Thursday, September 16, 2021

Quarterly update from the DMRC

Colleagues,

We would like to start this update by acknowledging our situation: this is not the place we hoped to be in the fall of 2021. We have experienced a number of setbacks in the COVID-19 pandemic, and its challenges continue to weigh on all of us. But through it all, the **research programs in the DMRC have excelled**.

We are grateful for the support you have shown to us and to each other. Thank you for the actions you each take, big and small, to keep diabetes and metabolism research moving forward and ensure that our community remains collegial and engaged.

Some people call **COVID-19 a marathon** (one that nobody would have signed up for), and Dr. Megan Call has some tips on how to get to the finish line together. Please continue to take care of yourselves, to cheer on your colleagues, and to let us know how we can help.

In the year ahead, we are looking forward to connecting with each of you, virtually and in-person

- The Seminars in Metabolism and the Health Behaviors Seminar Series will be held in hybrid formats—both in large lecture halls and on zoom. We encourage you to attend in-person, if you are able and comfortable.
- Save the date for the 2021 Diabetes and Metabolism Research Fall Retreat on November 8th through the 12th, from 12pm to 2pm. This year will again be conducted in a virtual format over around lunch time (to minimize zoom fatigue!).

Finally, welcome to the new members of the DMRC community: Drs. Chaix, Estabrooks, Hill and Lee! We are thrilled that you have joined us. We look forward to working with you and getting to know you better.

Take care,
Scott Summers & Jared Rutter, DMRC Co-Directors

Welcome new DMRC investigators!

Welcome to the four new DMRC investigators who recently joined or will soon join us at the University of Utah! Be sure to reach out to these new community members and introduce yourselves.

Amandine Chaix, PhD

Assistant Professor, Nutrition and Integrative Physiology, College of Health

Focus: Dynamic relationship between nutrition, metabolism, and the circadian clock inhealth and disease

Paul Estabrooks, PhD

Professor, Health and Kinesiology, College of Health (*starting January 2022*)

Focus: Dissemination and implementation science: physical activity promotion, healthful eating, and weight control

Jennie L. Hill, PhD

Associate Professor, Population Health Sciences, School of Medicine

Focus: Population-based health outcomes of obesity, physical activity and nutrition

Shinduk Lee, DrPH, MSPH

Assistant Professor, Division of Health Systems and Community-Based Care, College of Nursing

Focus: Healthy aging; chronic disease prevention and management

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Good News

Successful first cohort of the "Summer Research Program in Microbiology, Immunology, and Metabolism"

From left to right: Lethan Hampton (Fairfax lab), Keke Fairfax, Mya Coleman (Summers lab), Kennedy Chastang (Lamb lab), Lauryn Banks (Tantin lab), Kamiya Watkins (Maria Bettini lab)

The DMRC was proud to support the first cohort of the "Summer Research Program in Microbiology, Immunology, and Metabolism," a program held in partnership with the department of Pathology.

Under the direction of Keke Fairfax, five students from Spelman College and Howard University completed a summer internship in research labs at U of U Health. The students participated in professional development sessions, enjoyed fun activities across Salt Lake City, and presented their research projects in a final poster session (pictured above). Several students said they look forward to applying to graduate school at the U.

Contact Sara or Dr. Fairfax if you are interested in hosting a student next summer!

Dr. Bill Rutter (left) posing with Dr. Scott Summers (right)

Scott Summers Awarded William J. Rutter, PhD, Presidential Endowed Chair in Biochemistry

In August of 2021, Scott Summers was awarded the inaugural William J. Rutter, PhD, Presidential Endowed Chair in Biochemistry. This award recognize Scott's "transformative impact on U of U Health, the College of Health, and Department of Nutrition and Integrative Physiology as an academic leader and researcher."

About Dr. Bill Rutter

This award is given in honor of Dr. Bill Rutter (pictured above), a former Chair of UCSF's Department of Biochemistry and Biophysics and a co-founder of Chiron. As one of the early adopters of recombinant DNA technology, Rutter and his colleagues cloned and characterized the insulin genes and hepatitis viruses and produced the world's first recombinant vaccine (against Hepatitis B). Often described as the "Father of Biotechnology," Dr. Rutter received the Heinz Award "for his role in helping to create the biotechnology industry and for his interest in shaping the industry to serve society." He has been elected into the National Academy of Sciences and the American Academy of Arts and Sciences. In 2021, Rutter was awarded an honorary doctorate at the University of Utah.

Building Sustainable Equity, Diversity, and Inclusion (EDI) Initiatives

The DMRC has led or supported two large NIH proposals to support EDI community development at the U.

1. NIH FIRST Grant Update

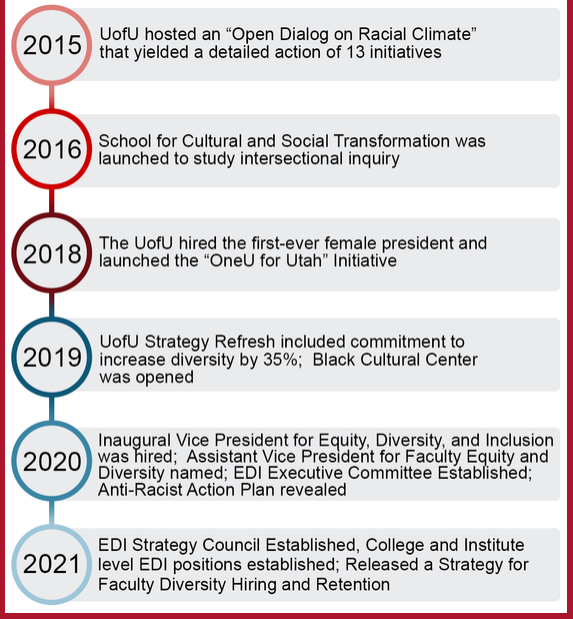
The U submitted an NIH FIRST application (PIs: Kola Okuyemi, Angela Fagerlin, Martin Tristani-Firouzi, Erin Rothwell) with a program called, the "Building Biomedical Research Inclusion & Diversity to Grow Excellence in Science (Building BRIDGES)" program. Building BRIDGES would fund faculty recruitment and development for investigators with a strong commitment to EDI.

We received a priority score of 24 and are waiting for notices of award to be released.

2. Building BRIDGES to a Diabetes Research Career – a postdoctoral and junior faculty training program

The DMRC submitted an application (PI: Scott Summers) to support postdoctoral recruitment and development. This program would leverage the platform of Building BRIDGES, and would support postdocs and junior faculty through a robust training and pilot and feasiblity program.

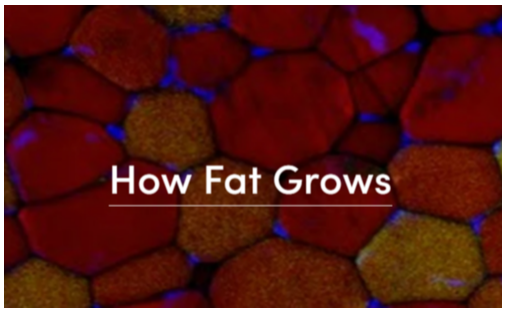
Scientific Merit Review will be held in November 2021.



UofU commitment to transforming the institutional EDI culture.

Research Highlights

Pioneering the Future is a series highlighting prominent health sciences discoveries made at the University of Utah. Check out these great stories featuring DMRC investigators.



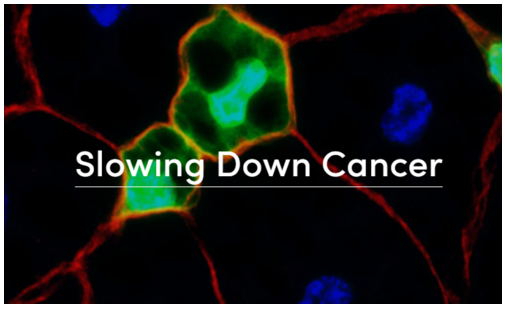
How Fat Grows

Sihem Boudina, PhD, studies how visceral fat forms and expands in response to excess calorie consumption. This kind of fat can increase in two ways: the fat cells can become larger, or they can summon a kind of stem cell that will spawn new fat cells. Boudina and her colleagues discovered a set of molecular signaling events that lead to fat cell growth. Learning more about how these different mechanisms work could reveal opportunities to intervene against intractable obesity or to stave off metabolic disease or cardiovascular disease.

Learning from Disease-Resistant Animals

The genetic factors that influence disease risk are not exclusively in our genes. Scattered throughout our genome are regulatory elements that influence when, where, and how much our genes are used. To find ways these regulatory elements can help stave off disease, Christopher Gregg, PhD, Elliot Ferris, PhD, and colleagues look to the genomes of animals with biomedical

superpowers. They have scoured the DNA of elephants, which rarely get cancer despite their large size and numerous cells; hibernating bats and squirrels, which pack on weight in preparation for a sedentary winter, yet don't become obese or develop metabolic problems.Their findings point researchers toward potential targets for preventing or treating human disease.

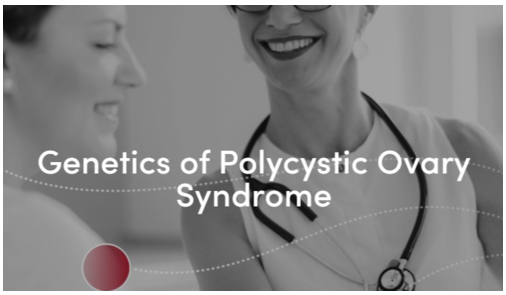


Slowing Down Cancer

Cells obtain energy from several different types of fuel, but the simple sugar glucose is particularly important in cancer cells. Normally, cells burn sugars for energy inside a mini-organ called the mitochondria. Cancer cells prevent pyruvate from entering the mitochondria, diverting it instead to metabolic pathways to produce building blocks.

Biochemist Jared Rutter, PhD, and colleagues discovered molecules called MPCs, for "mitochondrial pyruvate carriers," which act as doorways to let pyruvate enter the mitochondria. Their work revealed that the choice of whether to import pyruvate has far-reaching medical implications. As cancer cells accumulate genetic mutations that enable uncontrolled growth and reproduction, mutations that reduce MPC production make the tumor more aggressive and deadlier. Importantly, adding MPC back to the tumor can slow down its growth. "We hope that this information can be used to design therapies that are specifically toxic to cancer cells," Rutter says.

Genetics of Polycystic Ovary Syndrome



Large genetic analyses are helping researchers understand complex conditions such as polycystic ovary syndrome (PCOS), a hormonal disorder that disrupts menstrual cycles and arrests egg development. Women with PCOS have variable symptoms: Many develop acne and excess facial hair, and weight gain, type 2 diabetes, and depression are also common. A study led by Division of Endocrinology Chief Corrine Welt, MD, suggests that cases of PCOS share the same genetic origins regardless of which symptoms have been used to diagnose them. Welt and her team identified 14 gene variants associated with PCOS, including three that had not previously been linked to the disorder. Some of the variants affect genetic pathways also implicated in depression, type 2 diabetes and obesity. Understanding the genetic risk factors for PCOS could help physicians diagnosis the disorder earlier and better manage its potential complications.

Exercise Boosts Cells' Energy Effeciency

Molecular biologist Katsu Funai, PhD, recalls his mother injuring her ankle when she was just 44

years old. Even after several surgeries, her mobility remained limited, and she suffered from lifelong illnesses across multiple organ systems. That experience fuels Funai's drive to understand how exercise affects cellular metabolism. "My passion for medical research is driven by my conviction that the root of all these diseases is the inactivity that she suffered since her injury."

Funai and his colleagues discovered that exercise increased the amount of a certain fat molecule, called phosphatidylethanolamine (PE), in the inner membrane of the mitochondria. Having PE in the membrane made the mitochondria produce energy more efficiently. His research puts lipids into a new light: addressing their role on mitochondrial function could lead to therapies for treating diabetes and heart disease.

New Publications (abridged)

- Ingoglia F, Chong JL, Pasquali M, Longo N.. **Creatine metabolism in patients with urea cycle disorders.** Mol Genet Metab Rep. 2021 Aug 23;29:100791. doi: 10.1016/j.ymgmr.2021.100791. eCollection 2021 Dec.

  Petrocelli JJ, Mahmassani ZS, Fix DK, Montgomery JA, Reidy PT, McKenzie AI, de Hart NM, Ferrara PJ, Kelley JJ, Eshima H, Funai K, Drummond MJ.. **Metformin and leucine increase satellite cells and collagen remodeling during disuse and recovery in aged muscle.** FASEB J. 2021 Sep;35(9):e21862. doi: 10.1096/fj.202100883R.

  Litchman ML, Ng A, Sanchez-Birkhead A, Allen NA, Rodriguez-Gonzales B, Iacob E, Greenwood DA.. **Combining CGM and an Online Peer Support Community for Hispanic Adults with T2D: A Feasibility Study.** J Diabetes Sci Technol. 2021 Aug 20:19322968211032278. doi: 10.1177/19322968211032278. Online ahead of print.

  Shields KL, Broxterman RM, Jarrett CL, Bisconti AV, Park SH, Richardson RS.. **The passive leg movement technique for assessing vascular function: the impact of baseline blood flow.** Exp Physiol. 2021 Aug 19. doi: 10.1113/EP089818. Online ahead of print.

  Stewart KL, Gigic B, Himbert C, Warby CA, Ose J, Lin T, Schrotz-King P, Boehm J, Jordan KC, Metos J, Schneider M, Figueiredo JC, Li CI, Shibata D, Siegel E, Toriola AT, Hardikar S, Ulrich CM.. **Association of Sugar Intake with Inflammation- and Angiogenesis-Related Biomarkers in Newly Diagnosed Colorectal Cancer Patients.** Nutr Cancer. 2021 Aug 9:1-8. doi: 10.1080/01635581.2021.1957133. Online ahead of print.

  Fix DK, Ekiz HA, Petrocelli JJ, Mckenzie AM, Mahmassani ZS, O'Connell RM, Drummond MJ.. **Disrupted macrophage metabolic reprogramming in aged soleus muscle during early recovery following disuse atrophy.** Aging Cell. 2021 Aug 8:e13448. doi: 10.1111/acel.13448. Online ahead of print.

  Steinberg BA, Zhang M, Bensch J, Lyons A, Bunch TJ, Piccini JP, Siu A, Spertus JA, Stehlik J, Wohlfahrt P, Greene T, Hess R, Fang JC.. **Quantifying the Impact of Atrial Fibrillation on Heart Failure-Related Patient-Reported Outcomes in the Utah mEVAL**

Program. J Card Fail. 2021 Jul 26:S1071-9164(21)00299-2. doi: 10.1016/j.cardfail.2021.07.009. Online ahead of print.

Shankar TS, Ramadurai DKA, Steinhorst K, Sommakia S, Badolia R, Thodou Krokidi A, Calder D, Navankasattusas S, Sander P, Kwon OS, Aravamudhan A, Ling J, Dendorfer A, Xie C, Kwon O, Cheng EHY, Whitehead KJ, Gudermann T, Richardson RS, Sachse FB, Schredelseker J, Spitzer KW, Chaudhuri D, Drakos SG.. **Cardiac-specific deletion of voltage dependent anion channel 2 leads to dilated cardiomyopathy by altering calcium homeostasis.** Nat Commun. 2021 Jul 28;12(1):4583. doi: 10.1038/s41467-021-24869-0.

Schlegel A.. **Identifying Glucocorticoid Insufficiency in Silent Corticotroph Adenoma with Elevated Adrenocorticotropic Hormone.** Lab Med. 2021 Jul 16:lmab053. doi: 10.1093/labmed/lmab053. Online ahead of print.

Ost KS, O'Meara TR, Stephens WZ, Chiaro T, Zhou H, Penman J, Bell R, Catanzaro JR, Song D, Singh S, Call DH, Hwang-Wong E, Hanson KE, Valentine JF, Christensen KA, O'Connell RM, Cormack B, Ibrahim AS, Palm NW, Noble SM, Round JL.. **Adaptive immunity induces mutualism between commensal eukaryotes.** Nature. 2021 Aug;596(7870):114-118. doi: 10.1038/s41586-021-03722-w. Epub 2021 Jul 14.

Depner CM, Rice JD, Tussey EJ, Eckel RH, Bergman BC, Higgins JA, Melanson EL, Kohrt WM, Wright KP Jr, Swanson CM.. **Bone turnover marker responses to sleep restriction and weekend recovery sleep.** Bone. 2021 Nov;152:116096. doi: 10.1016/j.bone.2021.116096. Epub 2021 Jun 30.

Trott DW, Machin DR, Phuong TTT, Adeyemo AO, Bloom SI, Bramwell RC, Sorensen ES, Lesniewski LA, Donato AJ.. **T cells mediate cell non-autonomous arterial ageing in mice.** J Physiol. 2021 Aug;599(16):3973-3991. doi: 10.1113/JP281698.

Smith JD, Carroll AJ, Fu E, Berkel C.. **Baseline Targeted Moderation in a Trial of the Family Check-Up 4 Health: Potential Explanations for Finding Few Practical Effects.** Prev Sci. 2021 Jun 22. doi: 10.1007/s11121-021-01266-z. Online ahead of print.

Ose DJ, Viskochil R, Holowatyj AN, Larson M, Wilson D, Dunson WA, Deshmukh VG, Butcher JR, Taylor BR, Svoboda K, Leiser J, Tingey B, Haaland B, Wetter DW, Fisher SJ, Hashibe M, Ulrich CM.. **Understanding the Prevalence of Prediabetes and Diabetes in Patients With Cancer in Clinical Practice: A Real-World Cohort Study.** J Natl Compr Canc Netw. 2021 Mar 10;19(6):709-718. doi: 10.6004/jnccn.2020.7653.

Gibson B, Simonsen S, Barton J, Zhang Y, Altizer R, Lundberg K, Wetter DW.. **Motivation and Problem Solving Versus Mobile 360° Videos to Promote Enrollment in the National Diabetes Prevention Program's Lifestyle Change Program Among People With Prediabetes: Protocol for a Randomized Trial.** JMIR Res Protoc. 2021 Jun 14;10(6):e28884. doi: 10.2196/28884.

Opportunities

Postdoc Opening: Computational Approaches to Diabetes and Metabolism T32 Training Grant

- We are requesting for applications for one postdoctoral slot for the Computational Approaches to Diabetes and Metabolism T32 Training Grant. The goal of this program is to cross-train students in the computational sciences and in the biological basis of diabetes, metabolism, and obesity. Each trainee will be required to be co-mentored by a computational and biological mentor.
  Here is the RFA and coversheet. The application deadline is October 31, 2021.

Access the Cardiovascular Genetics Biobank

- The DMRC has acquired a large number of clinical serum samples from researchers from the prior Division of Cardiovascular Genetics. These include clinical studies relating to body habitus (e.g. studies of extreme familial thinness, familial obesity, gastric bypass), premature coronary artery disease, heart failure, diabetes, etc. These collections are indexed with electronic health records and contain extensive information about clinical outcomes. If you would like to discuss ways to collaborate and use these samples in your study, please contact Scott Summers.

Metabolomics Core Support Program

The goal of the Metabolism Core Support Program is to provide financial support for University of Utah faculty to either:

- develop new methodology in metabolism that will be used by the broader DMRC research community or
- to encourage new research explorations into metabolism that otherwise would not be possible without DMRC support.

Learn more here.

Save the Date!

The Diabetes and Metabolism Virtual Research Fall Retreat will be held every day the week of November 8-12, from 12-2pm daily.

Download the calendar invite here.

2021 DIABETES & METABOLISM VIRTUAL RESEARCH RETREAT

Monday, November 8 - Friday, November 12
12:00PM - 2:00PM daily

HEALTH
UNIVERSITY OF UTAH

#DMRC2021

MONDAY — RESEARCH TALKS & DISCUSSIONS

Research Talks, 12:00PM - 1:15PM
- Stavros Drakos, MD, PhD
- Corrine Welt, MD
- Jennie Hill, PhD

Breakout Discussions, 1:15PM - 2:00PM
- Faculty discussion & Trainee discussion

TUESDAY — KEYNOTE & POSTERS

Keynote Presentation, 12:00PM - 1:00PM
Barbara Kahn, MD
George R. Minot Professor of Medicine, Harvard Medical School, Senior Faculty, Division of Endocrinology, Diabetes and Metabolism, Beth Israel Deaconess Medical Center

Virtual Poster Session, part 1, 1:00PM - 2:00PM

WEDNESDAY — KEYNOTE & POSTERS

Keynote Presentation, 12:00PM - 1:00PM
Korey Hood, PhD
Professor of Pediatrics (Endocrinology and Diabetes) and of Psychiatry and Behavioral Sciences (Child and Adolescent Psychiatry), Stanford University

Virtual Poster Session, part 2, 1:00PM - 2:00PM

THURSDAY — RESEARCH TALKS & DISCUSSIONS

Research Talks, 12:00PM - 1:15PM
- Keke Fairfax, PhD
- Amy Locke, MD
- Maria Bettini, PhD

Breakout Discussions, 1:15PM - 2:00PM
- Faculty discussion & Trainee discussion

FRIDAY — RESEARCH TALKS & DISCUSSIONS

Research Talks, 12:00PM - 1:15PM
- Shinduk Lee, DrPH, MSPH
- Micah Drummond, PhD
- Matt Wahl, MD

Breakout Discussions, 1:15PM - 2:00PM
- Faculty discussion & Trainee discussion

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