The UCSD/UCLA/Salk/Cedars-Sinai DRC

The NIDDK Centers program is:
Diabetes Research Centers (DRC)
Grant number: P30 DK063491

The Components of the Center include:

A. Transgenic, CRISPR, and Knock-out Mouse Core
   Pamela L. Mellon

B. Mouse Metabolic and Molecular Physiology Core
   Andrea Hevener & Edward Dennis

C. Epigenetics and Genomics Core
   Chris Glass, and Nicholas Webster

D. Human Genetics Core
   Jerome Rotter & Leslie Raffel

E. Novel Target Discovery and Assay Development Core
   Julian Whitelegge

F. Pilot and Feasibility Program
   Peter Tontonoz

G. Enrichment Program
   Maike Sander & Mark Goodarzi

H. Administrative Component
   Jerrold M. Olefsky & Alan Saltiel

The website address is: http://DRC.ucsd.edu

The listserve address is: DRC-L@ucsd.edu

If you use our Cores or receive a P&F, please cite P30 DK063491 in the resulting publications and link them to the DRC in your my NCBI.
Listserv for DRC Members

Send announcements, communications, requests, etc., to your DRC colleagues:

DRC-L@UCSD.EDU

If you are receiving this newsletter directly, you are already subscribed. If you would like to subscribe, please email mellonadmin@ucsd.edu. This is a moderated listserv, so messages will be prescreened such that only relevant and important messages will reach you.

OUR WEBSITE
http://DRC.UCSD.EDU

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Organization of the UCSD/UCLA/Salk/Cedars-Sinai Diabetes Research Center for years 11-15
05/01/2013-04/30/2018

Upgrades and Expansion of our Cores

Our Biomedical Research Cores have undergone substantial growth and change since the founding of our Center in 2003. For example, the new Novel Target Discovery and Assay Development Core focuses on proteomic analysis of plasma and tissue samples and provides unique services in the generation of novel immunoassays for biologically relevant proteins of interest. The Transcriptional Genomics Core incorporates a variety of epigenetic technologies, which provide a major new strength for our DRC faculty. The Metabolic and Molecular Physiology Core includes a Lipidomics sub-core headed by Dr. Edward Dennis. Dr. Dennis is the Director of the LIPID MAPS Consortium at UCSD and his laboratory has developed many new methodologies for analyzing over 700 lipid species in blood as well as tissue samples from humans and mice. He is among the world’s leaders in this area, and the addition of these mass spec-based lipidomics methodologies and provide powerful new services available to our membership. This core has also acquired important new technologies in mitochondrial functional analyses, as well as ex vivo studies of insulin target tissues. The Transgenic and Knock-out Mouse Core has added new advanced technologies of CRISPR/Cas9, facilitating the advances of our DRC investigators in genetically modified mice. The Human Genetics Core has expanded its genotyping capabilities, adding specialized chips including the Cardio-Metabochip, the Immunochip, the Exome chip, and the HumanMethylation450 DNA Analysis BeadChip. Exome and targeted DNA sequencing, and induced pluripotent stem cells (iPSC) have been added. All of these advances reflect upgrading and expansion of our DRC Core Facilities for the support of our DRC Investigators.
2016 DERC P&F Grants AWARDED

Pilot and Feasibility Projects in Endocrinology & Diabetes

Pilot & Feasibility Program, Director: Peter Tontonoz

On behalf of the UCSD/UCLA Diabetes Research Center Pilot and Feasibility Grant Committee, the UCSD/UCLA DRC Center is delighted to announce that we have awarded 6 outstanding projects for seed funding in 2016 out of 18 superb applications. The number and quality of the applications is clear evidence for the remarkable scientific environment that exists in our universities for supporting diabetes research especially among promising young scientists. The UCSD/UCLA DRC funds four grantees per year at approximately $40,000-$50,000.

THE UCSD/UCLA DERC is Proud to Announce the 2016 P&F AWARDEES:

2016 Junior Faculty Developmental Award winner:

Kyle J. Gaulton, PhD, UCSD, for the proposal “The Impact of Type 2 Diabetes Risk Variants on Transcriptional Regulation During Pancreatic Development.” Partnered with UCSD Dean’s Research Award.

P&F awardees:

• Shannon M. Reilly, PhD, UCSD, for the proposal “An IL-6/Stat3 Autocrine Axis in Adipose Tissue.”

• Stephanie Stanford, PhD, UCSD, and LIAI, for the proposal “Elucidating the Role of LMPTP in Adipogenesis.”

• Li Zhang, PhD, UCLA, for the proposal “Novel Ubiquitination Pathways in Lipid Homeostasis.”

• Kellie Breen, PhD, and David Natale, PhD, UCSD, for the proposal “Glucocorticoid Disruption of Placental Junctional Zone Endocrine Function and the Downstream Prenatal Programming of Metabolic Syndrome.”

• Cathryn Kolka, PhD, CEDARS-SINAI, for the proposal “Energy Expenditure in Skeletal Muscle.” Partnered with the Cedars-Sinai Dean’s Research Award.

Please join us in congratulating these promising young investigators!

See a full history of our P&F awardees at: http://drc.ucsd.edu/pf/award-history.shtml

Final report and presentation at the annual retreat

A report on each pilot and feasibility study conducted will be provided at the end of the study period and an update will be provided yearly for four years after the completion of the award. These brief reports will contain professional career status at the time of the award and at the time of the report; an overview of the project including its significance and salient results; a list of resulting publications; and peer-reviewed subsequent funding in the same or related areas. Funded P&F investigators will attend the annual DRC retreat as well as a meeting of Regional P&F awardees, and present the results of their work in the year immediately following their award. Travel to these meetings will be charged to the individual P&F awards.

ALL PAPERS MUST CITE P30 DK063491
The Metabolic and Molecular Physiology CORE
Andrea Hevener, Ph.D. Professor of Medicine
http://derc.ucsd.edu/cores/mouse-phenotyping.shtml

The MMPC provides investigators from UCLA, UCSD, the Salk Institute and Cedars-Sinai with a series of state-of-the-art molecular and physiological assays of metabolic function not readily available from national mouse phenotyping centers. These include timely, cost-effective animal, tissue, and cellular analytic services. Mouse genetics combined with dietary, physiological and pharmaceutical interventions has advanced therapeutic target identification and improved patient care by moving information from the bench to the bedside. The MMPC will help to accelerate this process by providing facilities and instrumentation as well as consultation from leading experts in the fields of nuclear receptor biology, insulin action, substrate metabolism, and inflammatory signaling. The UCSD-UCLA MMPC boasts a comprehensive and highly specialized physiology core providing services to assess:

a) Insulin sensitivity and substrate metabolism (Andrea Hevener, Director): glucose/insulin tolerance, hyperinsulinemic-euglycemic clamps, whole animal indirect calorimetry, ex vivo tissue insulin action and fatty acid metabolism, and body composition (MRI).

b) Oxidative metabolism and mitochondrial biology tissue/cellular oxygen consumption using the XF-24 Extracellular Flux Analyzer, mitochondrial isolation, novel mitochondrial peptide analysis, and tissue/cellular preparation for advanced microscopy.

c) Lipidomics (Edward Dennis and Oswald Quehenberger, Co-Directors): fatty acyls, glycerol lipids, glycerophospholipids, sterol lipids, sphingolipids, and prenol lipids analyzed by liquid chromatography, gas chromatography, and mass spectrometry.

d) Inflammatory signaling including diabetes complications analysis of circulating hormones, cytokines, chemokines and adipokines in plasma or conditioned media using Luminex technology (human, mouse, cell), as well as assessment of atherosclerotic lesion area and complexity. Monocytes/macrophages can be isolated and phenotyped upon request.

New Technology Alert! The MMPC now offers analyses using the MSD Meso Scale QuickPlex SQ120 Analyzer. This instrument can replace standard ELISA and immunoblotting assays for assessing circulating factors (e.g. hormones, chemokines, and cytokines) and cell or tissue proteins/protein signaling events. Additionally, MSD offers assay development reagents and plates suitable for immunogenicity, PK (pharmacokinetics), serology, and cell binding. MSD provides an open technology platform that allows researchers to develop novel singleplex or multiplex assays quickly using their own in-house or commercially available capture/detection antibody pairs. This is particularly useful for researchers wanting to develop customized multiplex assays or wishing to convert ELISAs or other binding assays to the MSD platform. MSD uses MULTI-ARRAY technology combined with electrochemiluminescence to bring speed and high density of information to biological assays. In combination with MULTI-SPOT plates, this technology enables precise quantitation of multiple analytes in a single sample requiring less time and effort than other assay platforms.

Compared to EISA, MULTI-ARRAY technology offers increased dynamic range, improved sensitivity, reduced sample and reagent requirements, and a streamlined workflow.

Electrochemiluminescent labels generate light when stimulated by electricity in the appropriate chemical environment. This reaction is incorporated into our immunoassays to provide the light signal used to measure important proteins and other biomedical molecules. How does electrochemiluminescence work? High binding carbon electrodes in the bottom of MULTI-ARRAY and MULTI-SPOT microplates allow for easy attachment of biological reagents (10X greater binding capacity than polystyrene).
Cont.

1. MSD assays use electrochemiluminescent labels that are conjugated to detection antibodies. The labels are called SULFO-TAG, and allow for ultra-sensitive detection.
2. Electricity is applied to the plate electrodes by an MSD instrument leading to light emission by SULFO-TAG labels. Light intensity is then measured to quantify analytes in the sample.

Advantages of Electrochemiluminescence:

- **High sensitivity**: Multiple excitation cycles can amplify signals to enhance light levels.
- **Broad dynamic range**: The wide dynamic range of our detection systems means high and low expression levels can be measured without multiple sample dilutions.
- **Low background**: The stimulation method (electricity) is decoupled from the signal (light) allowing only labels near the electrode surface to be detected.
- **Easy to use**: Immunoassay method similar to conventional ELISA, but quicker.
- **Great flexibility**: Labels are stable, non-radioactive, and conveniently conjugated to biological molecules.
- **Unsurpassed performance and quality**: Electrochemiluminescence is a highly successful detection system that achieves clinical quality data in a variety of sample types, including cell supernatant, serum, plasma, and whole blood.

MULTI-SPOT plates, which offer arrays within the well for increased throughput and assay multiplexing, are available in 96- and 384-well formats, with up to 10 spots per well.

Advantages of MULTI-ARRAY technology:

- Conserves valuable samples by allowing multiple results from very low sample volumes
- Achieves sensitivity and speed comparable to conventional single-analyte assays with excellent precision across a wide dynamic range
- Enables the measurement of native levels of biomarkers in normal and diseased samples without multiple dilutions

For more information on MSD technology or kit availability and pricing, please visit www.mesoscale.com or contact Tanya Kalaydjian (818-515-9610, tkalaydjian@mesoscale.com) the MSD Sales Representative. There is currently no service fee or wait time associated with using the MSD instrument!

**DRC P&F Grant Announcement Updates**

**2017 Pilot and Feasibility Projects in Endocrinology & Diabetes**

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 2017.

Applications DUE: **February 10th, 2017**, to Dr. Peter Tontonoz at ptontonoz@mednet.ucla.edu

**P&F grant format**

Failure to meet the formatting requirements will lead to an administrative disqualification of the proposal. The P&F grant applications should include:
(a) Face page with the title of the grant, the name, email, academic title, department, and institution of the PI, the names of additional personnel and collaborators and a 200 word abstract.

(b) Biosketches for the PI and other key personnel (standard 5-page NIH format).

(c) The scientific proposal (5-page limit).

(d) References.

The entire grant must be submitted as a single emailed pdf file less than 2 MB in size. If the grant includes high-resolution images, these must be reduced to meet the size requirement. Failure to provide a single pdf file or a file that is too big will result in disqualification. No budget is required, but the scope of the work should be appropriate for a 1-year project and the funds cannot be used for PI salary.

Eligibility
All eligible investigators must have faculty appointments at UCLA, Salk, Cedars, or UCSD, and be independent investigators. To be eligible for a P&F grant you need to be eligible to submit an R01 as a PI at the end of the one-year grant period. A joint appointment at an affiliated institution is allowed. Post-doctoral fellows may submit a grant if they provide a letter from their Chair stating that they are about to be appointed to the faculty. Investigators eligible for pilot and feasibility funding generally will be expected to fall into three categories:

(Category 1) New investigators without current or past non-mentored NIH research support as a principal investigator (current or past support from other sources being modest).

(Category 2) Established investigators with no previous work in diabetes that wish to apply their expertise to a problem in this area.

(Category 3) Established investigators in diabetes/endocrinology research who propose testing innovative ideas that represent clear departure from ongoing research interests. Emphasis is placed on Category 1 applicants.

Interactions with other DRC components
It is expected that junior faculty will be able to rely on the advice and support of a senior DRC investigators and will have a priority access to DRC Cores, including an opportunity to discuss their projects in depth with the core directors in order to receive maximum benefits from their services. Similarly, investigators with no previous experience in diabetes/endocrinology research will be expected to have a DRC collaborator. P&F grantees will be encouraged and expected to utilize DRC core resources. However, the award is given only to the designated PI and not to collaborators.

Final report and presentation at the annual retreat
A report on each pilot and feasibility study conducted will be due at the end of the study period and an update will be requested yearly for at least four years after the completion of the award. These brief reports will contain professional career status at the time of the award and at the time of the report; an overview of the project including its significance and salient results; a list of resulting publications; and peer-reviewed subsequent funding in the same or related areas. Funded P&F investigators will be expected to attend the annual DRC retreats alternating between Los Angeles and La Jolla, and present the results of their work in the year immediately following their award and continue to attend the annual meetings for at least three years thereafter. Travel to these meetings can be charged to the individual P&F awards.

All papers must cite P30 DK063491 and obtain a PMCID number from NCBI for all publications.

Notification procedure:
After approval of the funding decisions by the DRC executive committee, funded and unfunded investigators will be notified and, when appropriate, a brief summary of the reviews will be sent to them by email (not a detailed critique). The expected activation date is 5/1/2017.