Committee, and a planning meeting for the Translational Advisory Committee.
- Submitted NIH Research Program Progress Report (RPPR) and the Scientific Information Reporting System (SIRS) reports on time.
- Initiated public outreach and stakeholder engagement to raise awareness of the benefits of hibernation research and its promised health benefits.

Challenges: Budget Cutbacks and COVID-19 Setbacks

UA Budget Cuts and Fiscal Exigency: Resulted in faculty departures and imposed hiring freezes, which impacted research being conducted by PI Duddleston and facility renovations for the AIMS Core. Altered work-loads will threaten research productivity and retention of successful faculty.

COVID-19 Setbacks:

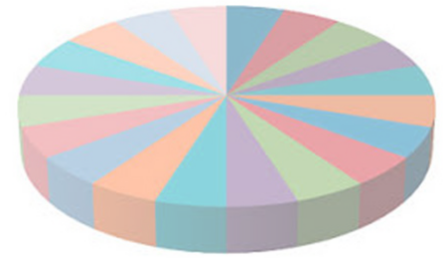
- Delayed submission of samples for ribosomal profile analysis needed by Project 1 which will affect the project's data analysis, project-related publications, and submission of a new collaborative R01 application by the PI and his advisor.
- Renovation work of the AIMS facility was temporarily put on hold due to partial closure of campus.
- Sample shipments from PI Duddleston's lab to the UC Denver metabolomics were delayed due to transportation barriers related to COVID-19.
- Postponed start of PI Coker's clinical trials as older adult participants are vulnerable to COVID-19. Trials will proceed when it is safe to do so as determined by NIH, Centers for Disease Control, and the project's advisors. PI Coker anticipates a new start date of November 1, 2020.
- Travel to conferences, training events, and meetings were cancelled impacting opportunities to make presentations and network with others working in the field.

Mitigation Efforts, Moving Forward

- Assembled COVID-19 related request for Carry Forward that will be submitted to NIH with the Federal Financial Report in mid-August 2020.
- AIMS Core is producing Virtual Transport Media (VTM) for the State's COVID-19 testing and receiving state funds to provide these services in addition to wastewater analysis for COVID-19 testing.
- Retention of successful and junior faculty and protection of research workloads was achieved, despite budget reductions.
- Access to Core resources continues with services sustained.

How we are doing it...

Business Model



Expenses

- Retain and nurture competitive investigators and Core resources
- Health and Metabolism Research (HaMR) Core
 - Clinical research capacity – Human
 - Clinical research capacity – Companion and working animals
- Advanced Instrumentation in Microbiome Sciences (AIMS) Core
 - Comprehensive services including organismal analysis, molecular analysis, and bioinformatics

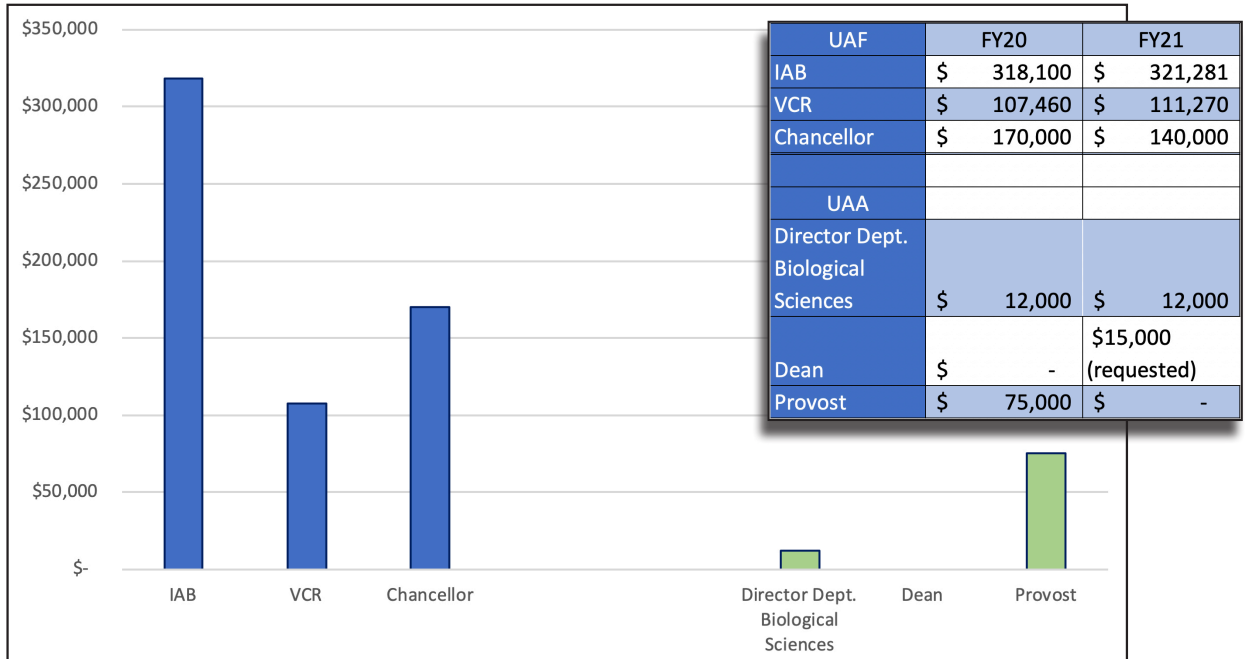
Revenue

- Current NIH COBRE award
- Competitive COBRE renewal in 2024
- Increase NIH R-series (for research) and equivalent funding
- Run cores as recharge centers. Expand core user base to offset UA support
- Develop discovery platforms for corporate partnering opportunities

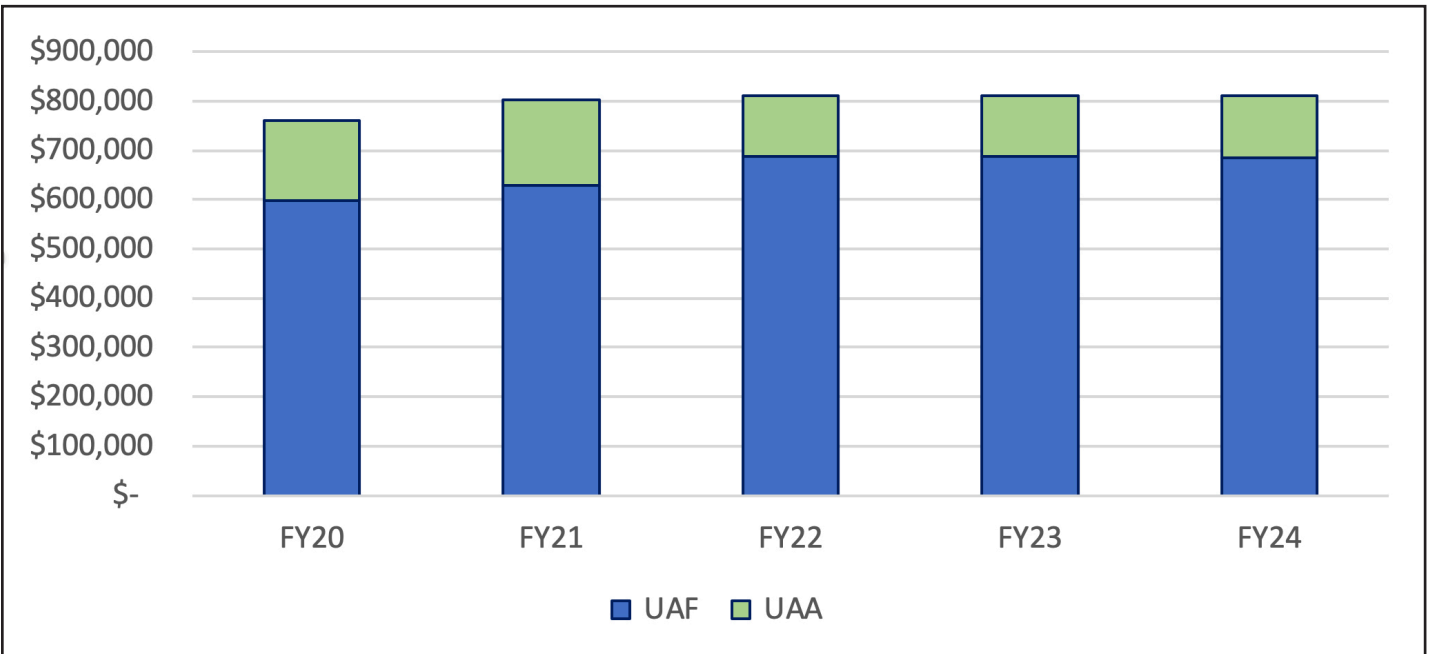
Revenues and Expenses

Overall TRiM Program		FY20	FY21	FY22	FY23	FY24
<u>Revenue</u>						
	COBRE Grant	\$ 754,775.77	\$ 1,439,148.00	\$ 1,440,306.00	\$ 1,440,306.00	\$ 1,440,306.00
	Other Grants	\$	\$	\$ -	\$ -	\$ -
	Other Support	\$ 266,139.00	\$ 189,000.00	\$ 194,000.00	\$ 194,000.00	\$ 194,000.00
	Forward "requested"	\$	\$ 224,000.00	\$ -	\$ -	\$ -
	Research User Fees	\$ 107,345.00	\$ 35,000.00	\$ 36,000.00	\$ 37,000.00	\$ 37,000.00
TOTAL REVENUE		\$1,128,259.77	\$ 1,887,148.00	\$ 1,670,306.00	\$ 1,671,306.00	\$ 1,671,306.00
<u>Expenses</u>						
Includes MIF	Salaries & Benefits	\$ 574,687.91	\$ 1,026,890.24	\$ 915,808.19	\$ 917,473.62	\$ 919,155.70
	Travel	\$ 14,394.65	\$ 72,916.00	\$ 53,259.00	\$ 51,859.00	\$ 51,859.00
	Contractual Services	\$ 202,452.14	\$ 340,832.00	\$ 310,520.00	\$ 314,020.00	\$ 312,570.00
	Commodities	\$ 176,136.85	\$ 200,195.00	\$ 384,044.00	\$ 381,944.00	\$ 383,394.00
	Equipment	\$ 45,055.99	\$ 51,000.00	\$ -	\$ -	\$ -
TOTAL EXPENSES		\$1,012,727.54	\$ 1,691,833.24	\$ 1,663,631.19	\$ 1,665,296.62	\$ 1,666,978.70
NET GAIN (LOSS)		\$ 115,532.23	\$ 195,314.76	\$ 6,674.84	\$ 6,009.38	\$ 4,327.30

FY20 Institutional Commitments Enhance Success and Sustainability of the *Center*



Projected Indirect (F&A) Dollar Amounts for UAA and UAF, FY20-FY24



Where we are going...

Opportunities on the Horizon

Developing new Research Collaborations

- ASCEND Hub, a NIH-sponsored coalition of 11 universities from western IDeA states formed to support innovation and entrepreneurship related to biomedical research, to identify opportunities for potential industry partnerships for TRiM's investigators and their research.
- Allen Brain Institute (ABI), Seattle Washington to share arctic ground squirrel (AGS) brain tissue samples collected by TRiM's investigators with ABI researchers that will be used to profile the molecular, genetic, anatomical and functional characteristics of AGS brain tissue.
- University of Kentucky to further understanding of muscle processes and the role they play in disuse muscle atrophy based on the work of PI Fedorov and his mentor, Dr. Dupont-Versteegden, UKY using an AGS animal model.
- Oxford University based on the work of Dr. Oivind Toien, HaMR Core to develop capabilities for sleep scoring in black bear.
- AIMS Core is actively supporting the research being conducted by PI Fedorov and PI Duddleston.

New pilot projects: Expected launch in FY22

Seeking UA-approval of Center status for the Transformative Research in Metabolism program. Why is this important? Because a Center status will:

- Build, strengthen, and leverage strategic investments made by UA to support biomedical and hibernation research in Alaska.
- Attract new funding (public and private investment), new partnerships (internal and external), and new investigators.
- Stimulate new biotech enterprise to increase partnerships between UA and the business community that will tap new revenue streams.
- Promote synergy of effort among UA programs in biomedical research to leverage resources and expand UA's funding base to grow our scientific capacity in biomedical research.
- Satisfy our commitment to NIH made in the grant application.
- Advance our long-term goal of increasing and sustaining Alaskan-based biomedical research scientists who are rooted in Alaska, care about our State's future, and committed to promoting the health and well-being of Alaskans.



Appendix A: Products resulting from TRiM's NIH COBRE award, July 16, 2019 through May 1, 2020 (GY01):

Manuscript published:

Fedorov V, Trucchi E, Goropashnaya A, Waltari E, Whidden SE, Stenseth NC. Impact of past climate warming on genomic diversity and demographic history of collared lemmings across the Eurasian Arctic, *Proceedings of the National Academy of Sciences of the United States of America*, January 27, 2020, doi: 10.1073/pnas.1913596117; PMID: 31988125. Funding Citations: National Science Foundation (10.13039/100000001) (EPS-0346770), (Grant 10.13039/100000057), NIH Alaska INBRE (P20GM103395), NIH COBRE (P20GM130443), and core funding of the Centre for Ecological and Evolutionary Synthesis, University of Oslo.

Vadim B. Fedorov, [_View ORCID Profile](#) Emiliano Trucchi, Anna V. Goropashnaya, Eric Waltari, Susan Erin Whidden, and Nils Chr. Stenseth

Meeting abstract, published:

Fedorov VB, Goropashnaya AV, Barnes BM, (2020) *Modulation of Gene Expression in Muscle of Hibernating Arctic Ground Squirrels (Urocitellus parryii)*, Federation of American Societies for Experimental Biology, Abstract published on-line, 4.19.2020. <https://doi.org/10.1096/fasebj.2020.34.s1.08897>. Funding Citations: NIH [R21AR064995]; NIH Alaska INBRE [P20GM103395]; **NIH COBRE [P20GM130443]**.

Other Publications by TRiM Investigators in Year 1 (names in bold):

Tian, Y., Wan, Y.-Y., Mu, H., H. Dong, **B.R. Briggs**, Zhang, Z (2019) *Microbial diversity in high temperature heavy oil reservoir*, *Geomicrobiology Journal*: doi:10.1080/01490451.2019.1662523. Funding Source: National Science Foundation.

Bishop M, Glasser, P, **Briggs, BR**, Pentrak, M, Stucki J., Boyanov, M. Kemmer, K, Kovarik, Dong H, (2019) *Reactivity of redox cycled Fe-bearing sediments towards hexavalent chromium reduction*. *Geochimica et Cosmochimica Acta*: 252:88-106. Funding Source: National Science Foundation.

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 multisite trials emanating from the CTSA Trial Innovation Network*. *J Clinical Translational Science*. 2020 Apr;4(2):75-80. doi: 10.1017/cts.2019.437. eCollection 2020 Apr. PubMed PMID: 32313695; PubMed Central PMCID: PMC7159807.

Coker MS, Ladd KR, Kim J, **Murphy CJ**, DeCort R, Newcomer BR, **Coker RH**, et al.

Essential amino acid supplement lowers intrahepatic lipid despite excess alcohol consumption.

Nutrients 2020;12, PMC7019240; *Nutrients* 2020, 12,254; doi:10.3390/nu12010254. Funding Source: NIH

Coker RH, Shin K, Scholten K, Johannsen M, Tsigonis J, Kim IY, Schutzler SE, Wolfe RR. *Essential amino acid-enriched meal replacement promotes superior net protein balance in older, overweight adults*, *Clinical Nutrition* 2019 Dec;38(6):2821-2826. doi: 10.1016/j.clnu.2018.12.013. Epub 2018 Dec 19. / PUBMED 30638738 / PMC6588419. Funding Source: NIH

Wilbur SM, Barnes BM, Kitaysky AS, **Williams CT**. *Tissue-specific telomere dynamics in hibernating arctic ground squirrels (Urocitellus parryii)*, *Journal of Experimental Biology*, 222(18), jeb204925, doi: 10.1242, PMID: 31515236, PMCID: PMC6765172. Funding Citations: NSF IOS-1558056 / NSF IOS-1558160 / NIH P20GM103395

Frare C, Jenkins ME, McClure KM, **Drew KL**. *Seasonal decrease in thermogenesis and increase in vasoconstriction explain seasonal response to N⁶-cyclohexyladenosine-induced hibernation in the Arctic ground squirrel (*Urocitellus parryii*)*, Journal of Neurochemistry, 2019 Nov;151(3):316-335. doi: 10.1111/jnc.14814. Funding Citations: TL4GM118992, NSF IOS-1258179, RL5 GM118990, NS081637, P20GM103395, TL4GM11899, R03NS081637.

Zhang Lin, Liu Xiao, **Duddleston Khrys**, Hines, Mark E. *The effects of pH, temperature, and humic-like substances on anaerobic carbon degradation and methanogenesis in ombrotrophic and minerotrophic Alaskan peatlands*, Aquatic Geochemistry, (4.6.2020) <https://doi.org/10.1007/s10498-020-09372-0>

Tomco Patrick L, Seefeldt Steven S, Rodriguez-Baisi Katinna, Hatton Jasmine J, **Duddleston Khry-styne**. *Sub-Arctic field degradation of metsulfuron-methyl in two Alaskan soils and microbial community composition effects*, Water, Air, & Soil Poll. 231:157 (2020) <https://doi.org/10.1007/s11270-020-04528-8>.

Manuscripts, pending in Year 1 (TRiM investigators and the TRiM COBRE grant citation in bold):

Dev S, Sachan A, Sachan F, Dehghani Ghose T, **Briggs BR**, Aggarwal S. *Mechanism of biological recovery of rare-earth elements from industrial and electronic wastes: A Review*. To be submitted to Chemical Engineering Journal. (2020). Funding Source: UNAC Faculty Initiative Fund.

Goropashnaya Anna V, Barnes Brian, **Fedorov Vadim B**. *Transcriptional changes in muscle of hibernating arctic ground squirrels (*Urocitellus parryii*): Implications for attenuation of disuse muscle atrophy*. Submitted to Scientific Reports (under review, submitted December 30, 2019).

Funding Citations: National Science Foundation (10.13039/100000001) (EPS-0346770), (Grant 10.13039/100000057) (P20GM103395), (**COBRE Grant P20GM130443**)

Coker, Melynda S, Ladd Kaylee, **Murphy, Carl J**, Ruby, Brent C, Shriver, Timothy C, Schoeller, Dale A, Newcomer BR, Bateman Terry, Bartlett Larry, **Coker Robert H**. *Alaska Backcountry Expeditionary Hunting Promotes Rapid Improvements in Metabolic Biomarkers in Healthy Males and Females*, To submit to Journal of Applied Physiology. Funding Citations: NIH Institutional Development Award (IDeA) under grant number P20GM103395 and the Biomedical Learning and Student Training Program (UL1GM118991, TL4GM118992, or RL5GM118990) and award number **P20GM130443** through the National Institute of General Medical Sciences of the National Institutes of Health. PubMed PMID: 30640843; PubMed Central PMCID: PMC6411444.

Rice, SA, Reisz, JA, Gehrke, S, D'Alessandro A, Deutz, N, **Drew, KL**. *Metabolic tracing in vivo shows nitrogen recycling and myofibrillar breakdown in hibernation*, in revision for Nature Metabolism. Funding Sources: NSF IOS 1258179; Institutional Development Award (IDeA) from NIGMS of the NIH 2P20GM103395 and **P20GM130443**; Boettcher Foundation Webb-Waring Early Career Award 2017; NIGMS RM1GM131968; and the National Heart, Lung, and Blood Institute (R01HL146442 and R01HL148151).

Appendix B: Conference/Meeting Presentations (GY01)

Briggs BB. *New Archaeal Phylum may be the Common Ancestor to Eukaryotes*, UAF Institute of Arctic Biology, Life Sciences Seminar, Fairbanks, AK, November 1, 2019.

Coker Robert. *Translational Medicine in the Mountain West*, Pharmacy Symposium, University of Wyoming, Laramie WY, February 1, 2020.

Coker Robert. *Identifying the Physiological demands in the Wildland Firefighter*, Rocky Mountain Wildland Fire, Boise State University, Boise ID, March 27, 2020.

Daniello Denise. *Transformative Research in Metabolism*, A Stakeholder Presentation, Alaska Commission on Aging and AgeNET Legislative Advocacy Meeting, Juneau, AK, February 2020.

Drew Kelly and Daniello Denise. *Transformative Research in Metabolism Overview*, NIH IDeA Western Regional Conference, Las Vegas, NV, October 8, 2019.

Kowalski MS, Bartlett L, Murphy CJ, Bateman T, Goropashnaya A., Fedorov V, Evans WJ, Coker RH. *Myogenic Responses to Alaska Backcountry Hunting*, Institute of Arctic Biology, Life Sciences Seminar Series, UAF, March 6, 2020.

Williams CT, Chmura HE, Duncan CM, Barnes BM, Buc CL, Christian, HC, Loudon, AS. *Re-imaging the Hibernating Brain: Hypothalamic Remodeling in an Arctic Hibernator*, Annual Meeting of the Society for Integrative and Comparative Biology, Austin, TX, January 2020 (co-author).

Williams CT, Shankar A, McCahon S, Callegari K, Seitz, T, Drown D. *SAD Rats: Effects of Short Photoperiod on Sleep Disruption, the Gut Microbiome, and Carbohydrate Consumption in Diurnal Grass Rats* Annual Meeting of the Society for Integrative and Comparative Biology, Austin, TX, January 2020 (co-author).

Williams CT, Duncan CM, Christian H, Chmura H, Buck CL, Barnes BM, Loudon A. *Ultrastructural Changes of Reproductive Neuroendocrine and Endocrine Responding Cells Associated with Circannual Timing in a Hibernating Mammal*, Austin, TX, January 2020 (co-author).

Williams CT. *Circannual Rhythms: From Molecular Mechanisms to Ecological Consequences*. University of Kentucky, Department of Biology Seminar Series, KY, January 2020 (invited speaker).

Posters

Coker Robert. *Alcohol Use Disorder*, Experimental Biology, San Diego, CA, April 5, 2020. (Event cancelled due to COVID-19).

Coker Robert. *Essential Amino Acid Supplement Lowers Intrahepatic Lipid in Individuals with Alcohol Use Disorders*, Experimental Biology, San Diego, CA, April 5, 2020. (Event cancelled due to COVID-19.)

Coker Robert, Coker, Melynda. *Translational Superior Influence of Reindeer Compared to Beef Ingestion on Protein Metabolism in Humans*, Experimental Biology, San Diego, CA, April 5, 2020. (Event cancelled due to COVID-19.)

Coker Robert, Coker, Melynda. *Rapid Improvements in Metabolic Health: Effect of Alaska Backcountry Expeditionary Hunting*; Obesity Week Conference, Las Vegas, NV, November 3-7, 2019.

Goropashnaya Anya, Barnes Brian, Fedorov Vadim. *Transcriptional changes in muscle of hibernating arctic ground squirrels (urocitellus parryii): implications for attenuation of disuse muscle atrophy*, One Health, One Future 2020 Conference, UAF, scheduled for 3.11.2020. (Event cancelled due to COVID-19 mandate.)

Goropashnaya Anya, Barnes Brian, Fedorov Vadim. *Modulation of Gene Expression in Muscle of Hibernating Arctic Ground Squirrels (urocitellus parryii) and Attenuation of Disuse Muscle Atrophy*, One Health, One Future 2020 Conference, UAF, scheduled for 3.11.2020. (Event cancelled due to COVID mandate.)

Williams CT, McCahol SL, Shankar A. *Effects of Short Photoperiod on Sleep and Carbohydrate Consumption in Diurnal Grass Rats*, Annual Meeting of the Society for Integrative and Comparative Biology, Austin, TX, January 2020.

Williams CT, Kynoch M., and Kielland, K. *Using Triaxial Accelerometers to Examine Activity and Hunt Rates in Canada Lynx (Lynx canadensis)*, Annual Meeting of the Alaska Chapter of The Wildlife Society, Anchorage, AK, February 2020.

Williams CT, Callegari K, Shankar A, Seitz T, Drown D. *Effects of Short Photoperiod and Carbohydrate Consumption of the Gut Microbiome of Diurnal Grass Rats*, Annual Meeting of the Alaska Chapter of The Wildlife Society, Anchorage, AK, February 2020.

Appendix C: Funding Proposals (GY01):

In Preparation:

Coker Robert. "Nutrient specific strategies for health and longevity," NIH R01 resubmission, \$1,147,435 (plan to submit on 7.5.2020).

Duddleston Khrys. "Toward microbial intervention for lean mass loss: The role of the gut microbiome in essential amino acid synthesis," NIH R01 resubmission, \$2,931,105 (plan to submit on 7.5.2020).

Submitted:

Coker Robert. "Sex-specific strategies for Health and Longevity," Administrative Supplement (NOT-GM-013), \$299,967 (submitted April 30, 2020), pending.

Williams Cory T. "Chronobiology of Predator-Prey Relationships in a Changing Arctic Ecosystem," National Science Foundation, \$775,305 (submitted in January 2020), pending.

List of all published works by investigator:

Kelly Drew, PhD, TRiM PI and Professor, UAF

<https://www.ncbi.nlm.nih.gov/myncbi/kelly.drew.1/bibliography/public/>

Vadim Fedorov, PhD, PI for *Post transcriptional mechanisms of muscle atrophy prevention in hibernating mammals*. Research Associate Professor, UAF

<https://www.ncbi.nlm.nih.gov/myncbi/1tAdSJFhcczQE/bibliography/public/>

Khrys Duddleston, PhD, PI for *Microbial provision of essential amino acids, protein conservation hibernation*. Professor and Director of Biological Sciences, UAA

<http://www.ncbi.nlm.nih.gov/sites/myncbi/khrystyne.duddleston.1/bibliography/45704998/public/>

Robert Coker, PhD, PI for *Nutritional strategies for metabolic health in aging*. Professor of Biology; Clinical Nutrition and Exercise Physiology, UAF

<https://www.ncbi.nlm.nih.gov/myncbi/robert.coker.1/bibliography/public/>

Melynda Sheri Coker, BS

<https://www.ncbi.nlm.nih.gov/myncbi/1pohkTjCSxRcdz/bibliography/public/>

Cory Williams, PhD, HaMR Core Lead and Assistant Professor of Biology, UAF

<https://scholar.google.com/citations?user=YsIVjdsAAAAJ&hl=en&oi=ao>

Brandon Briggs, PhD, AIMS Core Lead and Associate Professor, UAA

<https://scholar.google.com/citations?user=BSTge74AAAAJ&hl=en>

Carl Murphy, PhD, Molecular Imaging Facility Manager, UAF

<https://scholar.google.com/citations?hl=en&user=rRDM5icAAAAJ>

Oivind Toien, PhD, Animal Instrumentation Manager, UAF

<https://www.ncbi.nlm.nih.gov/myncbi/oivind.toien.1/bibliography/53972374/public/>

Appendix D: External Advisory Report, June 30, 2020

REPORT OF THE EXTERNAL ADVISORY COMMITTEE

1P20GM130443-01 “Mammalian Hibernation Research- A Path Towards a Center for Transformative Research in Metabolism” – Kelly Drew, Ph.D., Principal Investigator

June, 2020

On June 22-23, 2020, the External Advisory Committee (EAC) for 1P20GM130443-01 met to evaluate progress toward the goals of this COBRE grant. The COBRE, led by Dr. Kelly Drew as PI, is administratively located within the Institute of Arctic Biology (IAB) at the University of Alaska (UA), whose Director, Dr. Brian Barnes, strongly supports the Center’s mission. Both Drs. Drew and Barnes are world authorities on mammalian hibernation.

1P20GM130443-01 supports three research projects and three core facilities to study hibernation as a path to develop transformative approaches to mitigate human disease and improve health. One of the projects is a clinical trial, the first to be conducted in Fairbanks. Progress during Yr1 has been excellent. The team demonstrated resilience and adaptability to establish the new COBRE, overcoming COVID-19 impediments and geographic distance (Anchorage and Fairbanks are ~350 miles apart).

Intra-institutional challenges discussed include:

- Fiscal exigency of the UA system, exacerbated by the COVID-19 pandemic, and the resultant uncertainties regarding faculty retention and future teaching loads.
- Designation of the Center for Transformative Research in Metabolism (TRiM) as an official Center within IAB and the UA system.
- Faculty retention, particularly successful NIH R01-funded investigators.
- Uncertainty regarding eligibility of non-tenured faculty to serve as COBRE Project Leaders or IAB-supported pilot projects.

The EAC discussed that it will be critical for TRiM to increase project interactions to both strengthen the COBRE and increase the likelihood of extramural funding. A first step should be a series of internal meetings of COBRE investigators to discuss ideas to promote research collaborations and build on untapped synergisms. These activities could lead to the development of multi-PI R01 proposals and, as a longer-term goal, a P01 submission.

Retention of NIH-funded faculty was identified as a major concern. Continued communication and outreach to UAF and UAA Administrations are strongly recommended. The EAC was concerned by a comment from an administrator who stated that a UA PI who is awarded an NIH grant and then leaves UA reflects well on UA as a place for career growth. Although some institutional migration can be expected, this mindset may prevent the administration from taking steps to *improve* retention. Losing quality investigators affects morale as well as viability of the research enterprise. This perspective negatively affects the ability of research programs such as TRiM to realize their full potential and successfully compete for NIH support, as the perceived quality of institutional support and resources is a scored evaluation criterion of any NIH proposal. Leaders such as Drs. Barnes, Drew and Duddlestone have worked tirelessly to build successful research programs and are encouraged to keep reminding the administration and Legislature about their achievements. The PI is also advised to broaden the number of transformative/translational projects to realize the COBRE’s mission.

Appendix D (continued)

Specific recommendations are:

1. Continue submission of NIH R21 and R01 research grant proposals. Explore other funding mechanisms to support the Center's mission.
2. Use NIH Career Development Awards (K-awards) to develop/retain research investigators. Use individual NIH Fellowship (F-awards) to support new and visiting investigators in hibernation research. Such mechanisms could help develop/support clinically-oriented scientists to translate basic science findings.
3. Develop projects to test the effectiveness of newly-identified therapeutic approaches based on mammalian hibernation principles.
4. Advance opportunities to expand therapeutic applications of mammalian hibernation by planning a conference supported by an NIH R13 Conference Grant to discuss/develop science-based therapies.
5. Continue community outreach to raise awareness of the benefits from hibernation research and its promised health benefits.

Respectfully submitted,

Detlev Boison, Ph.D., Professor and Vice Chair of Research and Training, Dept of Neurosurgery, RWJMS and New Jersey Medical School at Rutgers, The State University of New Jersey.

Thomas S. Kilduff, Ph.D., Director, Center for Neuroscience, SRI International

David Lathrop, Ph.D., Consulting Scientist and former Chief of the Heart Failure and Arrhythmias Branch, Division of Cardiovascular Sciences, NHLBI/NIH.

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