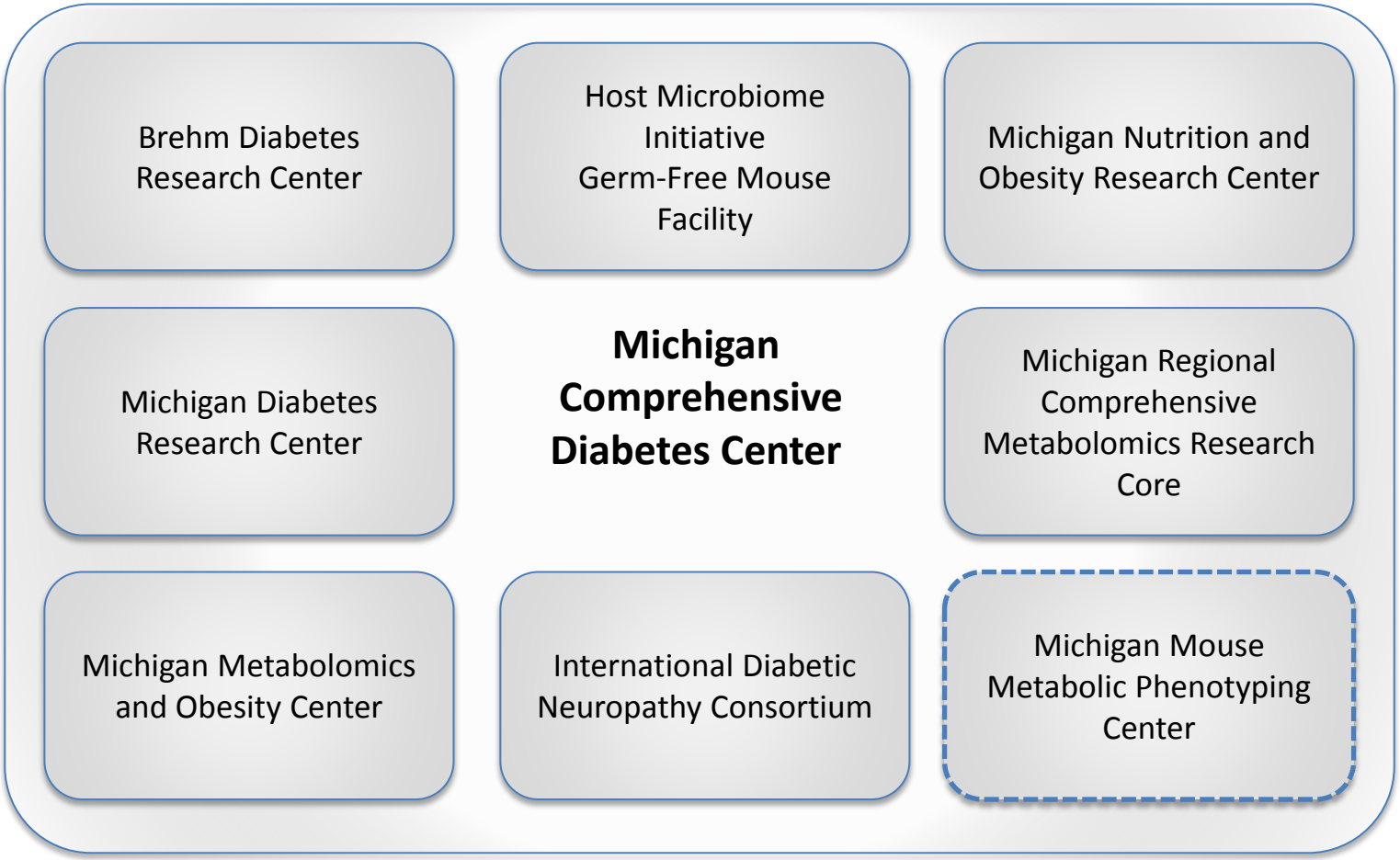
MMPC
Mouse Metabolic
Phenotyping Centers

Michigan MMPC

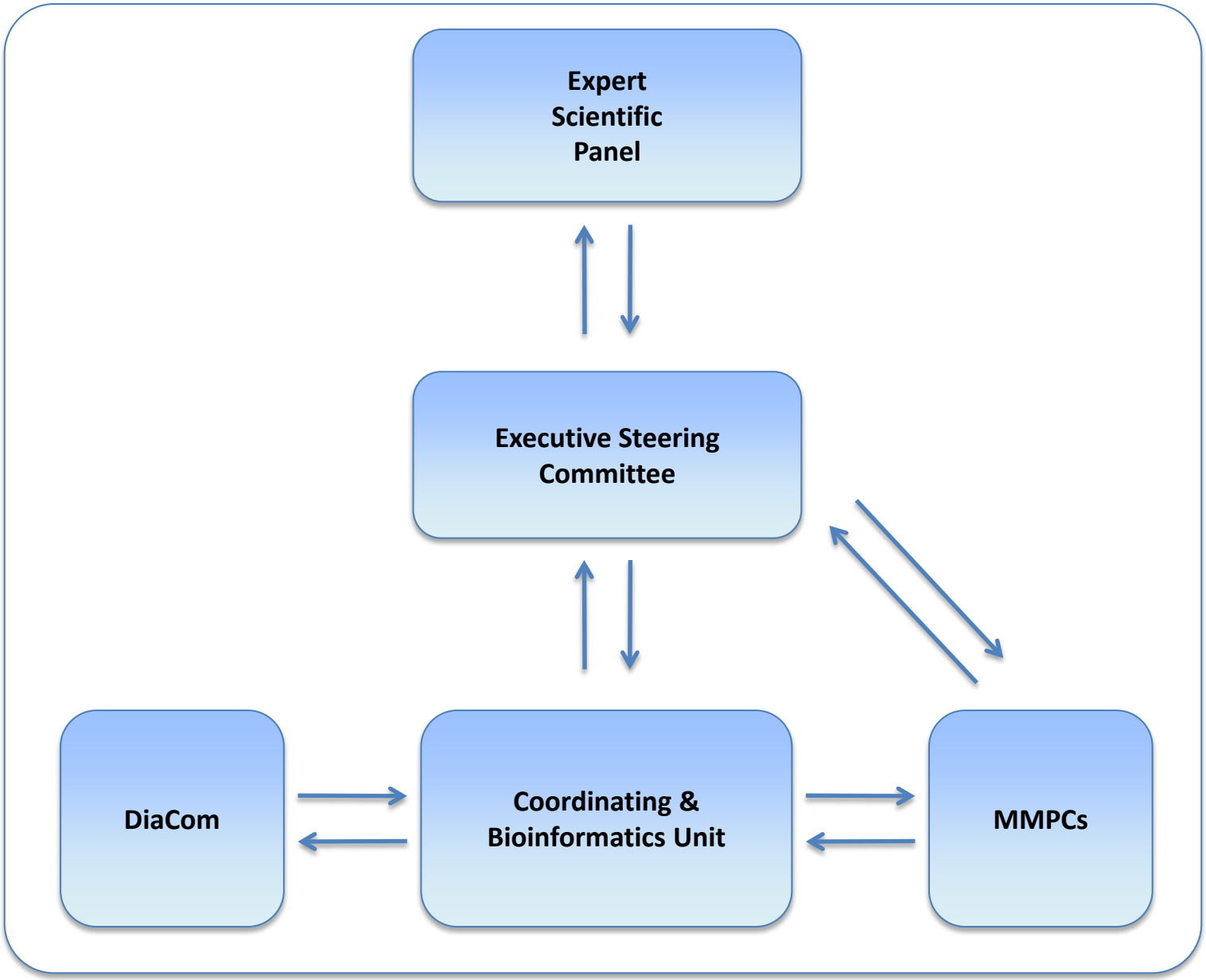
PI: Malcolm J. Low, MD, PhD

08/24/16

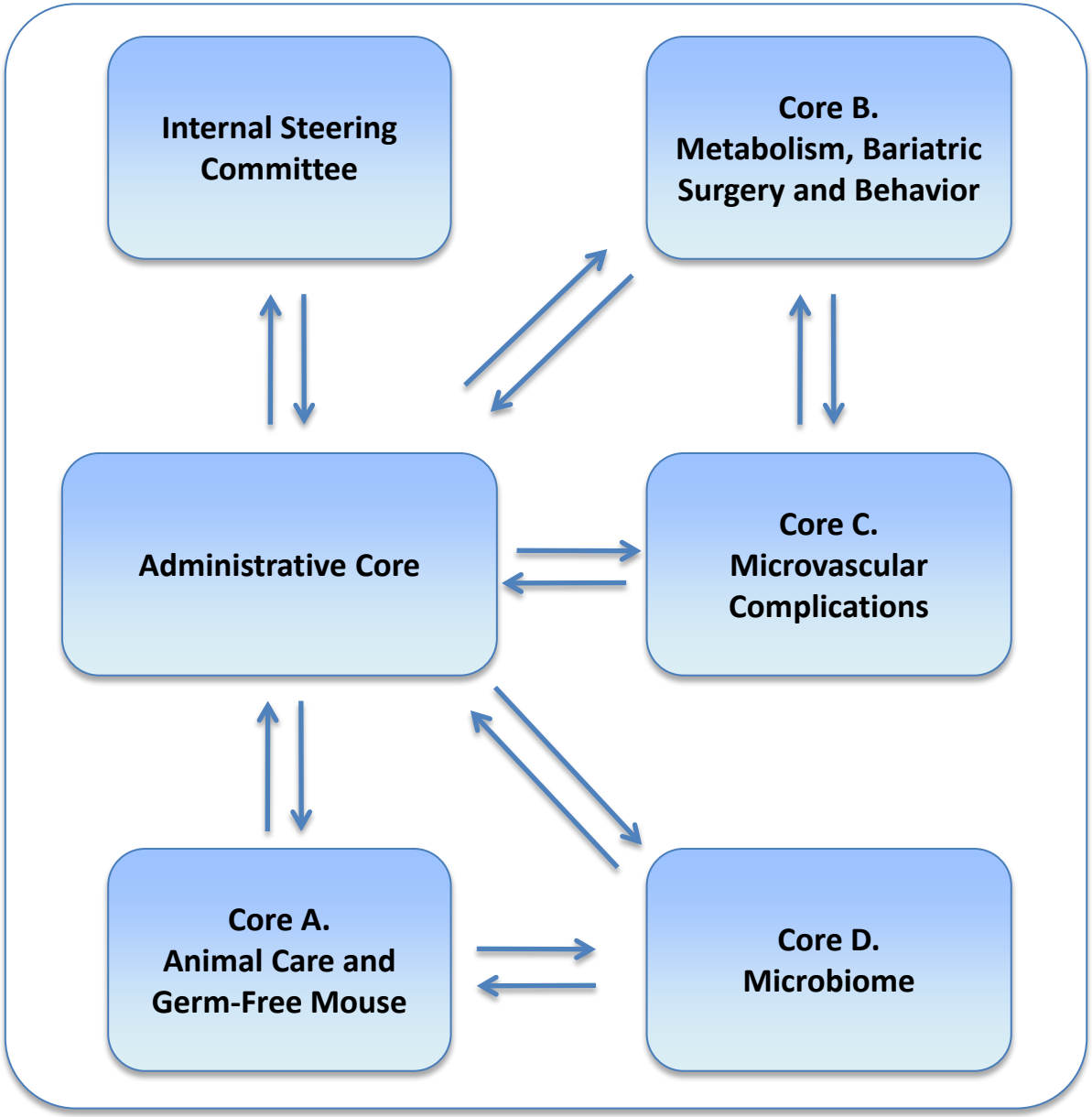
University of Michigan Diabetes and Obesity Initiatives



Organizational Chart for the MMPC Consortium



Michigan Mouse Metabolic Phenotyping Center



Adminstrative Core

Malcolm Low, MD, PhD – Admin. Core Director

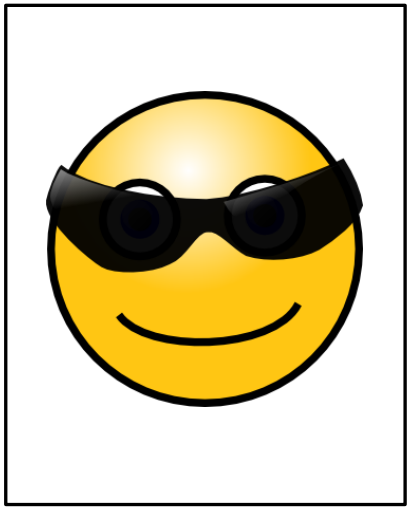
(Departments of Molecular & Integrative Physiology; Internal Medicine)

Randy Seeley, PhD – Admin. Core Assoc. Director

(Departments of Surgery; Internal Medicine)

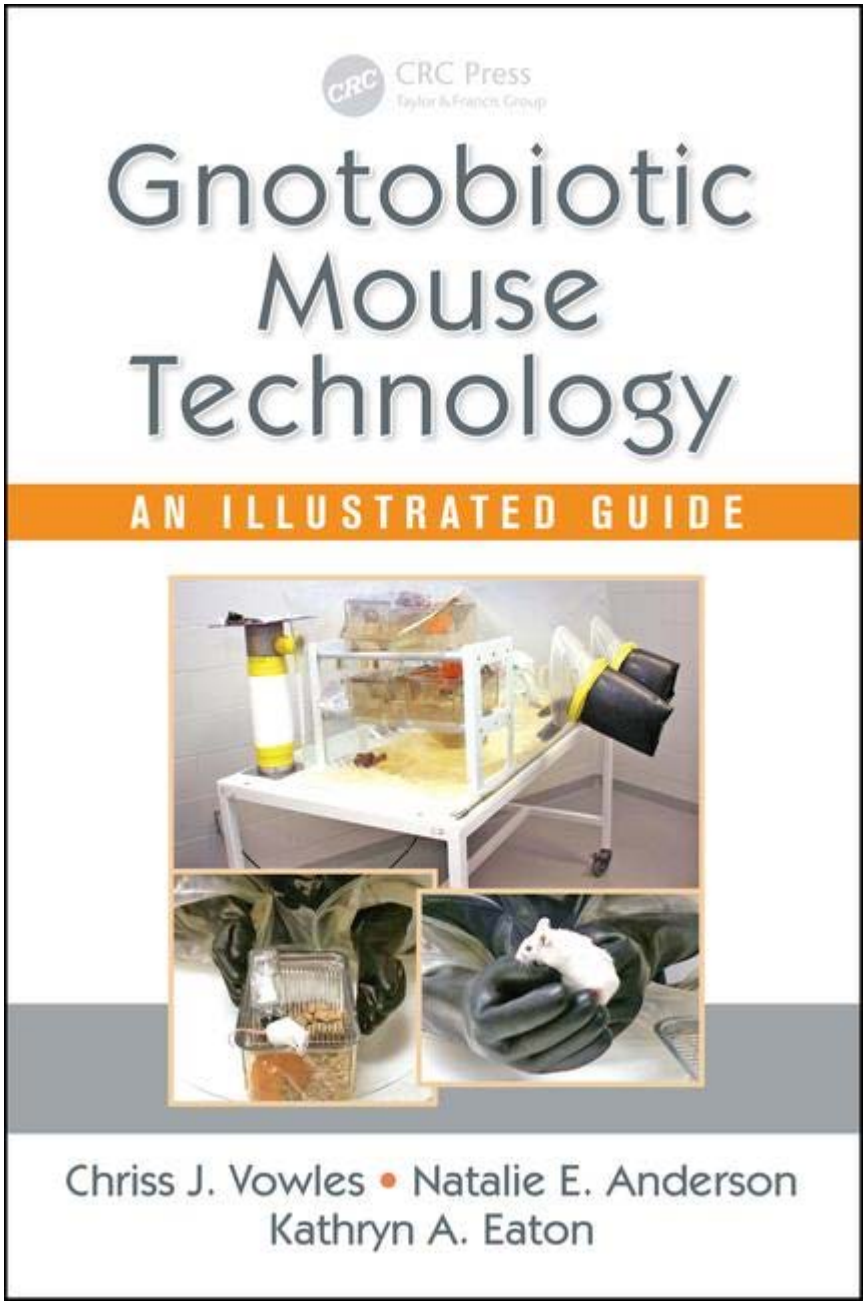
Animal Care and Germ-Free Mouse Core

Robert Sigler, DVM, PhD - Core Director
(Unit for Laboratory Animal Medicine)
Jennifer Lofgren, DVM, PhD - Core Co-Director
(Unit for Laboratory Animal Medicine)
Kathryn Eaton, DVM, PhD - Core Assoc. Director
(Department of Microbiology & Immunology and ULAM)



ULAM In-vivo Animal Core (IVAC)

- Animal diagnostic laboratory tests
- IVAC pathology
  - Necropsy services
  - Histology laboratory
- Digital slide scanning
  - Aperio AT2 digital slide capture and analysis



- Maintain and distribute several strains of germ-free mice
- Long term experiments with germ free or gnotobiotic housing
- Variety of technical services
- Rederivation of new germ free strains
- Ongoing collaborations with microbiome core

Metabolism, Bariatric Surgery and Behavior Core

Malcolm Low, MD, PhD - Core Director

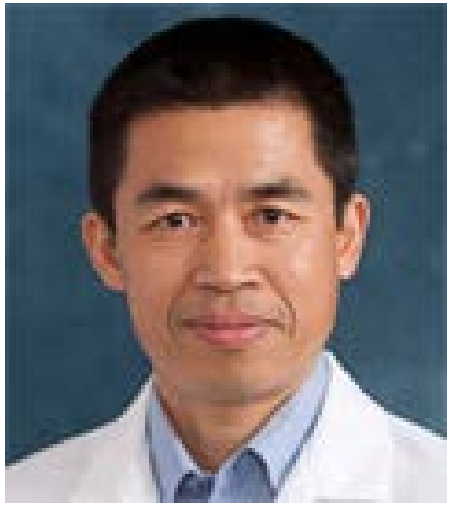
(Departments of Molecular & Integrative Physiology; Internal Medicine)

Nathan Qi, MD, PhD - Core Co-Director

(Department of Medicine)

Randy Seeley, PhD - Core Assoc. Director

(Departments of Surgery; Internal Medicine)



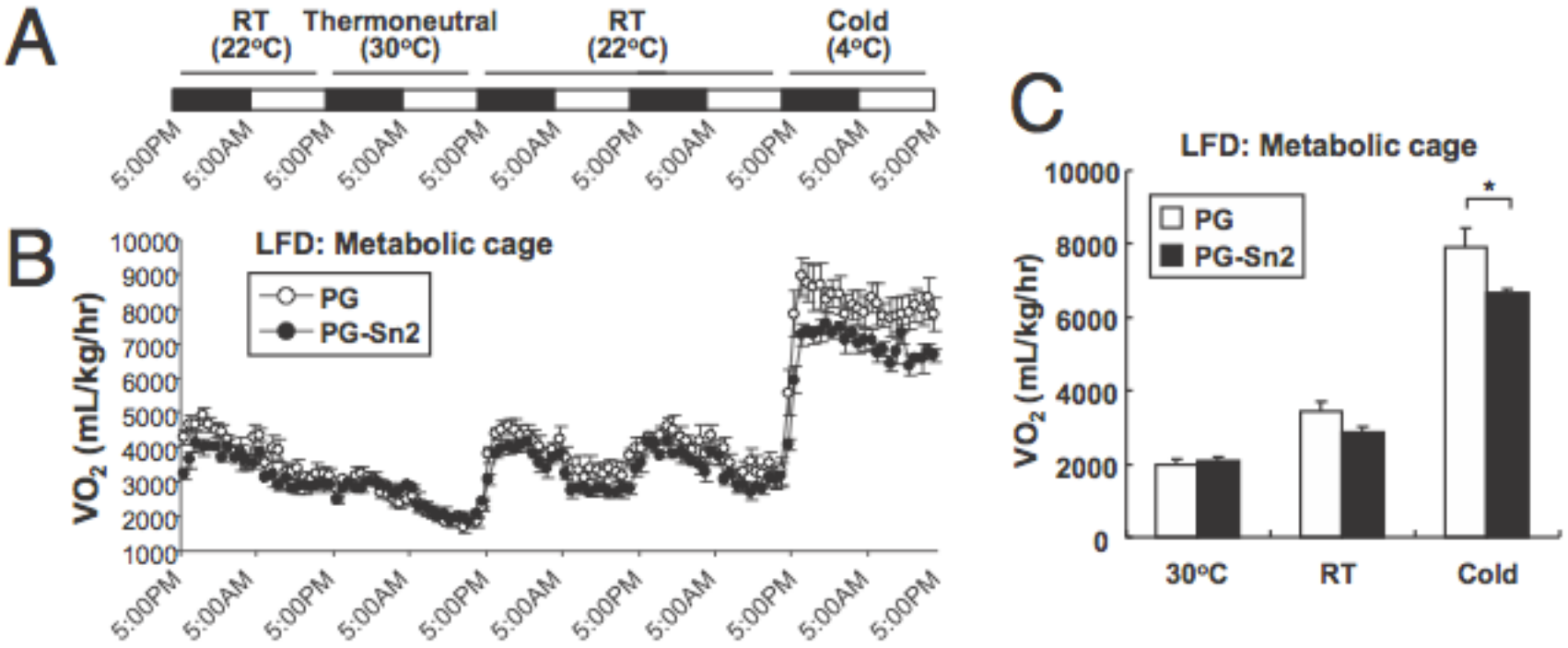
- **Surgical procedures**
  - **Vascular cannulation (carotid artery, jugular vein, portal vein)**
  - **Vertical sleeve gastrectomy, Roux-En-Y Gastric Bypass (in development)**
  - **Parabiosis**
- **Insulin sensitivity & substrate metabolism**
  - **Insulin and glucose tolerance tests**
  - **Hyperinsulinemic euglycemic clamps**
  - **IV glucose tolerance test (with dual cannulation)**
  - **Telemetric continuous blood glucose monitoring (DSI)**
- **Energy expenditure and activity**
  - **CLAMS (indirect calorimetry under temperature controlled conditions)**
  - **Body composition by NMR**
  - **Spontaneous locomotor activity**
- **Serial blood sampling and infusion, dual cannulation, Culex/Empis**
- **Open-field locomotor activity**
- **Consultation/training**
- **Operant Conditioning – Meal patterns and food reward**
- **Wide variety of behavioral tests relevant to motivation, anxiety, depression and cognition, Noldus**

Metabolism, Bariatric Surgery and Behavior Core

Serial Measurement of Energy Expenditure (CLAMS) at 30, 22 & 10 deg C

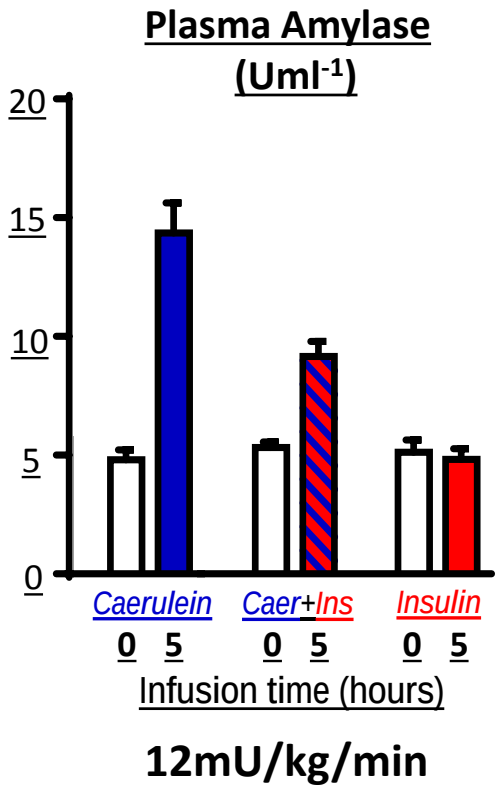
Sestrin2 inhibits uncoupling protein 1 expression through suppressing reactive oxygen species

Seung-Hyun Ro[a], Myeongjin Nam[a,b], Insook Jang[a], Hwan-Woo Park[a], Haeli Park[a], Ian A. Semple[a], Myungjin Kim[a], Jeong Sig Kim[a,c], Haewon Park[a], Paz Einat[d], Golda Damari[d,1], Maya Golikov[d], Elena Feinstein[d], and Jun Hee Lee[a,2]

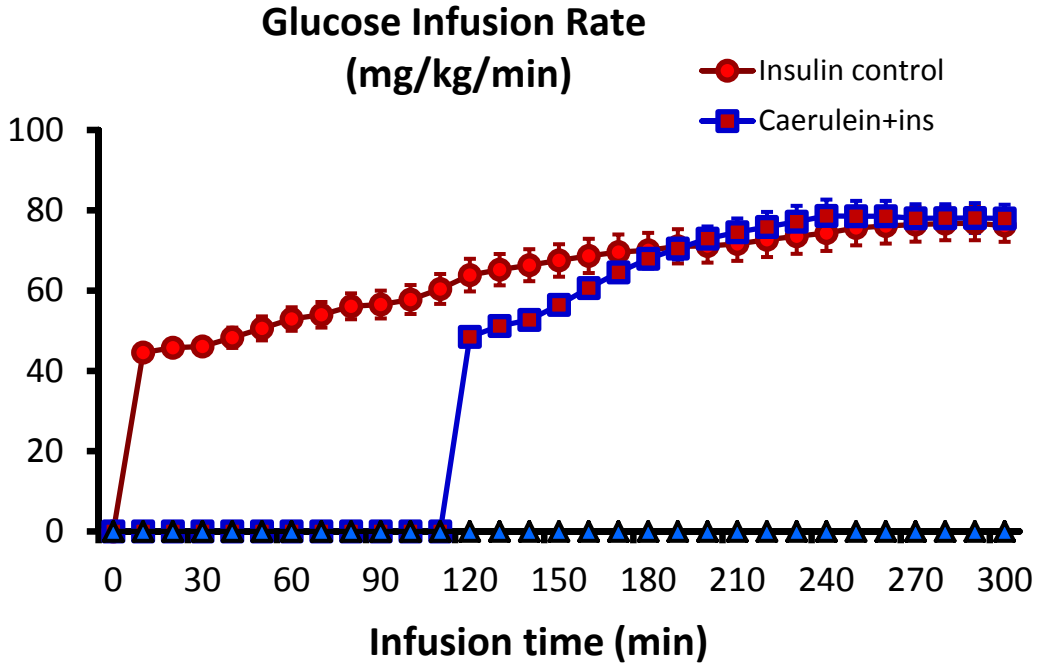


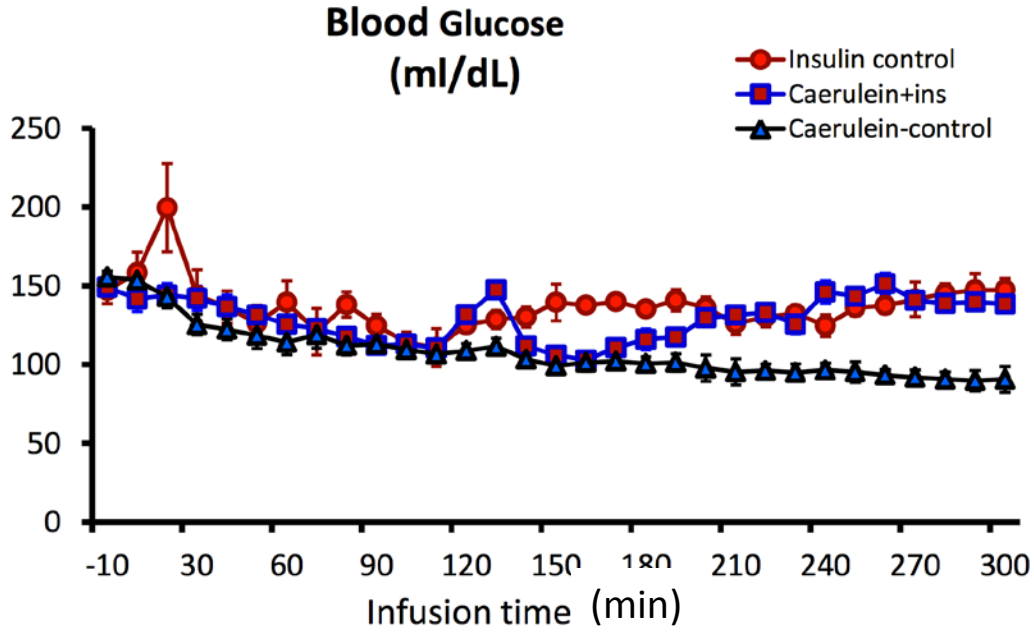
www.pnas.org/cgi/doi/10.1073/pnas.1401787111

Insulin infusion has a protective effect on Caerulein (CCK) induced acute pancreatitis

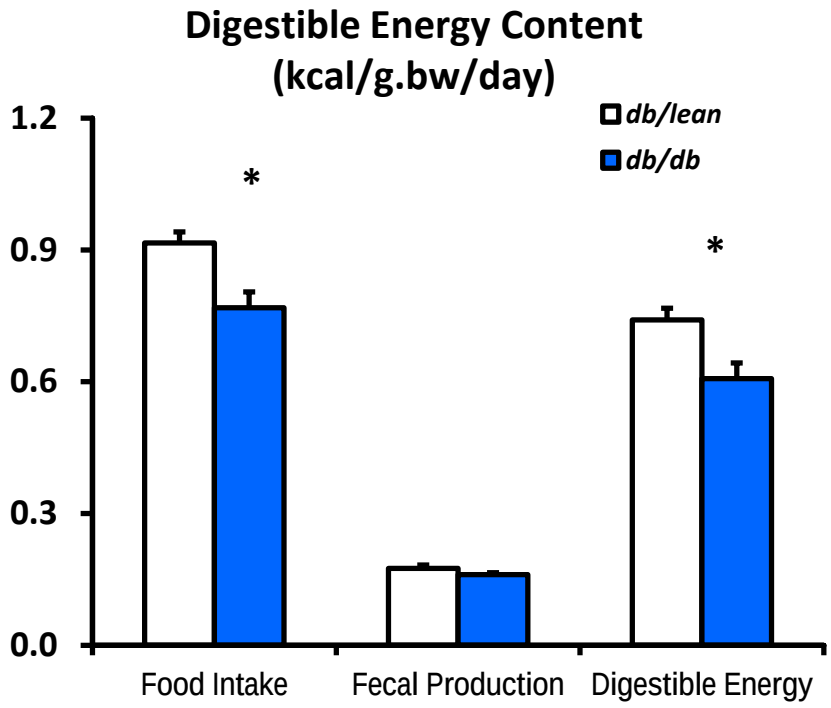


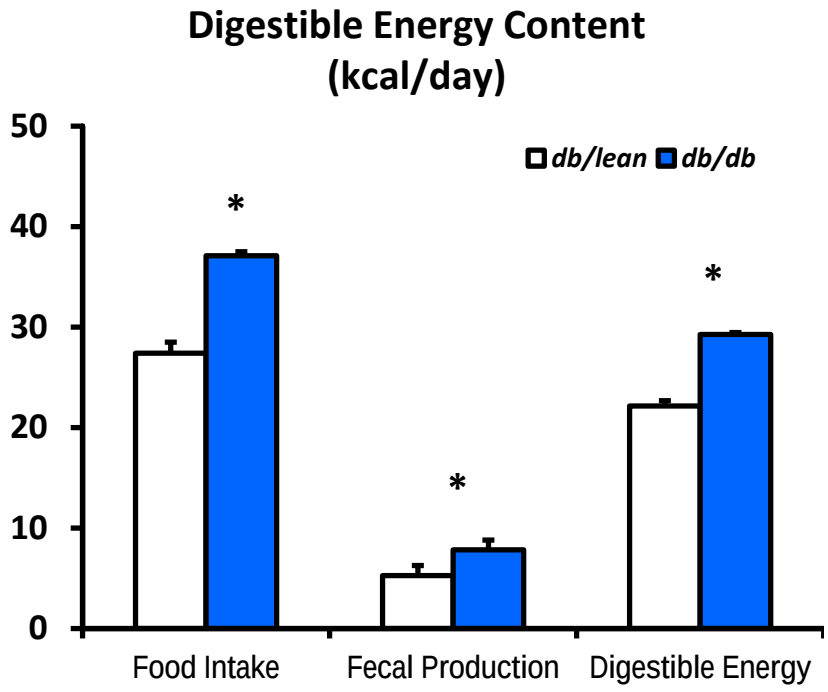
12mU/kg/min



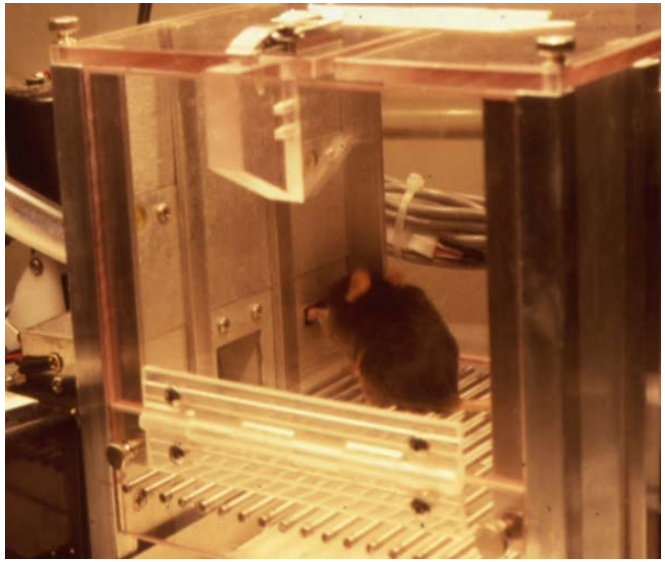
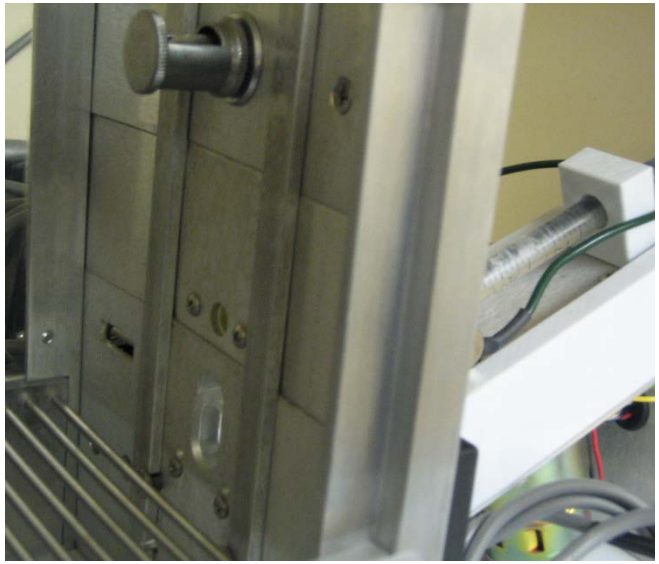


Bomb calorimetry to determine fecal loss of calories in *db/db* and *db/+* mice





Meal Pattern Analysis: Operant Paradigm

- **Lever presses**
- **Food pellet deliveries: Fixed ratio and Progressive ratio**
- **Licks from water sipper**
- **Inter-event time interval duration**
- **Video recording (behavioral satiety sequence)**

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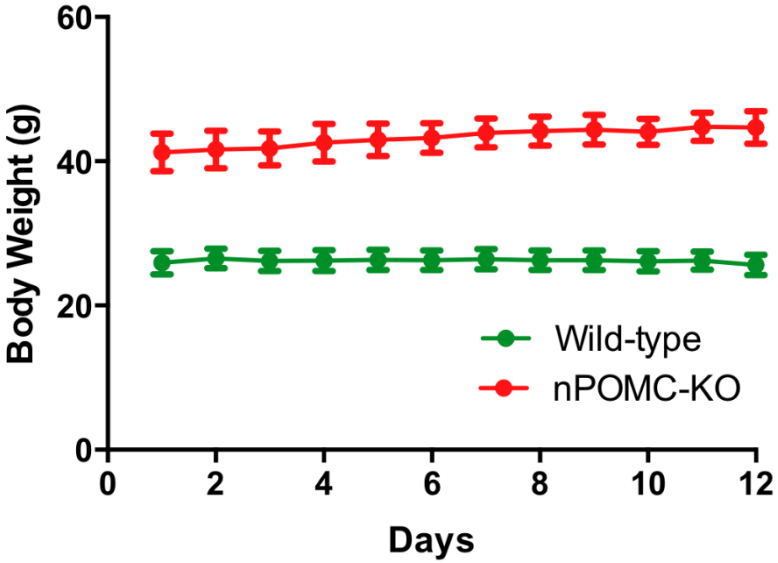
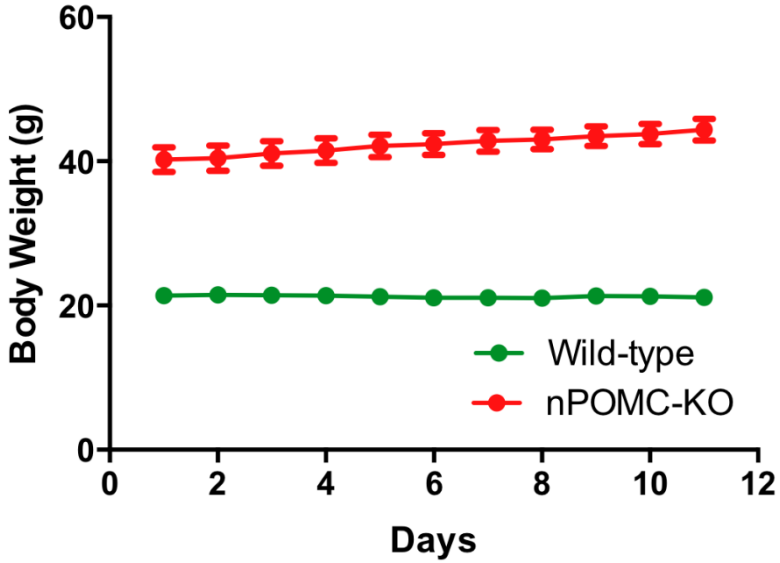
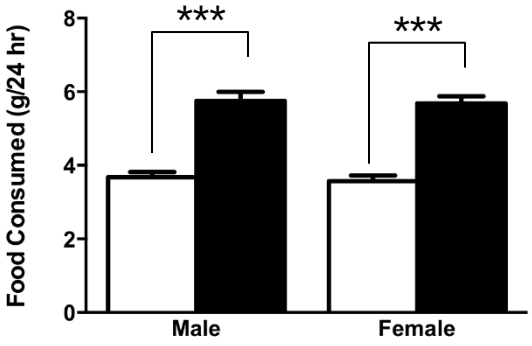
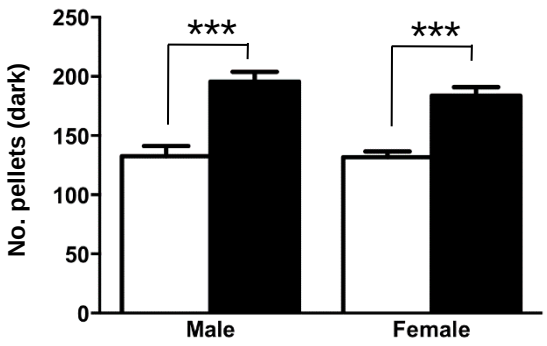
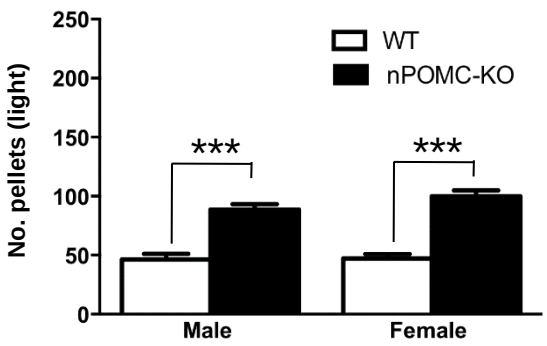
Bar pressing for 20 mg pellets using a fixed ratio 30











Jessica Adams and Samantha Spierling, unpublished data

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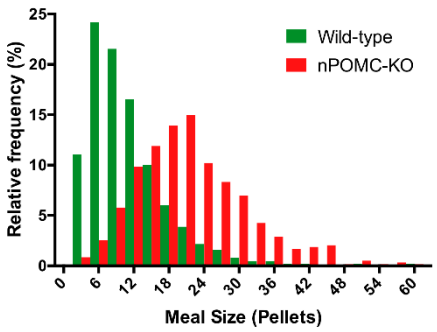
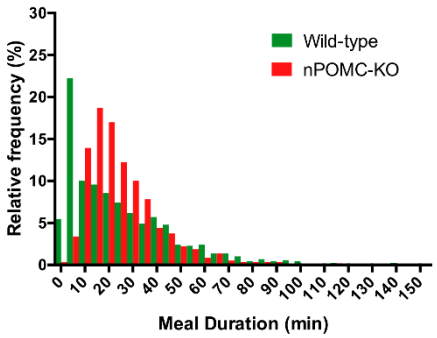
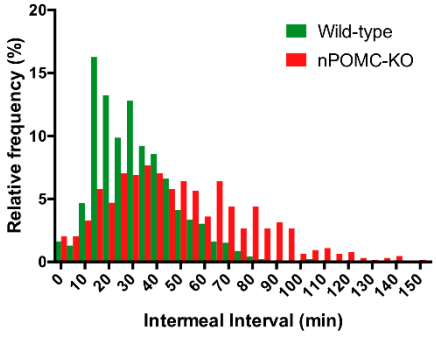
Meal Parameters Lights Off (6pm – 6am)

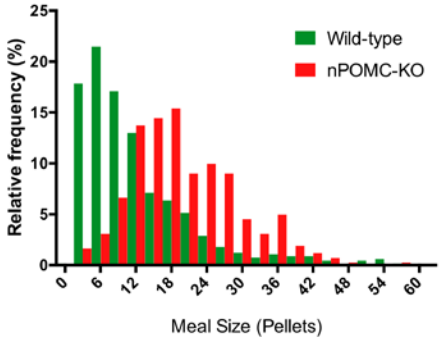
Male

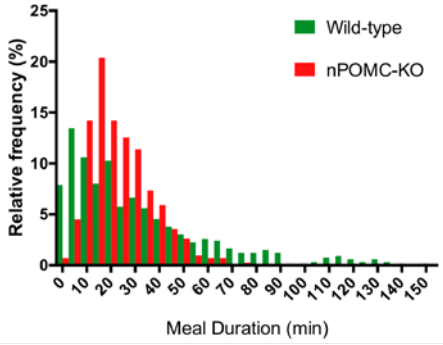


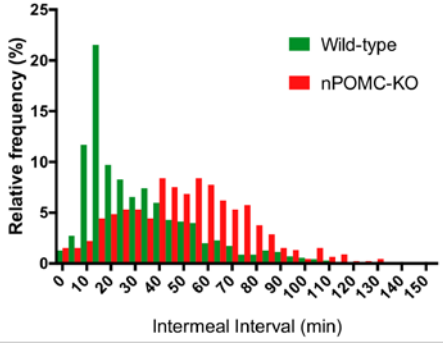


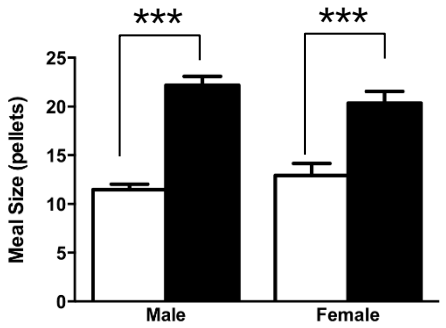


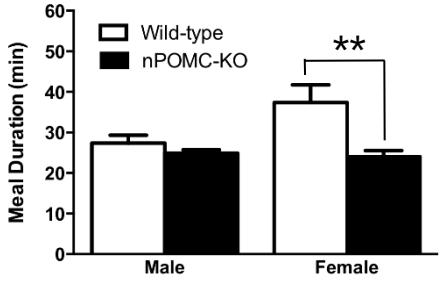
Female

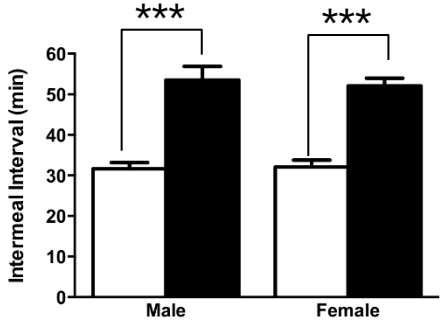












Jessica Adams and Samantha Spierling, unpublished data

Culex automated blood sampler & Empis infusion system (Basi, Inc.)

- Ratturn cages replace fluid swivels
- Tethered rats or mice have freedom of motion while their locomotor activity is recorded
- Animals can have combinations of vascular cannulae, intracranial cannulae, GI cannulae, microdialysis probes, optrodes and electrodes
- Serial biological samples can be obtained from, and substances infused into, nonanesthetized animals at preprogrammed intervals without human presence

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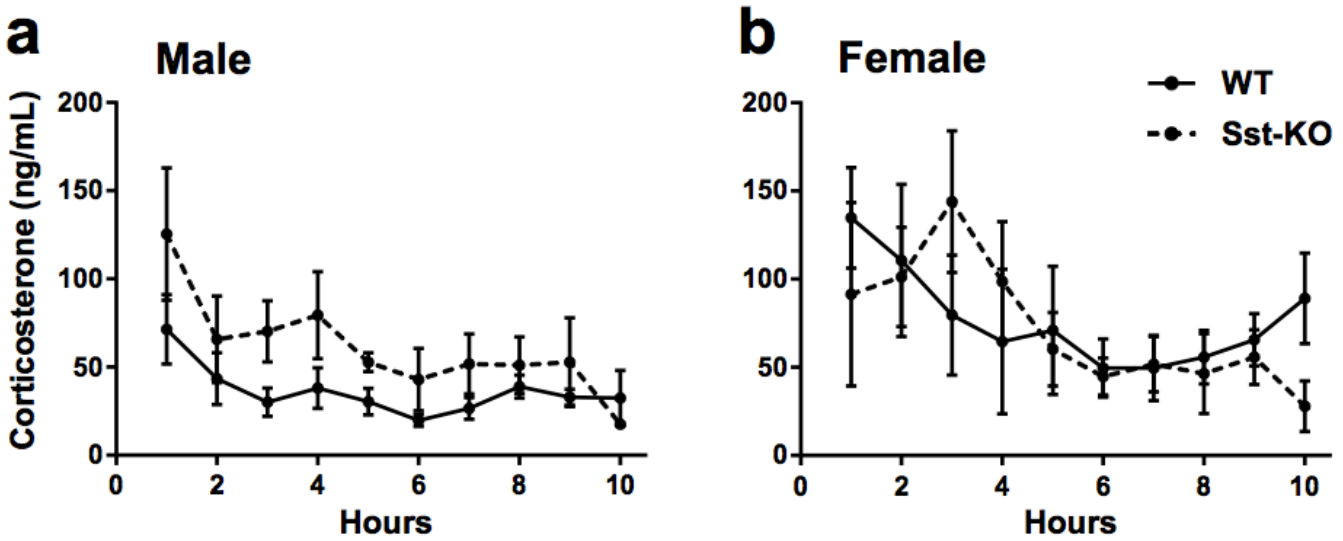
Culex Automated Blood Sampling 10ul q15 min x 44

Low Stress Indicated by Plasma Corticosterone



Adams J, et al. 2015
Endocrinology
156(3):1052–1065

Metabolism, Bariatric Surgery and Behavior Core

Culex Automated Blood Sampling 10ul q15 min x 44

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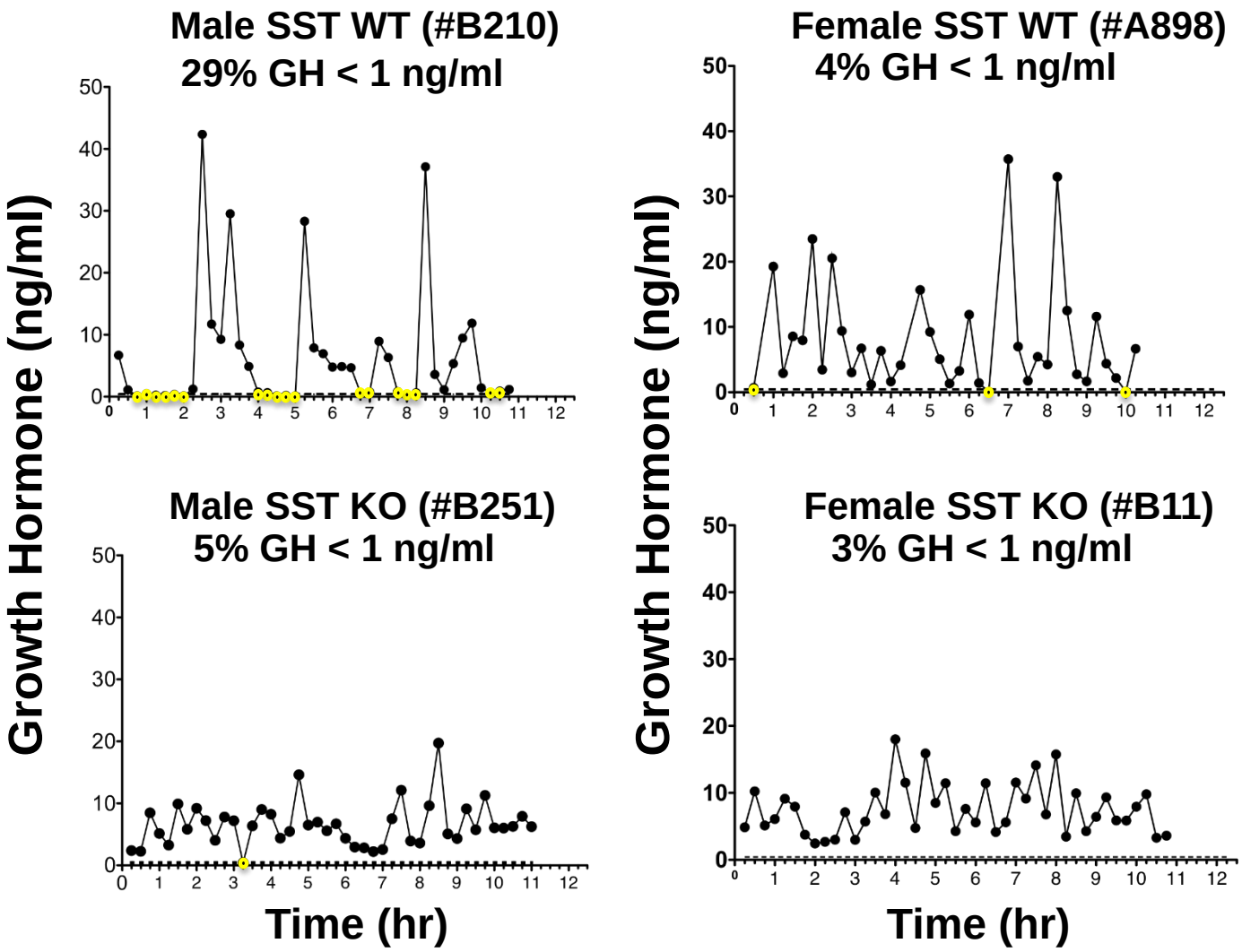
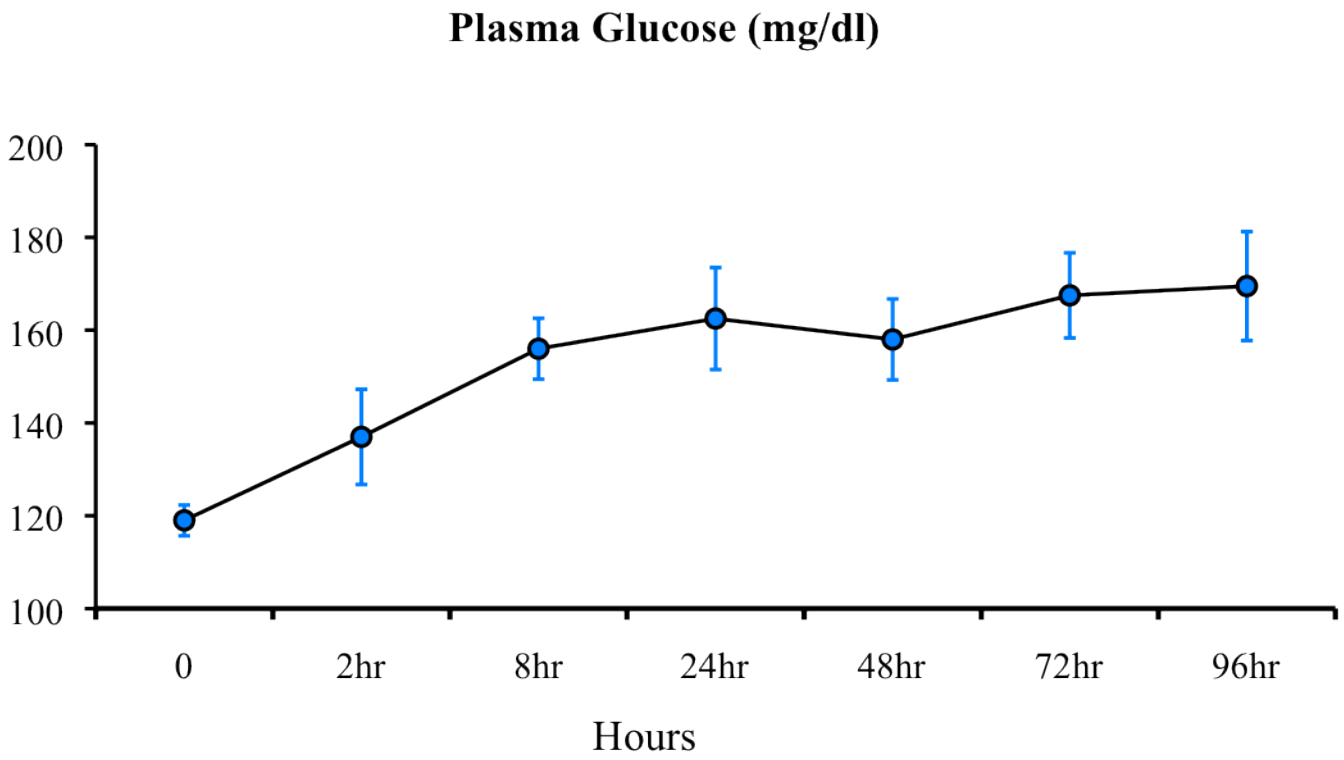


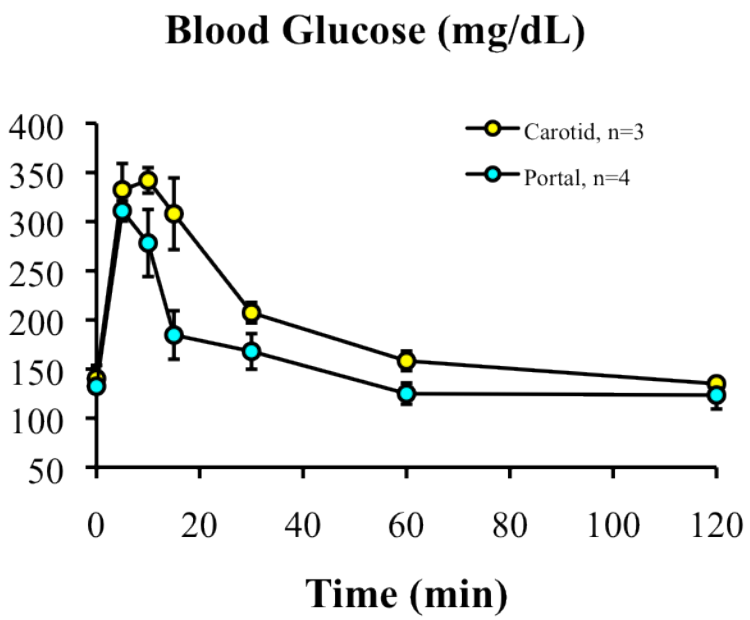
Maintenance of chronic hyperglycemia by constant iv infusion of glucose using the Culex apparatus in mice

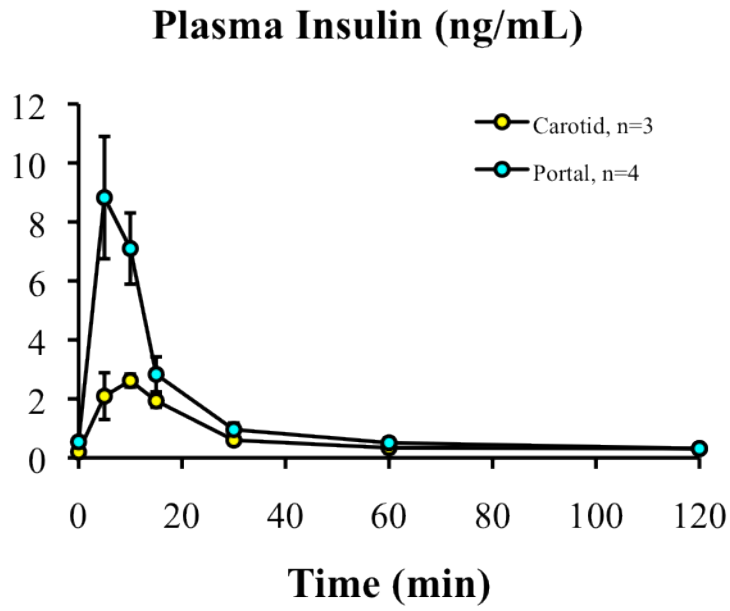


Qi, et al. unpublished data

Glucose infusion rate: 0.05-0.08 mL/g body weight

Differences between carotid artery vs. portal vein sampling of glucose and insulin during an OGTT





Blood sampling was perfomed with the Culex apparatus in freely moving mice. We propose to use this new approach when performing hyperinsulinemic, euglycemic clamps.

Qi, et al. unpublished data

Microvascular Complications Core

Eva Feldman, MD, PhD - Director

(Department of Neurology)

Jeffrey Hodgin, PhD - Co-Director

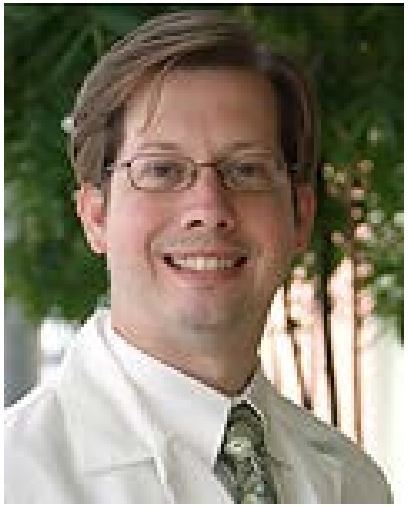
(Department of Pathology)

David Antonetti, PhD - Co-Director

(Departments of Ophthalmology & Visual Sciences; Molecular & Integrative Physiology)

Cheng-mao Lin, PhD - Coordinating Manager

(Department of Ophthalmology & Visual Sciences)



Microvascular Complications Core

- Provide a complete range of microvascular phenotyping of murine models of diabetes, obesity and metabolic disease

- Highly integrated with the other core laboratories that provide animal phenotyping, metabolomic, and bioinformatic support to fully perform multiscalar integration of phenotypic data

Complications Assessment

Complication	Conscious (Repeat Measures)	Anesthetized	Terminal
Peripheral Neuropathy: *Sural and sciatic nerves*	• Thermal Sensing • Mechanical Allodynia	• Nerve Conduction	• Morphological • Biochemical • Biomarkers
Nephropathy: *Kidney*	• Albuminuria/Creatine • Glomerular Filtration • Blood Pressure (tail-cuff)		• Morphological • Biochemical • Biomarkers
Retinopathy: *Retina*	• Visual Acuity • Contrast Sensitivity	• Morphological (OCT)	• Vascular Permeability • Biochemical • Biomarkers

Microbiome Core

Vincent Young, MD, PhD - Core Director

(Departments of Internal Medicine; Microbiology & Immunology)

Pat Schloss, PhD - Core Assoc. Director

(Department of Microbiology & Immunology)

Tom Schmidt, PhD - Core Assoc. Director

(Departments of Ecology & Evolutionary Biology (LSA); Internal Medicine, Microbiology & Immunology)

Christine Bassis, PhD - Research Investigator

(Department of Internal Medicine)