Welcome to the 2023 Newsletter for the UCSD/UCLA Diabetes Research Center! 2023 marks the 20th year of operation for our center; we started as one of the first regional Diabetes Centers funded by NIDDK and became a model for many others that followed. This past year has been a fruitful one for the Center, which continues to support the diabetes and metabolism research activities of two major universities within the UC system and three outstanding institutes in Southern California. Our four biomedical research cores continue to operate at the cutting edge, providing crucial services to a wide array of our DRC membership. Our research base has contributed with numerous important papers, and our P&F program again has supported outstanding young faculty to help launch their careers in biomedical sciences. We are in the midst of the 7th year of our highly successful Monthly Metabolism Meetings, featuring speakers from all of the institutions that comprise our Center. Our 2022 DRC Retreat, held at the Luskin Center at UCLA was a huge success, with Drs. Ron Evans from the Salk Institute and Shingo Kajimura from Beth Israel Deaconess and Harvard Medical School giving outstanding Keynote lectures. We closed with a luncheon for all attending participants who numbered over 200 people in total. This year’s retreat is scheduled for March 22, 2023, at the Sanford Stem Cell Center in La Jolla, featuring keynote lectures from Drs. Dale Abel of UCLA and Scott Sternson from UCSD.
2023 Retreat

Wednesday, March 22, 2023
9AM – 3:30PM
Sanford Consortium for Regenerative Medicine
2880 Torrey Pines Scenic Drive
La Jolla, CA 92037

KEYNOTE SPEAKER
Scott Sternson, Ph.D.

Neuroscience & Chemical Biology
University of California, San Diego
Professor of Neuroscience
“Algorithms for Appetite”
## OPENING ADDRESS

<table>
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<tr>
<th>Time</th>
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<tr>
<td>9:00 AM</td>
<td>Welcome and Introduction - DRC Director Dr. Alan Saltiel</td>
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| 9:10 AM  | E. Dale Abel, MD, PhD<br>
**Chair and Executive Officer of the Department of Internal Medicine, Professor of Medicine, Biochemistry, and Biomedical engineering – UCLA**<br>“Mitochondrial Dynamics and Cardiometabolic Disease” |

## 2023 PILOT AND FEASIBILITY AWARD TALKS

<table>
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<th>Time</th>
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| 10:10 AM | Vala Hamidi, MD<br>
**Assistant Clinical Professor – UCSD Health**<br>“The effect of Mirabegron on ADRB3 expression in subcutaneous white adipose tissue in humans” |
| 10:30 AM | Matthew Wortham, PhD<br>
**Assistant Adjunct Professor, Dept of Pediatrics - UCSD**<br>“Epigenomic control of cell state governs beta cell adaptation and failure” |
| 10:50 AM | Coffee Break                                             |
| 11:00 AM | Panel Discussion<br>
**Sustaining an Academic Career in Biomedical Research**<br>**Moderator:** Alan Saltiel<br>**Panelists:** Dale Abel, Peter Tontonoz, Andrea Hevener, Alexandra Newton, Ron Evans |
| 12:00 PM | Lunch                                                    |
| 1:30 PM  | Yuliya Skorobogatko, PhD<br>
**Assistant Project Scientist, Dept of Medicine – UCSD**<br>“GTPase RalA regulates nutrient transporters in adipose tissue” |
| 1:50 PM  | Francesca Telese, PhD<br>
**Assistant Professor, Dept of Medicine – UCSD**<br>“The effect of dietary withdrawal on histone dopaminylation in the brain” |
KEYNOTE ADDRESS

2:30 PM  Introduction: Peter Tontonoz, M.D, PhD

Scott Sternson, PhD  
Professor of Neuroscience  
University of California, San Diego  

“Algorithms for Appetite”

3:30 PM  Poster session and Reception
CALL FOR PROPOSALS

DRC P&F Grant Announcement

2023 Pilot and Feasibility Projects in Endocrinology & Diabetes

Pilot & Feasibility Program Director: Peter Tontonoz

As part of the mission of our UCSD/UCLA Diabetes Research Center (DRC) grant, the Pilot and Feasibility Grant Program will support grantees at approximately $40,000-50,000 direct costs (with additional ~55% indirect costs) in 2023. The maximum number of P&F awards an investigator may receive is two. Successful applicants can apply to have their first year of funding renewed for a second year by re-applying the following year or may submit a second application in a subsequent year.

Applications DUE: April 3rd, 2023, to Dr. Peter Tontonoz at ptontonoz@mednet.ucla.edu

ALL PAPERS MUST CITE P30 DK063491 and obtain a PMCID number from NCBI for all publications.
Zhenqi Zhou is an Assistant Professor in the Division of Endocrinology, Department of Medicine, UCLA. His laboratory focuses on the role of mitochondrial quality control in the pathophysiological of metabolic diseases. They are also interested in understating the molecular basis of skeletal muscle and liver cross-talk in the progression of nonalcoholic fatty liver disease, with the hope of developing new approaches to combat obesity, type-2 diabetes, and other metabolic disorders.
Anthony J. Covarrubias is an Assistant Professor in the Department of Microbiology, Immunology, and Molecular Genetics, UCLA. He is a macrophage biologist with expertise in immuno-metabolism, and how inflammation and metabolism are integrated to regulate metabolic health and disease states including aging. Dr. Covarrubias’ recent work is focused on how diet and aging-related inflammation impacts the aging process. In a recent manuscript he showed that the decline of NAD+ during aging is driven by the activation of tissue resident macrophages via senescent cells. As senescent cells progressively accumulate in aging tissues, these results highlight a new causal link between visceral tissue senescence, NAD+, and immuno-metabolic dysregulation during aging, an active area of investigation in the Covarrubias Lab at UCLA.

Vira Kravets is an Assistant Professor of Biomedical Engineering at UCSD. She obtained her Ms. Sci in Physics, with specialty “Photonics” from the Kyiv National University of Ukraine. She then moved to Colorado to obtain her Ph.D. in Physics. Her thesis focused on Plasmonic nano materials for bioimaging and biosensing applications. As a Postdoctoral Fellow at the Anschutz Medical Campus of the University of Colorado, Dr. Kravets studied role of heterogeneity of the insulin-producing cells in the formation of the neuro-endocrine networks in pancreatic islets. She discovered a “first-responder” cell population, which drives micro-organs’ response to blood glucose. Dr. Kravets is a recipient of multiple research awards and grants, including career awards from NIH and from the Burroughs Wellcome Fund.
Rajat Singh is interested in understanding how autophagy regulates systemic lipid metabolism in physiology and obesity states. He is interested in understanding the signaling mechanisms regulating lipophagy and the molecular mechanisms by which autophagy selectively identifies and degrades fat droplets, as well as unraveling new mechanisms by which the liver copes with the excessive influx of lipids during fasting and obesity. Finally, they explore how intermittent fasting remodels circadian autophagy to provide systemic benefits in mice and humans. Their long-term goal is to develop approaches to stimulate autophagy and prevent age- and obesity-related chronic diseases.

Nicolas Musi has recently joined Cedars Sinai Medical Center to serve as Professor and Director of the Center on Diabetes, Metabolism and Aging, and Director of the Endocrinology Division. Dr. Musi trained in Internal Medicine at the University of Miami and in Endocrinology, Diabetes and Metabolism at the Joslin-Beth Israel Deaconess Medical Center fellowship program. He joined the University of Texas Health Sciences Center at San Antonio (UTHSCSA) in 2003, where he rose through the ranks from Assistant Professor to Full Professor. Prior to joining Cedars Sinai, Dr. Musi directed the prestigious Sam and Ann Barshop Institute of UTHSCSA for 9 years. Dr. Musi has been continuously funded by NIH since 2007 and has published more than 130 peer-reviewed manuscripts and book chapters related to the pathophysiology of diabetes, obesity, and insulin resistance, and the biology of aging. Currently he is PI on two R01 awards, PI of a Clinical Center for the Molecular Transducers of Physical Activity Consortium (MoTrPAC), and multi-PI on a Tissue Mapping Center for the Cellular Senescence Network (SenNet). Dr. Musi was elected as a member of the American Society for Clinical Investigation in 2019.
XIA YANG
PhD

Xia Yang is a Professor, Department of Integrative Biology and Physiology and the Vice Chair of the Molecular, Cellular, and Integrative Physiology (MCIP) Ph.D Interdepartmental Program at UCLA. She focuses on developing and applying multi-tissue multi-omics systems biology approaches to understand the genetic and environmental network perturbations in complex human diseases, including diabetes, cardiovascular disease, and neurodegenerative disorders. With a PhD in Molecular Genetics with an emphasis on Bioinformatics and postdoctoral training in Systems Genetics and building on her industry experiences as Senior Research Scientist at Rosetta Inpharmatics/Merck & Co and as Principal Scientist and Director of Systems Biology at Sage Bionetworks, she has developed a broad research portfolio from computational tool development to disease mechanism investigations to drug discovery and toxicity studies.

SCOTT STERNSON
PhD

Scott Sternson is a Professor of Neuroscience at the University of California in San Diego and an Investigator with the Howard Hughes Medical Institute. Before this, he was a Group Leader at the Janelia Research Campus in Virginia. His research combines chemical, optical, and genetic tools to investigate the neural circuits that mediate the representation of physiological states and the implementation of behaviors related to hunger and eating. He has been honored with the Helmholtz Foundation Young Investigator in Diabetes Award, the Linda and Jack Gill Transformative Investigator Award, and the Phillip Sharp Lecture on Neural Circuits from MIT.
E. Dale Abel is the William S. Adams Distinguished Professor of Medicine, Chair and Executive Medical Director of the Department of Medicine in the David Geffen School of Medicine and UCLA Health. He was formerly a Professor of Medicine, Biochemistry and Biomedical Engineering, Chair of the Department of Medicine and Director of the Fraternal Order of Eagles Diabetes Research Center at the University of Iowa where he held the John B. Stokes III Chair in Diabetes Research and the François M. Abboud Chair in Internal Medicine. He has had a distinguished career in endocrine and metabolism research. His recent work focuses on mitochondrial mechanisms that mediate inter-organ crosstalk that may influence the pathophysiology of insulin resistance and mitochondrial pathways linking metabolism with increased risk for atherothrombosis. He is the recipient of numerous awards for scholarship and mentorship including being elected into the National Academy of Sciences (NAS).

Awards and Recognition

Dale Abel, M.D., Ph.D., Chairman of Medicine at UCLA was elected to the National Academy of Sciences in 2022.

Susan Taylor, Ph.D., Distinguished Professor of Pharmacology and Chemistry and Biochemistry at UCSD won the Herbert Tabor Research Award from ASBMB in 2022.

Alan Saltiel, Ph.D., Professor of Medicine and Pharmacology at UCSD was elected as a fellow of the American Society of Pharmacology and Experimental Therapeutics.
DRC four Core facilities

Transgenic and Knockout Mouse

The DRC Transgenic, CRISPR Mutagenesis, and Knock-out Mouse Core is a state-of-the-art facility that has an outstanding track record in the production of genetically altered mice. Transgenic mice carrying new or novel genes are created by microinjection of DNA into the pronuclei of fertilized eggs. Mice carrying directed mutations are created by injection of CRISPR guide RNAs with Cas9 mRNA/protein and template DNA. Knock-out mice lacking specific genes of interest are created by homologous recombination in embryonic stem cells followed by injection into blastocysts to create chimeric mice. Highly experienced personnel produce transgenic, CRISPR, and knock-out mice for DRC investigators at very reasonable cost and with very short lead times. The Core provides embryonic stem cell recombination, knockout mice, CRISPR mutant mice, transgenic mice (both standard and BAC transgenics), sperm or embryo cryopreservation, and pathogen-free embryonic rederivation to the DRC community at discounted rates. This UCSD-based Core Facility has been in operation since 1992.

Metabolic and Molecular Physiology

The MMPC provides full service in vivo and ex vivo phenotyping in rodents. We perform accurate, time efficient and cost effective metabolic studies in mice, tissues, and cells generated/obtained by DRC investigators. We promote interactions and synergy between DRC investigators and Biomedical Cores, and provide individualized and comprehensive assessment of metabolism, hormone action and inflammatory signaling.

Genomics and Epigenetics

The DRC Epigenetic and Genomics Core (EGC) is a state-of-the-art facility that facilitates high-throughput genomic approaches. High-throughput sequencing, data acquisition and analysis require expensive instrumentation and reagents and a highly skilled team of individuals who are experts in specific components of the overall procedure. These technologies therefore lie beyond the scope of most individual laboratories. The EGC, which is comprised of the Institute for Genomic Medicine (IGM) and the Center for Computational Biology and Bioinformatics, has been instrumental in providing DRC investigators access to these technologies. The EGC also provides consultation and training of students, postdoctoral fellows, investigators and technical staff regarding high-throughput sequencing methodologies and data analysis which is overseen by the Functional Genomics Specialist. Genomics services are available to the DRC community at subsidized rates.

Human Genetics

Genetic susceptibility contributes significantly to the development of diabetes and its complications. As shown by recent successes in genetic mapping, the technological capability now exists to identify many of the responsible genes.

To be successful in such endeavors, it is necessary to combine expertise in genetic epidemiology, clinical investigation, molecular genotyping, DNA sequencing, mathematical genetic analysis, and functional characterization. The goal of the Human Genetics Core is to offer such expertise to DRC investigators conducting studies into the genetics of diabetes, its complications and related disorders, so that they can employ cutting-edge molecular and analytic methodologies in this rapidly developing field.
The overall mission of the UCSD/UCLA DRC is to foster research in the prevention and treatment of diabetes and its complications, and to improve the lives of patients suffering from this devastating disease.

The UCSD-UCLA DRC functions not only to integrate research activities across our member institutions, but also serves as a hub for other research enterprises in the Southern California area and beyond. Together, the participating institutions constitute an unprecedented wealth of diabetes and metabolic research expertise and experience. In aggregate, the sponsored research programs at these institutions currently garner over $867 million dollars per year in direct costs, including over $76 million in diabetes and metabolic research to our DRC faculty.

These institutions incorporate outstanding research programs across the broad spectrum of basic and clinical diabetes research, and the DRC has cemented Southern California as a hub for innovation in diabetes research, education, and treatment.

The center is organized into five Biomedical Research Bases:

- Nuclear Receptors
- Cell Signaling
- Metabolism
- Complications
- Beta Cell Biology

The Center is an important resource for education, training, raising awareness of endocrine and diabetes research. It supports:

- Pilot and Feasibility grants for young and newly focused research scientists
- Hosts Monthly Metabolism Group Meetings
- Convenes and Annual retreat