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, Karen Reue, & 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 & Kuk-Wha Lee

G. Enrichment Program
   Maike Sander & Mark Goodarzi

H. Administrative Component
   Jerrold M. Olefsky, Pamela Mellon & Peter Tontonoz

Core contact information on following pages in the left column

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

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

UCSD-UCLA-Salk-Cedars Sinai Diabetes Research Center

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Andrea Hevener
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Core A. Transgenic & Knock-out Mouse
Pamela L. Mellon

Core B. Metabolic & Molecular Physiology
Andrea Hevener
Peter Tontonoz

Core C. Genomics & Epigenetics
Christopher K. Glass
Bing Ren

Core D. Human Genetics
Jerome Rotter
Leslie Raffel

Core E. Novel Target Identification & Assay Development
Julian Whitelegge
Junwiang Wan

Core F. Microarray
Sub-Core
Nicholas Webster

Core C. Lipidomics
Sub-Core
Edward Dennis

Core B. Microarray
Sub-Core

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 (see page 4). 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.
2015 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 DERC Center is delighted to announce that we have awarded 7 outstanding projects for seed funding in 2015 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 2015 P&F Awardees:

2015 Junior Faculty Developmental Award winner:

Jonathan Wanagat, MD, PhD, UCLA, for the proposal "Determining the effects of muscle mitochondrial DNA copy number and quality control on insulin sensitivity".

P&F awardees:

- **Timo Rieg, MD**, UCSD, for the proposal "Role of leptin in the regulation of intestinal sodium glucose co-transporter 1". Partnered with UCSD Dean's Research Award.
- **Joseph Cantor, PhD**, UCSD, for the proposal "CD98hc in pancreatic islet allograft rejection". Partnered with UCSD CTRI Research Award.
- **Thomas Hnasko, PhD**, UCSD, for the proposal "Role of brain triglycerides sensing in reward: why does fat taste so good?" Partnered with UCSD Dean's Research Award.
- **Elizabeth Tarling, PhD**, UCLA, for the proposal "Regulation of glucose and lipid homeostasis by the ubiquitin ligase RNF130". Partnered with UCLA CTSI Research Award.
- **Anne Beigneux, PhD**, UCLA, for the proposal "Molecular mechanisms underlying LPL physiology".
- **Run Yu, MD, PhD**, CEDARS-SINAI, for the proposal "Regulation of pancreatic a cell mass by glucagon signaling". Partnered with Cedars-Sinai Dean's Research Award.

Please join us all in congratulating these promising young investigators and we all look forward to seeing the fruits of their research in the literature and in future DRC meetings.

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.
Transgenic Mouse and Embryonic Stem Cell Core provides Germline Modification of the Mouse Genome by CRISPR/Cas9 Technology

Pamela L. Mellon

http://cancer.ucsd.edu/research-training/shared-resources/transgenic-core/Pages/default.aspx

The Transgenic Mouse and Embryonic Stem Cell Core has established a highly successful new service that provides investigators at UCLA, UCSD, the Salk Institute and Cedars-Sinai with state-of-the-art CRISPR/Cas9 modification of the mouse genome. The new service can generate targeted specific internal deletions, targeted single base or clustered multi-base mutations, specific small insertions, or add tags to specific genes to generate tagged proteins in vivo, as well as many other manipulations in a highly targeted and specific manner directly into the mouse genome.

CRISPR Mutagenesis and Internal Deletion

For internal deletion, a CRISPR guide RNA that targets the desired gene region is co-injected with commercial Cas9 mRNA (provided by the Core). For specific mutations or short insertion/deletions, a CRISPR guide RNA that targets the desired gene region is co-injected with commercial Cas9 mRNA and a template DNA that harbors the mutation. These are injected into fertilized one-cell embryos, which are then implanted in pseudopregnant dams. Resulting pups are returned to the Client. The Client will then analyze these by PCR and sequencing to determine the presence of the given transgene.

CRISPR injection is used to create internal deletions, insertions, or to mutate specific basepairs directly in the mouse germline.

- New clients consult with Jun Zhao (juzhao@ucsd.edu) and Ella Kothari (ekothari@ucsd.edu)
- Client designs and generates single guide RNA (sg RNA) and single-stranded oligo or double-stranded DNA fragment if applicable
- Core can provide client with pretested Cas9 mRNA (acquired from Life Technologies) for a nominal fee
- Client prepares RNA injection mixture to give to the Core for injection
- Core prepares pronuclear stage embryos
- Core injects RNA mix into cytoplasm of the embryos
- Core implants embryos into foster females
- Core arranges for transfer of 7-10 day old pups and foster dams to client’s vivarium
- Client screens resulting pups for transgene

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 subjects. Transgenic subjects 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 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 subjects. 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), embryo freezing, and pathogen-free embryonic rederivation to the DRC community at discounted rates. This Core Facility has been in operation since 1992.