MMPC MICROMouse Program

Maren Laughlin

October, 2019

2019 Leaders

- Jack Rutledge (chair) --UC-Davis
- Julio Ayala --Vanderbilt
- Yvonne Ulrich-Lai --U Cincinnati
- Randall Friedline --U Mass
- Christine Bassis --U Michigan

- Rick McIndoe --Augusta University

- Outreach: Dawn Rowe --UC-Davis

What is the MICROMouse?

Pilot and Feasibility projects in mouse metabolic research.

Who can apply?

Eligible Project Directors/Principal Investigators:

- Applicants must hold a doctoral level position.
- Young investigators and post-doctoral fellows are encouraged to apply.
- Applicants can be in or outside an MMPC institution.

MICROMouse Guidelines

$75K direct costs, 1 year. PI can request 2nd year.

PI sends letter of intent to MMPC, applications reviewed 4x/year (2-3 expert reviewers, scores and comments)

-managed by Jack, Julio, Yve, Randle, Christine

Applications chosen for award by simple majority of MMPC Steering Committee (also decides if they can resubmit)

-managed by Rick

Awards made from the CBU, typically via subcontract. F&A costs negotiated.

-overseen by Rick

Progress report submitted at termination of award period.

Review Process

Proposals are assigned to ~three reviewers

- Members of MMPC external advisors
- External scientists with expertise in area of proposal
- Often use previous MICROMouse applicants

Reviewers are reminded that preliminary data should get less weight in the case of younger PIs

Unsuccessful proposals can be resubmitted by invitation

Competitive renewal possible for 1 additional year

Two Types of MICROMouse:

Resource-development projects

- Develop or miniaturize technologies
- Adapt existing technologies for use in mice
- Provide new tests to phenotype mouse models of metabolic disease
- Establish new types of mathematical models, informatics, databases or products that augment the mission of the center.
- Travel and housing funding to visit and learn MMPC tests
- Funding for short meetings or courses relevant to the MMPC

Two Types of MICROMouse:

Resource-related research projects

- Investigate biological phenomena or parameters that are broadly applicable to metabolic disease research using mouse models

Examples: impact of temperature, physical activity, stress, housing conditions, husbandry issues, microbiota, circadian rhythms, diets and feeding behavior, hormone patterns, growth, surgical models, etc.

- The pursuit of novel biological questions where the information can enrich or inform an MMPC and otherwise foster its mission.
- Use of the bariatric surgery models, the role of microbiome in metabolic diseases, studies that employ information found in the MMPC database

New in 2018

Encourage young investigators:
"All academic biomedical researchers who have a doctoral-level position can apply. **Post-doctoral fellows and junior faculty are especially encouraged to apply. Applications from post-doctoral fellows must include two letters of recommendation from senior mentors.** Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH support."

Police responsiveness regarding the MMPC mission:
"A brief letter of intent with description of the proposed project is due two weeks prior to submission of an application**. The letter will be promptly reviewed by the MMPC MICROMouse committee for responsiveness and for the relevance of the project to the MMPC mission**. Applications will be accepted only with permission from the MICROMouse committee."

6 Year Award Summary

Year	Applications MMPC/External	Awards MMPC/External	Investigators early/established
2014	18 10/8	4 3/1	2 assist prof 2 full prof
2015	10 8/2	5 5/0	1 post doc 4 full prof
2016	14 9/5	5 3/2	1 post doc, 1 assist prof 3 full prof
2017	18 9/9	5 2/3	1 post doc, 1 instr,1 assist 1 assoc prof, 1 full prof
2018 Micromouse (Q1,2,4)	21 6/15	5 1/4	1 research investigator 2 assist prof, 2 full prof
2018 Microbiome (Q3)	22 6/16	6 1/5	3 research investigator 3 assoc/full prof
2019	14 (3 qtrs) 3/11	2 (2 qtrs) 0/2	1 asst prof 1 assoc prof

6 Year Award Summary

Year	Resource-Development Research			Resource-Related Research		
	Applications	Awards	Success Rate	Applications	Awards	Success Rate
2014	10	3	30%	8	1	12%
2015	6	4	66%	4	1	25%
2016	7	4	57%	7	1	14%
2017	6	5	83%	12	0	0%
2018 (Q1,2,4)	1	0	0%	20	5	25%
2019 (Q1,2)	2	0	0%	6	2	33%

2018 MMPC Mouse Microbiome Metabolic Research Program

- $125,000 (total costs) for one year
- Pilot and feasibility projects that incorporate microbiome research into mouse metabolic phenotyping studies
- all studies should demonstrate clear potential to advance the mission of the MMPC
- any independent investigator or post-doctoral fellow at a US institution is eligible to apply.

22 applications

15 professor, 7 ‘research scientist/post doc’

6 awards

3 professor, 3 ‘research investigator’

5 from Universities outside the MMPC institutions

Cholera toxin, microbiome and obesity
Susan Erdman—Research Investigator
Massachusetts Institute of Technology

Development of a humanized mouse model to study the association between the gut microbiome and urinary stone disease
Joshua Stern—Associate Professor
Albert Einstein College of Medicine

Effects of Estradiol and Gut Microbiota on Energy Metabolism in Female Mice
Kalpana Acharya—Research Investigator
Wellesley College

Gut microbiota-regulated metabolism through MicroRNA-204
Kaikobad Irani--Professor
University of Iowa

Mouse Microbiome and Liver Tumorigenesis
Yu-Jui Yvonne Wan--Professor
University of California - Davis

The role of the microbiome in the metabolic benefits of NAD precursors
Karthikeyani Chellappa—Staff Research Associate
University of Pennsylvania

MICROMouse Funded 2018

Resource-Related projects

Effect of isocaloric restriction on high fat diet induced cognitive impairment
Jennifer Rutkowsky
University of California Davis

Mouse liver epigenome
Jeffrey Pessin
Albert Einstein College of Medicine

Development of lower urinary tract symptoms in diabetic mice
Warren Hill
Beth Israel Deaconess Medical

The effects of vertical sleeve gastrectomy on the celiac ganglia
Ana Emiliano
Columbia University

Individual variability in the metabolic response to fructose
Fernando Gomez-Pinilla
University of California Los Angeles

Funded 2019 to date

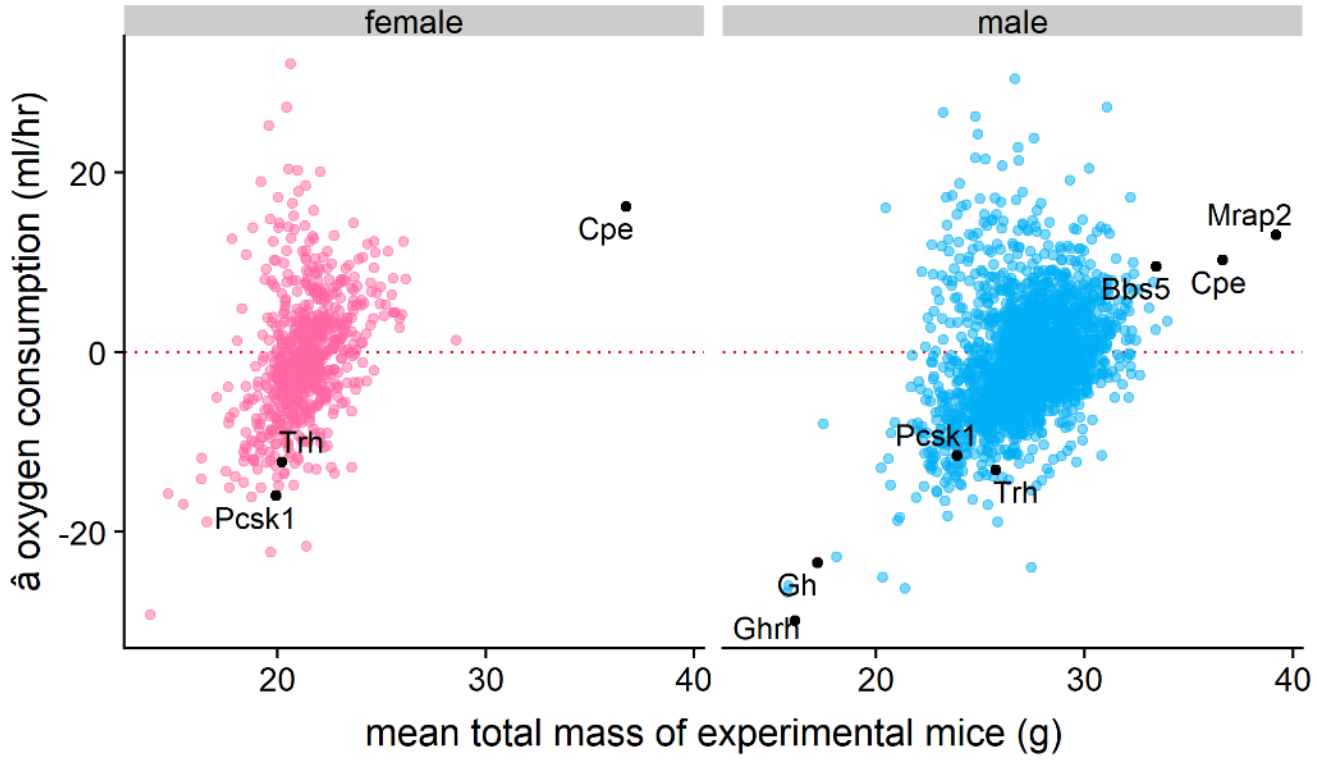
Resource Related Projects

Housing temperature impacts mouse energy metabolism during physical activity
E. Matthew Morris
University of Kansas Medical Center

Maximizing data to phenotype islet function in mouse models with low pancreatic islet content
Craig Nunemaker
Ohio University-Main Campus

2017 An Open-Source Resource for Analysis of Mouse Energy Balance Experiments (CalR) Alexander Banks

“Analysis of 30,000 mice (MMPC/IMPC) including 10,000 wild type C57Bl/6 mice -- largest experimental variance is derived from institutional site and acclimation to metabolic chambers.



Mina AI, LeClair RA, LeClair KB, Cohen DE, Lantier L, Banks AS. CalR: A Web-Based Analysis Tool for Indirect Calorimetry Experiments. Cell Metab. 2018;28(4):656-66 e1.

2017 In Vivo Imaging of Retinal Hypoxia in a Preclinical Model of Diabetic Retinopathy. MD Imam Uddin, Ph.D.

1.Targeted imaging of VCAM-1 mRNA in a mouse model of laser-induced choroidal neovascularization (LCNV) using antisense hairpin-DNA functionalized goldnanoparticles. Uddin, M. I.; Kilburn, T.C.; Rong, Y.; McCollum, G.W.; Wright, D.W.; Penn, J.S. Mol. Pharmaceutics, 2018, 15(12), 5514-5520.

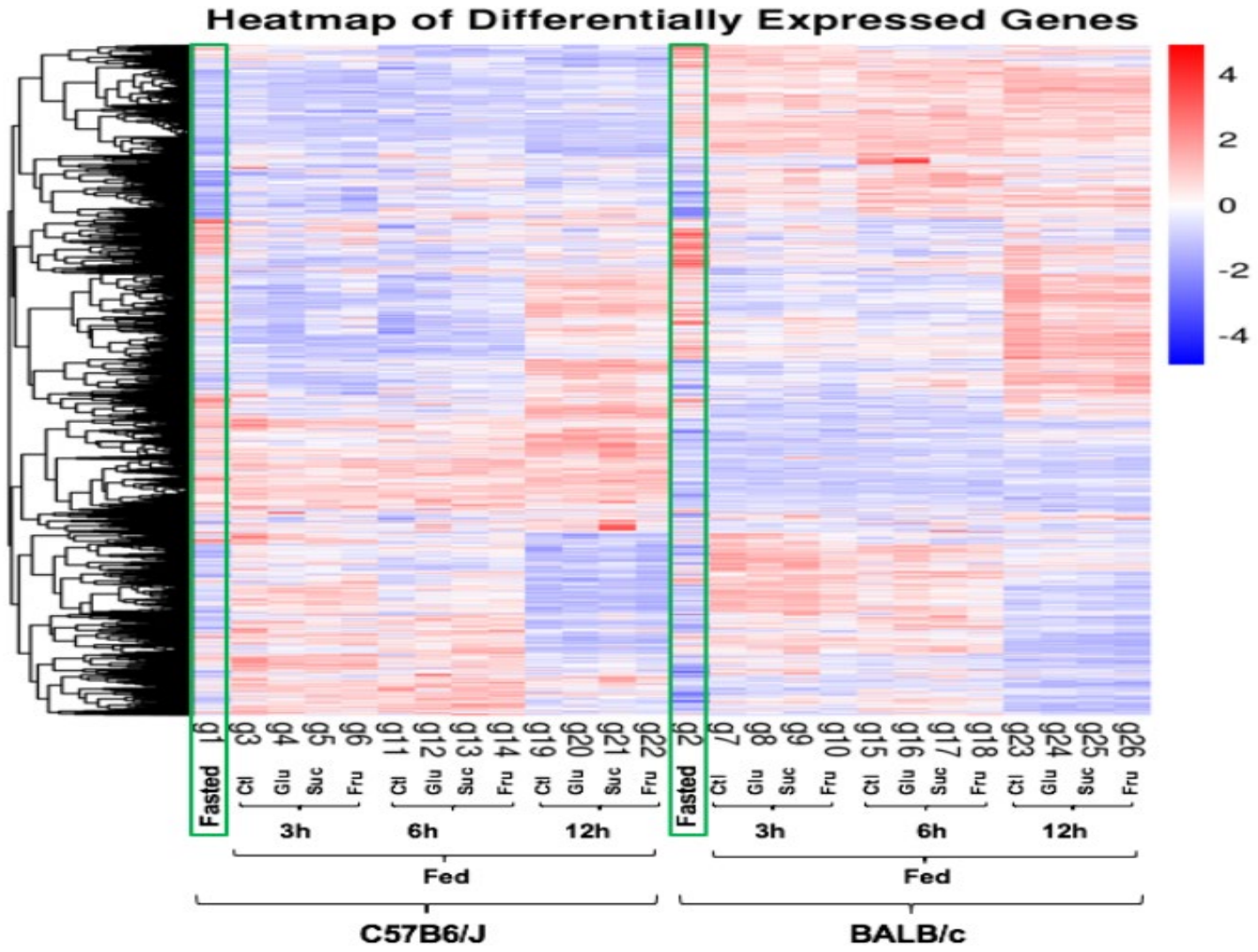
2. Real-time imaging of VCAM-1 mRNA in TNF-α activated retinal microvascular endothelial cells using antisense hairpin-DNA functionalized gold nanoparticles. Uddin, M. I.; Jayagopal, A.; Wong, A.; McCollum, G. W.; Wright, D. W.; Penn, J. S. Nanomedicine:NBM, 2018, 14(1), 63-71.

3. In Vivo Imaging of Retinal Hypoxia using HYPOX-4-dependent Fluorescence in a Mouse Model of Laser-induced Retinal Vein Occlusion (RVO). Uddin, M. I.; Jayagopal, A.; McCollum, G. W.; Rong, Y.; Penn, J. S. Invest. Ophthalmol. Vis. Sci. 2017, 58(9), 3818-3824.

2017 Validation of a Novel MS-based Method for Muscle Glucose Flux Analysis in Mice Ashley S. Williams

Williams AS, Muoio DM, Zhang G. A fast and sensitive method combining reversed phase chromatography with high resolution mass spectrometry to quantify 2-fluoro-2- deoxyglucose and its phosphorylated metabolite for determining glucose uptake (2019). ChemRxiv [Preprint]. February 27, 2019. Available from: https://doi.org/10.26434/chemrxiv.7771142.v1

2018 Mouse liver epigenome
Jeffrey Pessin
Albert Einstein College of Medicine



MICROMouse FOA Proposal

Proposal:

Funding Opportunity Announcement for original research that uses the MMPC database for at least one specific aim of a project.

Goals:

- Test and improve the public interface
- Provide a proof-of-concept test of MMPC data utility.

Logistics:

- Application receipt date(s)
- Size and duration of awards
- Number of awards