



UCDAVIS  
MMPC

Mouse Metabolic Phenotyping Center



*established 2011*

# MMPC at UC Davis Annual Report (Y04)

NIH U24 DK092993



National Institutes of Health



National Institute of  
Diabetes and Digestive  
and Kidney Diseases

MMPC Steering Committee Annual Meeting  
NIH, Bethesda, MD



[www.mousebiology.org](http://www.mousebiology.org)

2795 2nd Street Suite 400

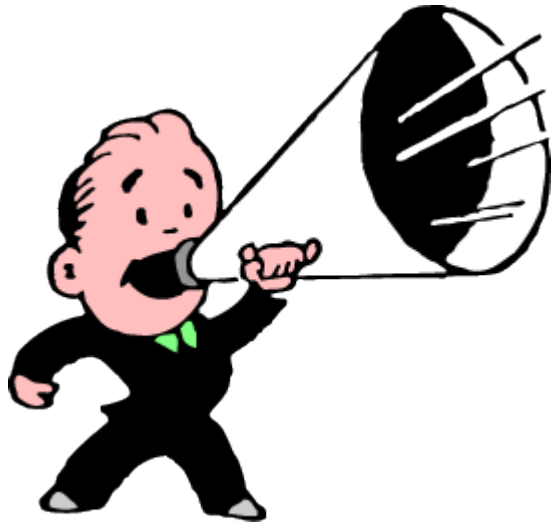
[mbp@ucdavis.edu](mailto:mbp@ucdavis.edu)

Davis, CA 95616

[@mousebiology](https://twitter.com/mousebiology)

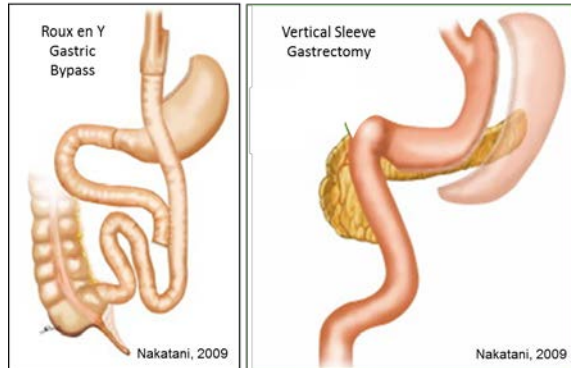
(530) 754-MOUSE

# Highlights!



Bariatric Models  
Brain Imaging  
Continuous glucose monitoring (CGM)  
iv Glucose Tolerance Test (GTT)  
Telemetry  
Gut Microbiome  
Gnotobiotic Mouse Research Center  
Gut Permeability  
Energy Expenditure  
Metabolomics  
Ultrasonographic imaging  
Website  
Metrics

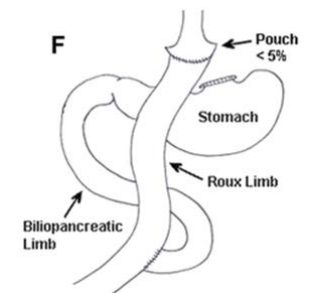
# Bariatric Surgery Models (Core B, Animal Care)



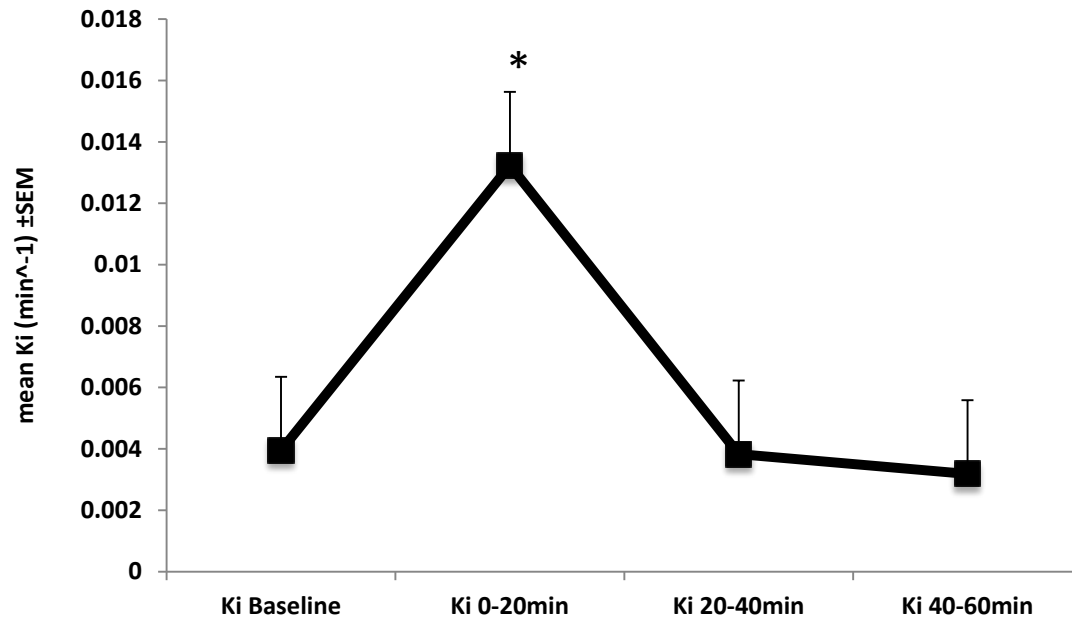
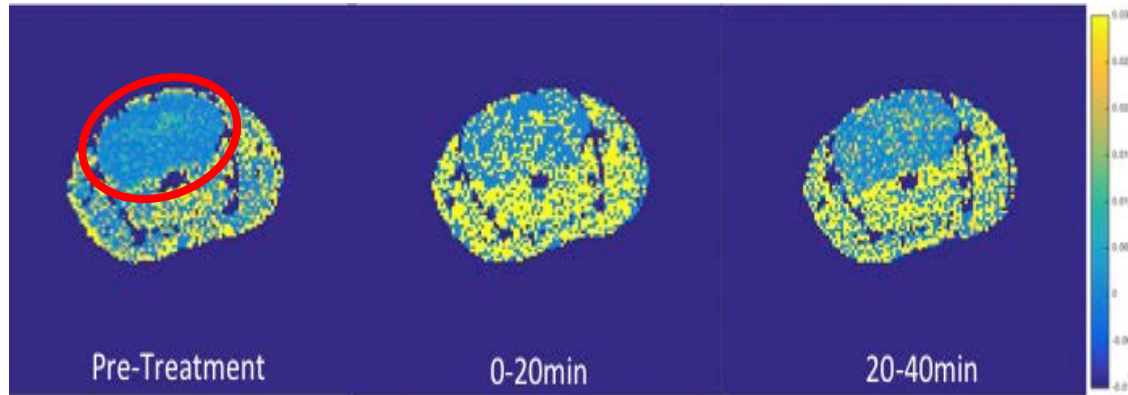
	VSG		RYGB	
	Sham	Surgery	Sham	Surgery
Number of survival surgeries	64	127	51	83
Number (%) survived at one month post-op	52 (81%)	103 (81%)	48 (94%)	56 (68%)

Models  
Development  
Update:

- VSG Validation study underway, UC Davis portion completed
  - males and females
  - microbiome, energy expenditure (CLAMS), fecal digestible energy, DEXA, ivGTT (VSG versus pair fed and ad lib sham controls)
- VSG models offered as service and for distribution
  - 4 requests underway
- RYGB models offered as service and for distribution
  - Refining procedure (modification of Hao *et al*, 2013)
- Cores C&D participating in service (functional analysis)
- Ileal transposition coming next



# Blood Brain Barrier Permeability by MRI (Core E, Cardio/Pathology)



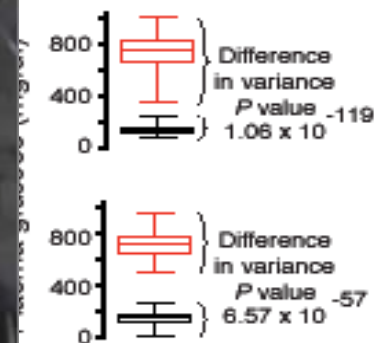
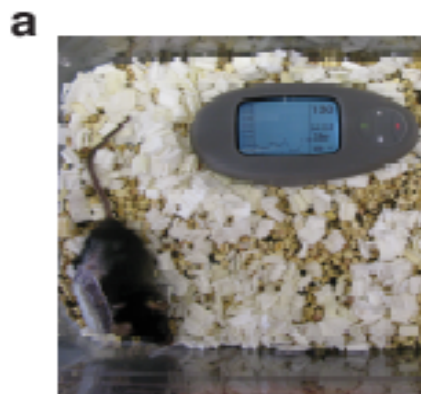
## Procedure Update:

- T1 weighted MRI data is collected with 7T Bruker Biospec MRS/MRI system using Magnevist (gadolinium based) contrast agent
- Assay could be applied to kidney or tumor biology (with some modifications to protocol)

# Continuous Glucose Monitoring-CGM (Core C, Endocrinology & Metabolism)

van der Meulen, T., et al., Nat Med, 2015. 21(7): p. 769-76

Glucose measurements every 5 min in diabetic ob/ob (red) and lean control (black) mice

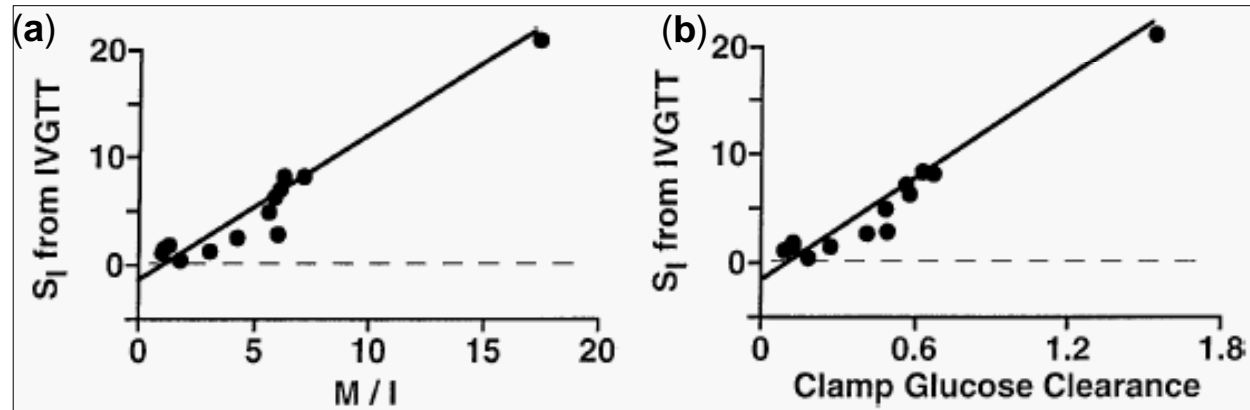


Procedure Update:

(Core B)  
Concentrations in

# Intravenous Glucose Tolerance Test-ivGTT (Core C, Endocrinol & Metabol)

(Ahren and Pacini, Am. J. Physiol., 1998, 1999, 2001, 2002)



## Validation with insulin sensitivity and glucose clearance assessed with Clamps

Insulin sensitivity index ( $S_1$ ) as measured by (a) IVGTT is well-correlated ( $r = 0.97$ ;  $p < 0.0001$ ) with insulin sensitivity and glucose clearance rates measured by (b) hyperinsulinemic, euglycemic clamps. M/I, glucose infusion rate during the 2<sup>nd</sup> h / mean insulin level at 60-120 min.

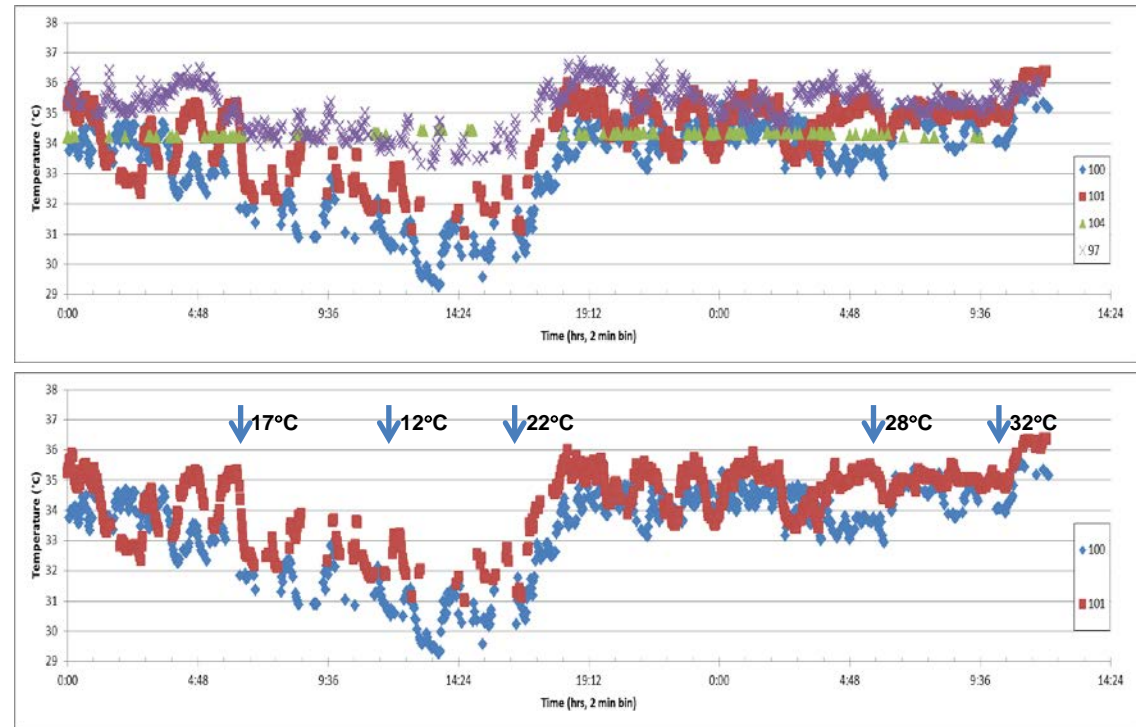
Assay  
Update:

- Requires 7 small (40 $\mu$ l) blood samples over 50 minutes following glucose IV (Core B).
- Faster & higher throughput than clamps - can also assess insulin secretion, insulin mediated + insulin independent glucose disposal (DI).
- Analysis simple math formula (computer modeling not needed; Am. J. Physiol., 2009).
- Offered as service (Core C&B) (e.g., insulin sensitivity in bariatric surgery mice)

# Murine Telemetry System (Core E, Cardiovascular & Pathology)

## Data Scientific Intl. Telemetry System

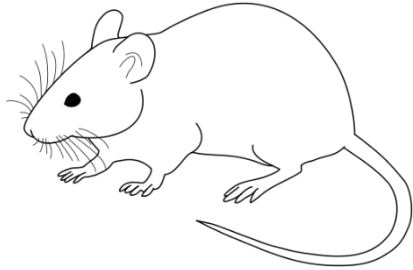
- HD-X11 or TA-F10 implantable telemeter
- Pressures: arterial, venous, left ventricular, ocular, bladder
- Biopotentials: ECG, EMG, EEG, EOG
- Temperature
- Activity (relative)
- Option of temperature controlled, or in CAMS



## Assay Update:

- First (pilot) study completed (with Core D: temp ramp with RynR mutant)
- Currently accommodates 4 mice/run (upgradable to 8-16)
- Fully installed, offered as service (Core D&B)

# Host-Microbiome Analysis (Core D, Body Composition)



## Host

### Host function

#### Gut

- Permeability (Ussing chambers)
- GI tract transcriptomics

#### Systemic

- Plasma or tissue metabolomics
- Bacterially derived metabolites



## Microbiome/Microbiota

Archaea, **Bacteria**, Fungi, Viruses

### Phylogenetic Classification

Variable region sequencing/alignment to database (targeted metagenomics)

- 16S rRNA (Bacteria & Archaea)
- ITS (internal transcribed spacer) rRNA (fungi)
- VLP purification & amplification (virus)

### Functional Activity

- Shotgun metagenomics (putative)
- Metatranscriptomics (active pathways)
- Metabolomics

Host-Microbe Interactions

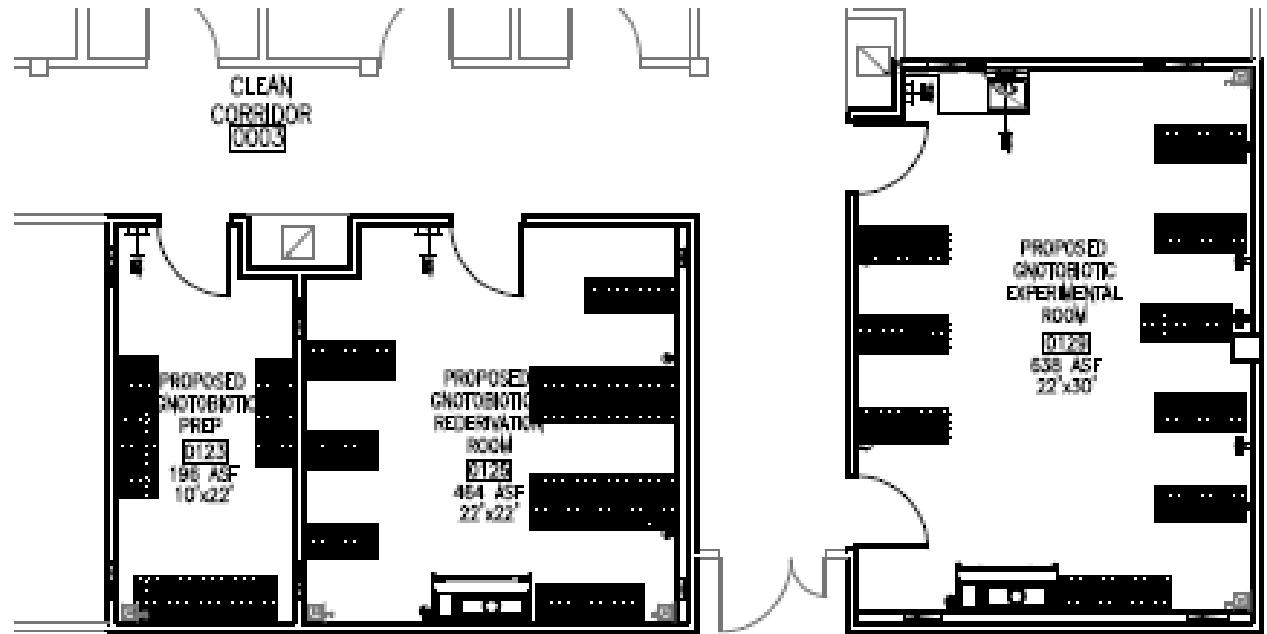
### Integrative Pathway Analysis

Metabolites

Gene activity

Microorganism identification

# Gnotobiotic Mouse Research Center (Core B, Animal Care)

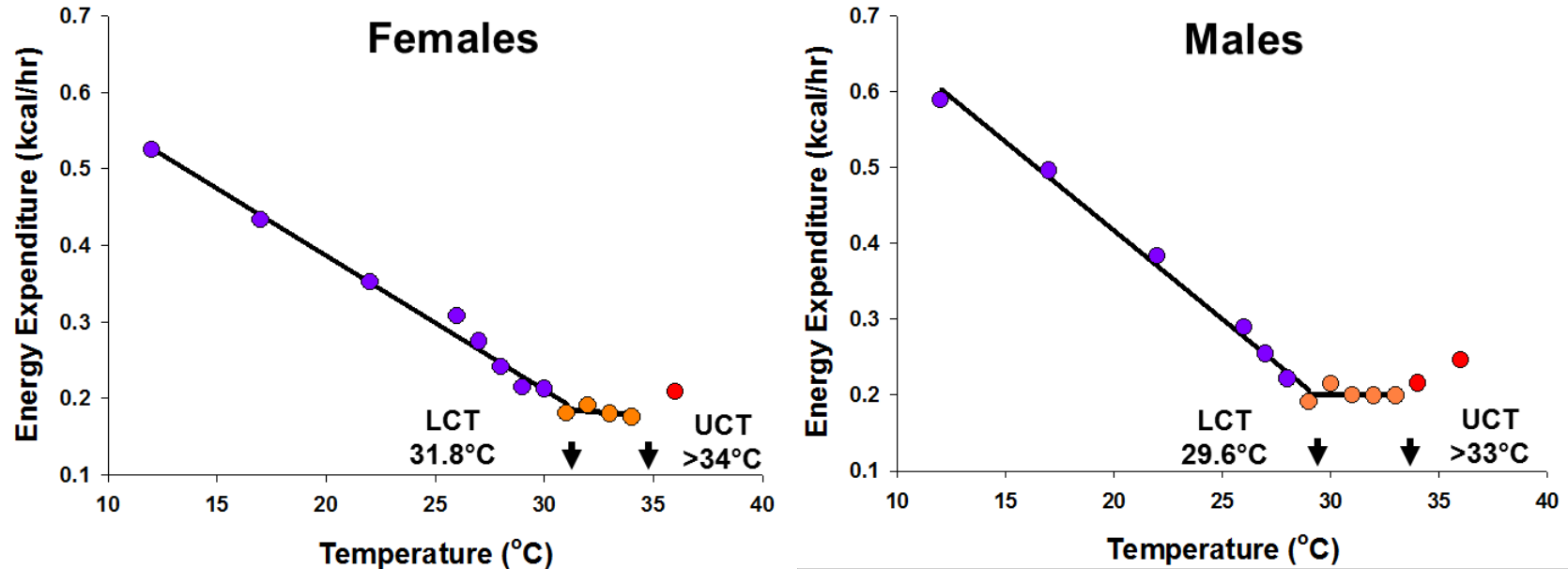


Facility  
Update:

- Enable experimental manipulation of gut microbiome
- Numerous services (rederivation, knockout/transgenic/Cas9 mice, diet)
- Capacity (340 cages: 100 rederivation/breeding, 240 microbial challenge)
- In-service July 2016

# Temperature Challenge (Core D, Body Composition)

Enables one to determine how shifts in the thermoneutral zone or energy expenditure response to cold contribute to weight gain.



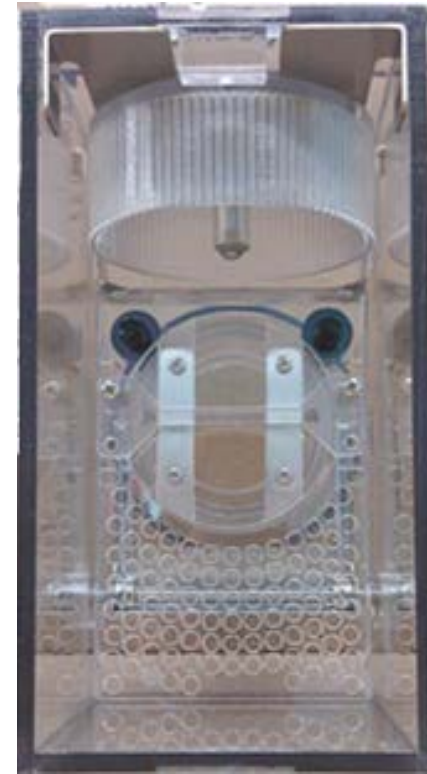
The relationship between ambient temperature and energy expenditure in male and female mice

Service  
Update:

- Determination of thermoneutral zone (lower and upper critical temperatures)
- Energy expenditure in response to cold or heat stress
- In-service 2015

## Physical Activity (Core D, Body Composition)

Enables determination of the extent to which physical activity-related energy expenditure is altered in mouse models.



Calorimetry chamber with running wheel

Service  
Update:

- Energy expenditure measured with running wheel access
- Energy expenditure during treadmill running
- In-service 2015

## Exercise (Core E, Cardiovascular & Pathology)



### **Starr Life sciences in-cage running wheels (20 wheels)**

- Evaluate the effect of voluntary exercise
- Can be paired with other metabolic measurements (i.e. CLAMS, insulin sensitivity, DEXA)
- Measures: distance, speed, intervals of running
- Provide enrichment



Service  
Update:

- First cohort to be run in Feb 2016
- To be offered as service later 2016

# Metabolomics (Core C, Endocrinology & Metabolism)

## Adapting for small volume biofluids, low amount tissues

Metabolomics @ UC Davis



~ 1000-fold less organ tissue in mouse v. human

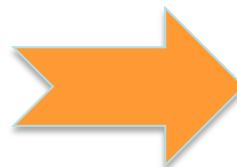
Liver 1.20 g in mouse → 1,561 g in human

Lung 0.13 g in mouse → 840 g in human

Heart 0.12 g in mouse → 300 g in human

~ 1000-fold less typical blood withdrawal

mouse < 100 ul → human 10 ml



### increased sensitivity needed

### micro-LC

reduce peak volume  
→ more sensitivity



### ~ 5 fold more sensitive

### high-recovery vials

reduce vial volume  
→ more total sample injected



### ~ 3 fold less sample

### ion mobility focusing

peak focusing like in electrophoresis



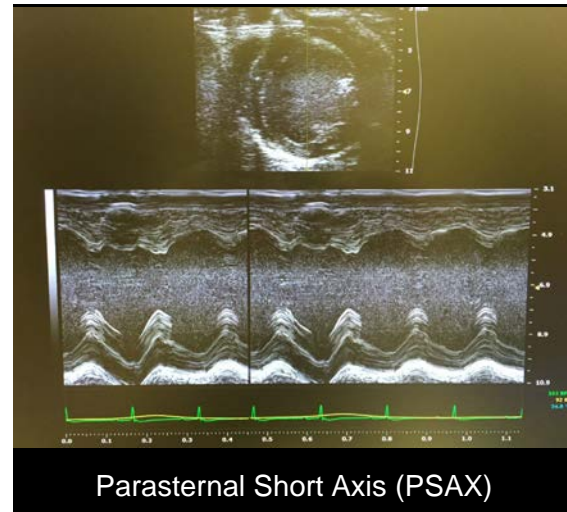
### ~ 10 fold better s/n

# Echocardiography (Core E, Cardiovascular & Pathology)

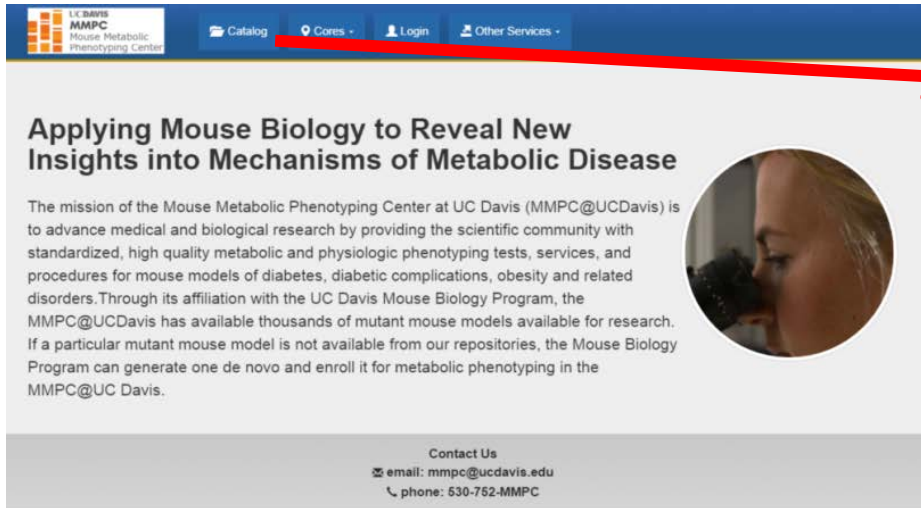
- Non-invasive technique
- Able to detect:
  - Localized or generalized hypertrophy
  - Thinning of the myocardium of the left ventricle
  - Presence of regional or global wall motion abnormalities associated with systolic dysfunction
- Applications of transmittal Doppler analysis allows the detection of abnormal filling patterns associated with left ventral diastolic dysfunction

Service  
Update:

- Technicians trained
- LIMS established
- In-service Fall 2015



# Website (Core A, Administration)



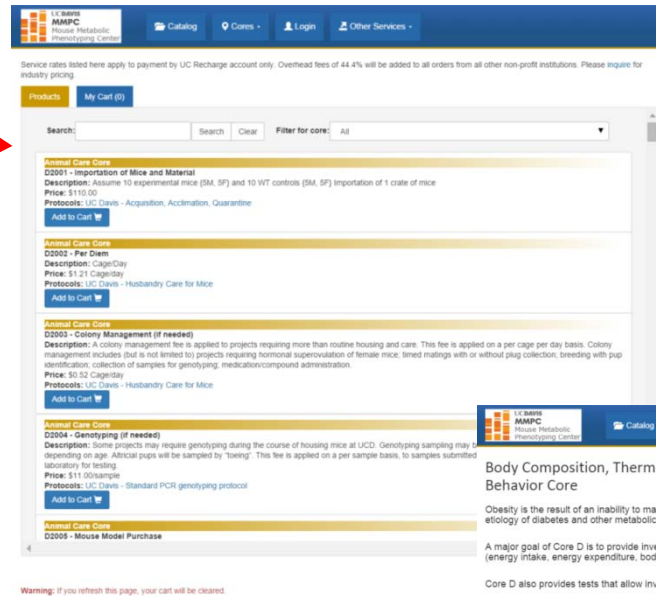
UC Davis MMPC Mouse Metabolic Phenotyping Center

Catalog Cores Login Other Services

## Applying Mouse Biology to Reveal New Insights into Mechanisms of Metabolic Disease

The mission of the Mouse Metabolic Phenotyping Center at UC Davis (MMPC@UCDavis) is to advance medical and biological research by providing the scientific community with standardized, high quality metabolic and physiologic phenotyping tests, services, and procedures for mouse models of diabetes, diabetic complications, obesity and related disorders. Through its affiliation with the UC Davis Mouse Biology Program, the MMPC@UCDavis has available thousands of mutant mouse models available for research. If a particular mutant mouse model is not available from our repositories, the Mouse Biology Program can generate one de novo and enroll it for metabolic phenotyping in the MMPC@UC Davis.

Contact Us  
email: [mmpc@ucdavis.edu](mailto:mmpc@ucdavis.edu)  
phone: 530-752-MMPC



UC Davis MMPC Mouse Metabolic Phenotyping Center

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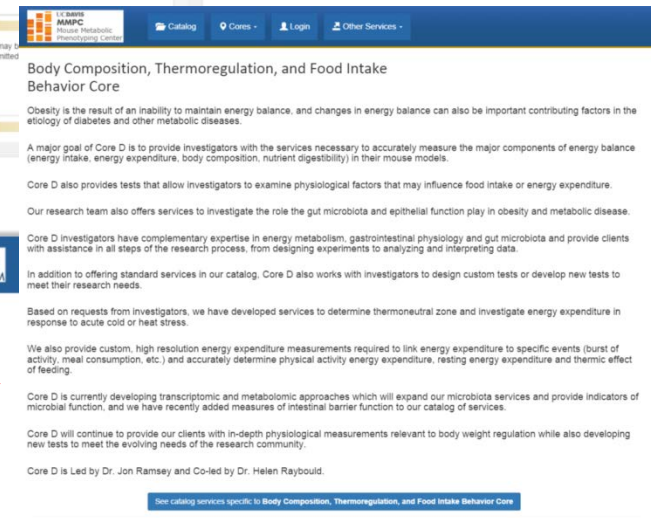
Service rates listed here apply to payment by UC Recharge account only. Overhead fees of 44.4% will be added to all orders from all other non-profit institutions. Please inquire for industry pricing.

Products My Cart (0)

Search: [input] Search Clear Filter for core: All

- Animal Care Core**  
D2001 - Importation of Mice and Material  
Description: Assume 10 experimental mice (5M, 5F) and 10 WT controls (5M, 5F) importation of 1 crate of mice  
Price: \$110.00  
Protocols: UC Davis - Acquisition, Acclimation, Quarantine  
Add to Cart
- Animal Care Core**  
D2002 - Per Diem  
Description: Cages/Day  
Price: \$1.21/Cage/Day  
Protocols: UC Davis - Husbandry Care for Mice  
Add to Cart
- Animal Care Core**  
D2003 - Colony Management (if needed)  
Description: A colony management fee is applied to projects requiring more than routine housing and care. This fee is applied on a per cage per day basis. Colony management includes but is not limited to projects requiring hormonal suppression of female mice, timed matings with or without plug collection, breeding with pup identification, collection of samples for genotyping, medicament/compound administration.  
Price: \$0.52/Cage/Day  
Protocols: UC Davis - Husbandry Care for Mice  
Add to Cart
- Animal Care Core**  
D2004 - Genotyping (if needed)  
Description: Some projects may require genotyping during the course of housing mice at UC Davis. Genotyping sampling may depend on age. Aftical pups will be sampled by "toeing". This fee is applied on a per sample basis, to samples submitted laboratory for testing.  
Price: \$11.00/sample  
Protocols: UC Davis - Standard PCR genotyping protocol  
Add to Cart
- Animal Care Core**  
D2009 - Mouse Model Purchase  
Add to Cart

Warning: If you refresh this page, your cart will be cleared.



UC Davis MMPC Mouse Metabolic Phenotyping Center

Catalog Cores Login Other Services

## Body Composition, Thermoregulation, and Food Intake Behavior Core

Obesity is the result of an inability to maintain energy balance, and changes in energy balance can also be important contributing factors in the etiology of diabetes and other metabolic diseases.

A major goal of Core D is to provide investigators with the services necessary to accurately measure the major components of energy balance (energy intake, energy expenditure, body composition, nutrient digestibility) in their mouse models.

Core D also provides tests that allow investigators to examine physiological factors that may influence food intake or energy expenditure.

Our research team also offers services to investigate the role the gut microbiota and epithelial function play in obesity and metabolic disease.

Core D investigators have complementary expertise in energy metabolism, gastrointestinal physiology and gut microbiota and provide clients with assistance in all steps of the research process, from designing experiments to analyzing and interpreting data.

In addition to offering standard services in our catalog, Core D also works with investigators to design custom tests or develop new tests to meet their research needs.

Based on requests from investigators, we have developed services to determine thermoneutral zone and investigate energy expenditure in response to acute cold or heat stress.

We also provide custom, high resolution energy expenditure measurements required to link energy expenditure to specific events (burst of activity, meal consumption, etc.) and accurately determine physical activity energy expenditure, resting energy expenditure and thermic effect of feeding.

Core D is currently developing transcriptomic and metabolomic approaches which will expand our microbiota services and provide indicators of microbial function, and we have recently added measures of intestinal barrier function to our catalog of services.

Core D will continue to provide our clients with in-depth physiological measurements relevant to body weight regulation while also developing new tests to meet the evolving needs of the research community.

Core D is Led by Dr. Jon Ramsey and Co-led by Dr. Helen Raybould.

[See Catalog services specific to Body Composition, Thermoregulation, and Food Intake Behavior Core](#)

## Cores at MMPC-UCD

- A** Administrative Core
- B** Animal Care Core
- C** Endocrinology and Metabolism Core
- D** Body Composition, Thermoregulation, and Food Intake Behavior Core
- E** Complications and Pathology Core

## Other Services

- Mouse Biology Program**  
For all your needs working with genetically altered mice
- KOMP Repository**  
Obtain KOMP resources and services
- KOMP Phenotype**  
Explore KOMP phenotyping results
- MMRRC MMRRC @ UC Davis**  
Mutant Mouse Resource and Research Center (at UC Davis)
- IMPC**  
International Mouse Phenotyping Consortium

## Our Goals:

- Broaden the scope of metabolic phenotyping tests for mice available to investigators.
- Standardize key methodologies.
- Expedite the completion of research.
- Compile a database of information relevant to mouse models of diabetes, obesity, and diabetic complication

## News & Events

January 22, 2015 NIH West Coast Metabolomics Center at UC Davis (WCMC) requests pilot project applications

November 6 - 9, 2013 UC Davis will be hosting this year's annual meeting including a pre-meeting symposium on Using Mouse Models to Understand Obesity and Diabetes and a post-meeting Imaging Symposium.

## MMPC Project Report

View MMPC Data



## Y04 Metrics (Core A, Administration)

### ➤ **Outreach campaign**

*Targeted e-mails sent to over 113,123 recipients*

### ➤ **Response Tracking for e-mail inquiries**

*230 message inquiries received since May '14*

### ➤ **Working Groups participation**

*Bariatric Surgery, Imaging, Energy Balance*

### ➤ **Catalog of UCD tests and services**

*91 services described online, 94% with SOP's*

### ➤ **Utilization since opening (October 1, 2011)**

*25 institutions, 92 client orders, 23,936 tests*

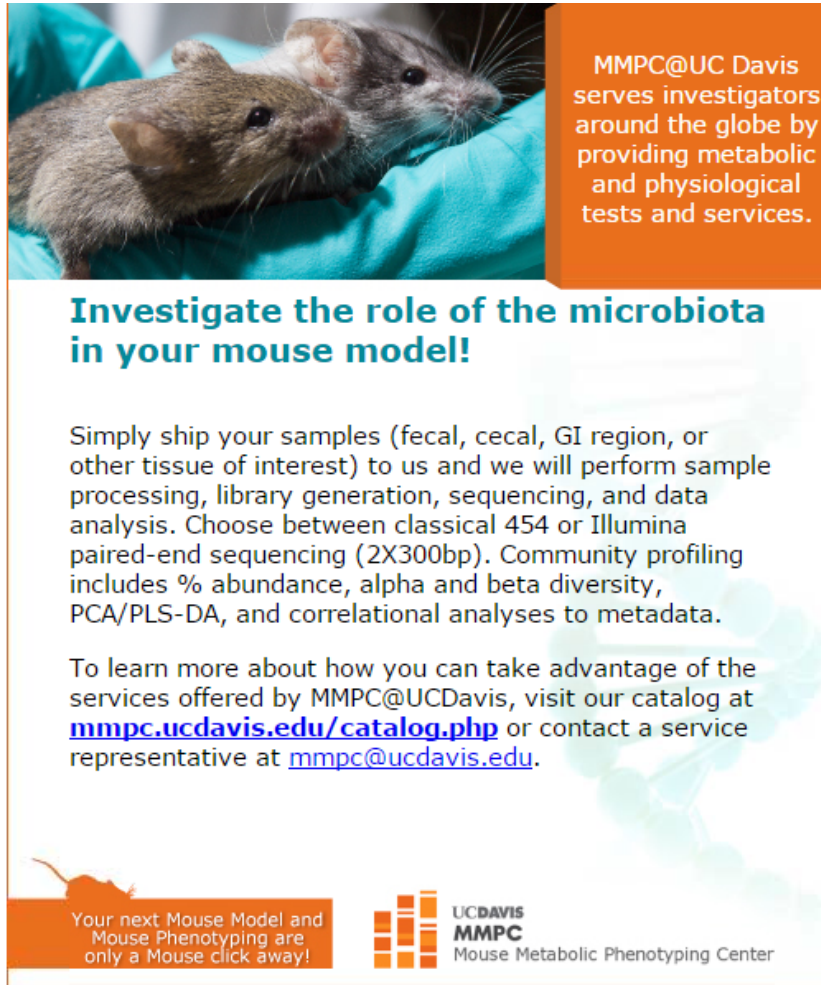
### ➤ **Publications linked to MMPC Grant#U24DK092993**

*43 with/10 without Center co-authorship*



# Y04 Outreach (Core A, Administration)

## example of email flyer:



MMPC@UC Davis serves investigators around the globe by providing metabolic and physiological tests and services.

**Investigate the role of the microbiota in your mouse model!**

Simply ship your samples (fecal, cecal, GI region, or other tissue of interest) to us and we will perform sample processing, library generation, sequencing, and data analysis. Choose between classical 454 or Illumina paired-end sequencing (2X300bp). Community profiling includes % abundance, alpha and beta diversity, PCA/PLS-DA, and correlational analyses to metadata.

To learn more about how you can take advantage of the services offered by MMPC@UCDavis, visit our catalog at [mmpc.ucdavis.edu/catalog.php](http://mmpc.ucdavis.edu/catalog.php) or contact a service representative at [mmpc@ucdavis.edu](mailto:mmpc@ucdavis.edu).

Your next Mouse Model and Mouse Phenotyping are only a Mouse click away!

UC DAVIS  
**MMPC**  
Mouse Metabolic Phenotyping Center

## Targeted, bi-monthly e-mail campaign, 2014 - 2015

113,123 targeted e-mails sent covering the following topics

2014 (13,126 emails)

- Metabolic Phenotyping of Dementia Mouse Models
- Metabolic Phenotyping of Parkinson's Mouse Models
- Metabolic Phenotyping of Alzheimer's Mouse Models
- Metabolic Phenotyping of Stroke Mouse Models

2015 (99,997 emails)

- Mouse Models of diabetes, obesity, or related disorders.
- Mouse Models for Bariatric surgery
- Gut Microbiome Analysis

[mmpc@ucdavis.edu](mailto:mmpc@ucdavis.edu)

[mmpc.ucdavis.edu](http://mmpc.ucdavis.edu)

855-UCD-MMPC (toll free)



UCDAVIS  
MMPC

Mouse Metabolic Phenotyping Center



NIH U24 DK092993

also...

Rick McIndoe



ADMINISTRATIVE CORE	<p>Samrrah Raouf</p> <p>Suzann Wadsworth</p> <p>Dave Clary</p> <p>Craig Warden</p> <p>Laurel Beckett</p>
ANIMAL CARE CORE	<p>Kristin Evans</p> <p>Stephen Griffey</p> <p>Kristin Grimsrud</p> <p>Christopher Pivetti</p> <p>Leslie Stewart</p> <p>Amy Kuhn</p> <p>Todd Tolentino</p>
ENDOCRINOLOGY & METABOLISM	<p>Peter Havel</p> <p>Fawaz George Haj</p> <p>Oliver Fiehn</p> <p>Mark Huising</p> <p>James Graham</p>
BODY COMPOSITION, THERMOREGULATION, AND FOOD INTAKE BEHAVIOR	<p>Jon Ramsey</p> <p>Helen Raybould</p> <p>Trina Knotts</p> <p>Charlotte Ronveaux</p>
COMPLICATIONS AND PATHOLOGY CORE	<p>John Rutledge</p> <p>Sue Bodine</p> <p>Dennis Wilson</p> <p>Nip Chiamvimonvat</p> <p>Jan Nolta</p> <p>Simon Cherry</p> <p>Amparo Villablanca</p> <p>Jennifer Rutkowsky</p>



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