Notice of Award

CENTER GRANT
Department of Health and Human Services
National Institutes of Health

Federal Award Date: 01/18/2019

NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Grant Number: 5P30DK020572-42
FAIN: P30DK020572

Principal Investigator(s):
Martin G Myers, MD

Project Title: Michigan Diabetes Research Center

Ms. Maxwell, Terese G
REGENTS OF THE UNIVERSITY OF MICHIGAN - ANN ARBOR
3003 South State Street
1040 Wolverine Tower
Ann Arbor, MI 481091274

Award e-mailed to: creynolds-gov@umich.edu

Period Of Performance:
Budget Period: 12/01/2018 – 11/30/2019
Project Period: 12/01/1996 – 11/30/2022

Dear Business Official:

The National Institutes of Health hereby awards a grant in the amount of $1,740,654 (see "Award Calculation" in Section I and "Terms and Conditions" in Section III) to The Regents of the University of Michigan in support of the above referenced project. This award is pursuant to the authority of 42 USC 241 42 CFR 52 and is subject to the requirements of this statute and regulation and of other referenced, incorporated or attached terms and conditions.

Acceptance of this award including the "Terms and Conditions" is acknowledged by the grantee when funds are drawn down or otherwise obtained from the grant payment system.

Each publication, press release, or other document about research supported by an NIH award must include an acknowledgment of NIH award support and a disclaimer such as "Research reported in this publication was supported by the National Institute Of Diabetes And Digestive And Kidney Diseases of the National Institutes of Health under Award Number P30DK020572. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health." Prior to issuing a press release concerning the outcome of this research, please notify the NIH awarding IC in advance to allow for coordination.

Award recipients must promote objectivity in research by establishing standards that provide a reasonable expectation that the design, conduct and reporting of research funded under NIH awards will be free from bias resulting from an Investigator's Financial Conflict of Interest (FCOI), in accordance with the 2011 revised regulation at 42 CFR Part 50 Subpart F. The Institution shall submit all FCOI reports to the NIH through the eRA Commons FCOI Module. The regulation does not apply to Phase I Small Business Innovative Research (SBIR) and Small Business Technology Transfer (STTR) awards. Consult the NIH website http://grants.nih.gov/grants/policy/coi/ for a link to the regulation and additional important information.

If you have any questions about this award, please contact the individual(s) referenced in Section IV.

Sincerely yours,

MARY K. ROSENBERG
Grants Management Officer
NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Additional information follows

SECTION I – AWARD DATA – 5P30DK020572-42

Award Calculation (U.S. Dollars)

Salaries and Wages	$551,878
Fringe Benefits	$176,601
Personnel Costs (Subtotal)	$728,479
Materials & Supplies	$16,929
Travel	$3,500
Other	$366,896
Federal Direct Costs	$1,115,804
Federal F&A Costs	$624,850
Approved Budget	$1,740,654
Total Amount of Federal Funds Obligated (Federal Share)	$1,740,654
TOTAL FEDERAL AWARD AMOUNT	$1,740,654
AMOUNT OF THIS ACTION (FEDERAL SHARE)	$1,740,654

SUMMARY TOTALS FOR ALL YEARS		
YR	**THIS AWARD**	**CUMULATIVE TOTALS**
42	$1,740,654	$1,740,654
43	$1,740,654	$1,740,654
44	$1,740,654	$1,740,654
45	$1,740,654	$1,740,654

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

Fiscal Information:

CFDA Name:	Diabetes, Digestive, and Kidney Diseases Extramural Research
CFDA Number:	93.847
EIN:	1386006309A1
Document Number:	PDK020572J
PMS Account Type:	P (Subaccount)
Fiscal Year:	2019

IC	CAN	2019	2020	2021	2022
DK	8472281	$1,740,654	$1,740,654	$1,740,654	$1,740,654

Recommended future year total cost support, subject to the availability of funds and satisfactory progress of the project

NIH Administrative Data:
PCC: DJH DCTR / **OC**: 414E / **Released** eRA Commons User Name 01/17/2019
Award Processed: 01/18/2019 12:04:37 AM

SECTION II – PAYMENT/HOTLINE INFORMATION – 5P30DK020572-42

For payment and HHS Office of Inspector General Hotline information, see the NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm

SECTION III – TERMS AND CONDITIONS – 5P30DK020572-42

This award is based on the application submitted to, and as approved by, NIH on the above-titled project and is subject to the terms and conditions incorporated either directly or by reference in the following:

a. The grant program legislation and program regulation cited in this Notice of Award.
b. Conditions on activities and expenditure of funds in other statutory requirements, such as those included in appropriations acts.
c. 45 CFR Part 75.
d. National Policy Requirements and all other requirements described in the NIH Grants

Policy Statement, including addenda in effect as of the beginning date of the budget period.

e. Federal Award Performance Goals: As required by the periodic report in the RPPR or in the final progress report when applicable.
f. This award notice, INCLUDING THE TERMS AND CONDITIONS CITED BELOW.

(See NIH Home Page at http://grants.nih.gov/grants/policy/awardconditions.htm for certain references cited above.)

Research and Development (R&D): All awards issued by the National Institutes of Health (NIH) meet the definition of "Research and Development" at 45 CFR Part§ 75.2**.** As such, auditees should identify NIH awards as part of the R&D cluster on the Schedule of Expenditures of Federal Awards (SEFA). The auditor should test NIH awards for compliance as instructed in Part V, Clusters of Programs. NIH recognizes that some awards may have another classification for purposes of indirect costs. The auditor is not required to report the disconnect (i.e., the award is classified as R&D for Federal Audit Requirement purposes but non-research for indirect cost rate purposes), unless the auditee is charging indirect costs at a rate other than the rate(s) specified in the award document(s).

This institution is a signatory to the Federal Demonstration Partnership (FDP) Phase VI Agreement which requires active institutional participation in new or ongoing FDP demonstrations and pilots.

An unobligated balance may be carried over into the next budget period without Grants Management Officer prior approval.

This grant is excluded from Streamlined Noncompeting Award Procedures (SNAP).

This award is subject to the requirements of 2 CFR Part 25 for institutions to receive a Dun & Bradstreet Universal Numbering System (DUNS) number and maintain an active registration in the System for Award Management (SAM). Should a consortium/subaward be issued under this award, a DUNS requirement must be included. See http://grants.nih.gov/grants/policy/awardconditions.htm for the full NIH award term implementing this requirement and other additional information.

This award has been assigned the Federal Award Identification Number (FAIN) P30DK020572. Recipients must document the assigned FAIN on each consortium/subaward issued under this award.

This award is not subject to the Transparency Act subaward and executive compensation reporting requirement of 2 CFR Part 170.

In accordance with P.L. 110-161, compliance with the NIH Public Access Policy is now mandatory. For more information, see NOT-OD-08-033 and the Public Access website: http://publicaccess.nih.gov/.

In accordance with the regulatory requirements provided at 45 CFR 75.113 and Appendix XII to 45 CFR Part 75, recipients that have currently active Federal grants, cooperative agreements, and procurement contracts with cumulative total value greater than $10,000,000 must report and maintain information in the System for Award Management (SAM) about civil, criminal, and administrative proceedings in connection with the award or performance of a Federal award that reached final disposition within the most recent five-year period. The recipient must also make semiannual disclosures regarding such proceedings. Proceedings information will be made publicly available in the designated integrity and performance system (currently the Federal Awardee Performance and Integrity Information System (FAPIIS)). Full reporting requirements and procedures are found in Appendix XII to 45 CFR Part 75. This term does not apply to NIH fellowships.

Treatment of Program Income:

SECTION IV – DK Special Terms and Conditions – 5P30DK020572-42

Clinical Trial Indicator: No
This award does not support any NIH-defined Clinical Trials. See the NIH Grants Policy Statement Section 1.2 for NIH definition of Clinical Trial.

In accordance with the Salary Limitation in NIH Guide Notice NOT-OD-19-031, Notice of Fiscal Policies in Effect for FY2019, none of the funds in this award shall be used to pay the salary of an individual at a rate in excess of Executive Level II. Therefore, this award and/or future years are adjusted accordingly, if applicable. See the Salary Cap Summary for a historical record of the salary cap, including effective dates.

Submitted budget has been reviewed and found not to represent significant rebudgeting, and the award is issued consistent with previous commitments.

This award is consistent with the NIDDK policy of level total cost funding for Centers; it represents the previous commitment level of total cost funding for this Center and reflects use of the full appropriation.

The issuance of this award has been delayed due to administrative funding considerations. According to NIH policy, if pre-award costs are necessary, they may be approved by the authorized Institution Official(s).

This award includes $546,000 ($350,000 direct costs and $196,000 associated F&A costs) for pilot and feasibility (P&F) studies. These funds are restricted and may not be used for any other purpose without the written prior approval of the Awarding Office. Funds awarded for P&F and/or for support of a New Investigator Award, though restricted and not available for expenditure for other purposes, may be carried over to the next budget period and used for the originally awarded purposes.

Pilot and Feasibility Study Budget Breakdown:

Funds in the amount of $390,000 ($250,000 direct costs and $140,000 associated F&A costs) are for University of Michigan pilot and feasibility (P&F) studies.
Funds in the amount of $156,000 ($100,000 direct costs and $56,000 associated F&A costs) are for expanded pilot and feasibility (P&F) studies outsided of University of Michigan.

Future Years of Support: Each budget period will be individually negotiated based on study progress and availability of funds.

This award includes funds to support the following cores. No additional cores may be supported with awarded funds without prior approval from NIDDK: **Administrative Core; Animal Studies Core; Clinical Core; Microscopy Imaging and Cellular Physiology Core; Molecular Genetics Core.**

In addition to the PI, the following individuals are named as key personnel: **Darleen Sandoval (Core001: Animal Studies Core) William Herman (Core002: Clinical Core) David Antonetti (Core003: Microscopy Imaging and Cellular Physiology Core) David Olson (Core004: Molecular Genetics Core) Christin Carter-Su (P&F Director).** Written prior approval is required if any of the individuals named above withdraws from the project entirely, is absent from the project during any continuous period of 3 months or more, or reduces time devoted to the project by 25 percent or more from the level that was approved at the time of award.

This grant is in response to RFA-DK-16-020. Acceptance of this award requires compliance with this solicitation. See the NIH Guide at http://grants.nih.gov/grants/guide/index.html for copy of the RFA that includes administrative and programmatic requirements specific to this award.

In accordance with NIH policy http://grants.nih.gov/grants/policy/hs/index.htm and the NIH Guide Notice NOT-OD-15-078, the awardee institution is required to submit the following documentation in their annual progress report for any P&F projects selected in the prior year that involve human

subjects: http://grants.nih.gov/grants/how-to-apply-application-guide/forms-d/supplemental-instructions-forms-d.pdf

- Institutional Review Board (IRB) approval
- Protection of Human Subjects section
- Inclusion Enrollment Report
- Education in the Protection of Human Research Participants certifications
- Description of progress on previously awarded projects

No funds may be drawn down from the payment management system and no obligations/expenditures may be made against Federal funds for research involving human subjects at any site engaged in such research for any period not covered by both an OHRP-approved Assurance and by an IRB approval consistent with 45 CFR Part 46.

The NIH is mandated by law (Public Health Service Act sec. 492B, 42 U.S.C. sec. 289a-2) to ensure the inclusion of women and minority groups in clinical research. The goal is to ensure that individuals are included in clinical research in a manner that is appropriate to the scientific question under study.

Investigators must report sex/gender, race, and ethnicity information using the Inclusion Management System (IMS) module in the eRA Commons. Separate Inclusion Data Records should be created for each individual P&F project.

No funds may be drawn down from the payment system and no obligations may be made against Federal funds for research involving live vertebrate animals for any site engaged in such research for any period not covered by both an OLAW-approved Assurance and an IACUC approval consistent with the PHS Policy on Humane Care and Use of Laboratory Animals.

The grantee is required to follow the model organism sharing plan included in the original application and may not implement any changes in the plan without the written prior approval of the NIDDK.

Prior Approval of Pilot Projects

Awardee-selected projects that involve clinical trials or studies involving greater than minimal risk to human subjects require prior approval by NIH prior to initiation.

The awardee institution will provide NIH with written study protocols that address risks and protections for human subjects in accordance with NIH's Instructions for Preparing the Human Subjects Section of the Research Plan.

The awardee institution will provide NIH with specific plans for data and safety monitoring, and will notify the IRB and NIH of serious adverse events and unanticipated problems, consistent with NIH DSMP policies.

Grantees can determine which progress reports are due through the website located at: https://public.era.nih.gov/chl/public/search/index.jsp , and should periodically check the site, which is updated on or around the 30th of each month. Progress report due dates are also available in the eRA Commons Status system. In addition, automatic e-mail notifications are sent to the PD/PI prior to due date.

As of October 17, 2014, the National Institutes of Health (NIH) requires grantees to submit all type 5 progress reports using the eRA Research Performance Progress Report (RPPR) module. Annual progress reports submitted in any format other than the RPPR will not be processed by the NIH and will require resubmission through the RPPR module in accordance with NIH Guide Notice Number: NOT-OD-15-014 released October 16, 2014.

STAFF CONTACTS

The Grants Management Specialist is responsible for the negotiation, award and administration of this project and for interpretation of Grants Administration policies and provisions. The Program Official is responsible for the scientific, programmatic and technical aspects of this project. These individuals work together in overall project administration. Prior approval requests (signed by an

Authorized Organizational Representative) should be submitted in writing to the Grants Management Specialist. Requests may be made via e-mail.

Grants Management Specialist: Christina Coriz
Email: corizc@niddk.nih.gov **Phone**: 301-594-8848

Program Official: James F Hyde
Email: hydej@niddk.nih.gov **Phone**: (301) 594-7692 **Fax**: (301) 480-3503

SPREADSHEET SUMMARY
GRANT NUMBER: 5P30DK020572-42

INSTITUTION: The Regents of the University of Michigan

Budget	Year 42	Year 43	Year 44	Year 45
Salaries and Wages	$551,878	$551,878	$551,878	$551,878
Fringe Benefits	$176,601	$176,601	$176,601	$176,601
Personnel Costs (Subtotal)	$728,479	$728,479	$728,479	$728,479
Materials & Supplies	$16,929	$16,929	$16,929	$16,929
Travel	$3,500	$3,500	$3,500	$3,500
Other	$366,896	$366,896	$366,896	$366,896
TOTAL FEDERAL DC	$1,115,804	$1,115,804	$1,115,804	$1,115,804
TOTAL FEDERAL F&A	$624,850	$624,850	$624,850	$624,850
TOTAL COST	$1,740,654	$1,740,654	$1,740,654	$1,740,654

Facilities and Administrative Costs	Year 42	Year 43	Year 44	Year 45
F&A Cost Rate 1	56%	56%	56%	56%
F&A Cost Base 1	$1,115,804	$1,115,804	$1,115,804	$1,115,804
F&A Costs 1	$624,850	$624,850	$624,850	$624,850

A. OVERALL COVER PAGE

Project Title: Michigan Diabetes Research Center	
Grant Number: 5P30DK020572-42	**Project/Grant Period:** 12/01/1996 - 11/30/2022
Reporting Period: 02/27/2018 - 11/30/2018	**Requested Budget Period:** 12/01/2018 - 11/30/2019
Report Term Frequency: Annual	**Date Submitted:** 09/27/2018
Program Director/Principal Investigator Information: MARTIN G MYERS , BA MD PHD **Phone number:** (734) 647-9515 **Email:** mgmyers@umich.edu	**Recipient Organization:** UNIVERSITY OF MICHIGAN AT ANN ARBOR 3003 SOUTH STATE STREET 1st Floor Wolverine Tower ANN ARBOR, MI 481091276 **DUNS:** 073133571 **EIN:** 1386006309A1 **RECIPIENT ID:** 17-PAF02413
Change of Contact PD/PI: N/A	
Administrative Official: COLLEEN L VOGLER University of Michigan ORSP 3003 S. State St., Room 1044 ANN ARBOR, MI 481091274 **Phone number:** 7346472179 **Email:** clv@umich.edu	**Signing Official:** COLLEEN L VOGLER University of Michigan ORSP 3003 S. State St., Room 1044 ANN ARBOR, MI 481091274 **Phone number:** 7346472179 **Email:** clv@umich.edu
Human Subjects: Yes HS Exempt: No Exemption Number: Phase III Clinical Trial:	**Vertebrate Animals:** Yes
hESC: No	**Inventions/Patents:** No

B. OVERALL ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The mission of the MDRC is to promote new discoveries and enhance scientific progress through the support of cutting-edge basic and clinical research by its highly interactive research base. The MDRC research base comprises 145 members: 118 members with $56.8 million of annual direct cost diabetes-related funding at the University of Michigan (UM) along with 27 regional members with $8.6 million of annual funding at three nearby Regional Partner Institutions: Michigan State University (MSU), Wayne State University (WSU) and the University of Toledo (UT). The investigators that make up the MDRC research base perform ground-breaking research in five broad areas relevant to diabetes: Cellular Aspects of Diabetes and Metabolism; Integrative Aspects of Diabetes and Metabolism; Islet Biology; Diabetic Complications; and Clinical Research in Diabetes and Metabolism. To support and empower research by its members, the MDRC will:
1. Coordinate activities that raise awareness of, interest in, and support for basic and translational research in diabetes, its complications, and related endocrine and metabolic disorders at the University of
Michigan and beyond.
2. Advance learning and promote scientific exchange related to diabetes, endocrinology and metabolism.
3. Provide research cores that provide shared, specialized technical resources and expertise that enhance the efficiency, productivity, and multidisciplinary nature of research performed by MDRC investigators.
4. Support a Pilot and Feasibility studies grant program.
5. Provide support for research in diabetes, its complications, and related endocrine and metabolic disorders at Regional Partner Institutions. The MDRC provides membership, enrichment activities, an
expanded Pilot and Feasibility Grant Program, and access to the MDRC Molecular Genetics Core for researchers at Regional Partner Institutions who study diabetes, its complications, and related endocrine and metabolic disorders.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

Yes

Revision/ Supplements #	Revision/ Supplements Title	Specific Aims	Accomplishments
P30DK20572-40S1	Administration of the NIDDK-based website	The focus of the supplement activities is improved design, development, support, and maintenance of three NIDDK funded web sites: Diabetes Research Centers, Centers for Diabetes Translation Research, and Cystic Fibrosis Research and Translation Centers. The web sites provide a central portal to facilitate progress in diabetes research, diabetes-related translational research, and cystic fibrosis basic and clinical research, including cystic fibrosis-related diabetes, with the goal of bringing together investigators from relevant disciplines in a manner that will enhance and extend the effectiveness of their research.	DRC: Web content added and updated for DRC centers and cores, funding opportunities, upcoming symposia and meetings, as well as center news, P&F reviewers, and diabetes related resources. The P&F reviewers has an improved design with the ability to search by publication keyword. Pilot studies & awardees added to highlight the center's study grant programs. CDTR & CFRTC: Web services are monitored and maintained. Summaries and biographies of centers and center directors, overviews of the centers' services and cores, and selected publications are reviewed and updated. The CDTR annual meeting book is available to view online and download. CFRTC web pages have new CF links and an improved layout

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The MDRC will continue to support the programs central to its mission, and to support the development of new resources, technologies, and core services to support the mission of the center and its members.

B.2 What was accomplished under these goals?

As described in the individual component reports, we operated cores, provided interaction and enrichment activities, and supported a UM-based and regional Pilot and Feasibility component. We helped to expand the services of the cores and continue to develop new services, including in the Animal Studies Core (additional islet assays; new laser for optogenetics), MICPC (in vivo fiber photometry), Molecular Genetics Core (more advanced rabies tracers; new AAV serotypes), and Clinical (consolidation of services in the Diabetes CRU). We continue to update our website.

Furthermore, the MDRC received a supplemental award, with which it supports the work of Jodee Allen in administering the NIDDK-based center website.

In the 18 months since our last progress report, our members have received 166 new diabetes-related research awards totaling over $221 million (126, totaling over $214 million from NIH); these are listed in the attached table. In addition to the vast majority of these that represent research awards, these include the renewals of several T32 awards that interact with and benefit from the MDRC- including “Training in Clinical and Basic Neuroscience”, which has a major focus in diabetic neuropathy and the “Michigan Vision Clinical Scientist Development Program,” which has a major focus in diabetic retinopathy. Also, the MDRC interacts with and provided support for the recent renewal of the Michigan O’Brien Renal Center (P30), including the proposed co-support of Pilot grants that focus on Diabetic Nephropathy, the UM Center for Gastrointestinal Research (P30), which utilizes the MDRC Molecular Genetics Core, and the Core Grant for Vision Research (P30), which shares tissue sectioning and imaging equipment and services with the MDRC MICPC Core.

The following publications exemplify progress made during the current funding period (center members listed in Bold):
1. Chambers AP, Sorrell JE, Haller A, Roelofs K, Hutch CR, Kim KS, Gutierrez-Aguilar R, Li B, Drucker DJ, D'Alessio DA, **Seeley RJ**, **Sandoval DA**. The Role of Pancreatic Preproglucagon in Glucose Homeostasis in Mice. Cell Metab. 2017 Apr 4;25(4):927-934.e3. doi: 10.1016/j.cmet.2017.02.008. Epub 2017 Mar 16. PubMed PMID: 28325479; PubMed Central PMCID: PMC5385998.
Glucagon-like peptide 1 (GLP-1) is necessary for normal gluco-regulation, and it has been widely presumed that this function reflects the actions of GLP-1 released from enteroendocrine L cells. To test the relative importance of intestinal versus pancreatic sources of GLP-1 for physiological regulation of glucose, the authors administered a GLP-1R antagonist, exendin-[9-39] (Ex9), to mice with tissue-specific reactivation of the preproglucagon gene (Gcg). Ex9 impaired glucose tolerance in wild-type mice but had no impact on Gcg-null or GLP-1R KO mice, suggesting that Ex9 is a true and specific GLP-1R antagonist. Unexpectedly, Ex-9 had no effect on blood glucose in mice with restoration of intestinal Gcg. In contrast, pancreatic reactivation of Gcg fully restored the effect of Ex9 to impair both oral and i.p. glucose tolerance. These findings suggest an important new model whereby islet-derived GLP-1 plays an important role in regulating glucose homeostasis.

2. Sas KM, Kayampilly P, Byun J, Nair V, Hinder LM, Hur J, Zhang H, Lin C, Qi NR, Michailidis G, Groop PH, Nelson RG, Darshi M, Sharma K, Schelling JR, Sedor JR, **Pop-Busui R**, Weinberg JM, **Soleimanpour SA**, **Abcouwer SF**, **Gardner TW**, **Burant CF**, **Feldman EL**, **Kretzler M**, **Brosius FC 3rd**, **Pennathur S**. Tissue-specific metabolic reprogramming drives nutrient flux in diabetic complications. JCI Insight. 2016 Sep 22;1(15):e86976. PubMed PMID: 27699244; PubMed Central PMCID: PMC5033761.
Diabetes is associated with altered cellular metabolism, but how altered metabolism contributes to the development of diabetic complications is unknown. The authors used the BKS db/db diabetic mouse model to investigate changes in carbohydrate and lipid metabolism in kidney cortex, peripheral nerve, and retina. A systems approach using transcriptomics, metabolomics, and metabolic flux analysis identified tissue-specific differences, with increased glucose and fatty acid metabolism in the kidney, a moderate increase in the retina, and a decrease in the nerve. In the kidney, increased metabolism was associated with enhanced protein acetylation and mitochondrial dysfunction. To confirm these findings in human disease, the authors analyzed diabetic kidney transcriptomic data and urinary metabolites from a cohort of Southwestern American Indians. The urinary findings were replicated in 2 independent patient cohorts, the Finnish Diabetic Nephropathy and the Family Investigation of Nephropathy and Diabetes studies. Increased concentrations of TCA cycle metabolites in urine, but not in plasma, predicted progression of diabetic kidney disease, and there was an enrichment of pathways involved in glycolysis and fatty acid and amino acid metabolism. These findings

highlight tissue-specific changes in metabolism in complication-prone tissues in diabetes and suggest that urinary TCA cycle intermediates are potential prognostic biomarkers of diabetic kidney disease progression.

3. Scott LJ, Erdos MR, Huyghe JR, Welch RP, Beck AT, Wolford BN, Chines PS, Didion JP, Narisu N, Stringham HM, Taylor DL, Jackson AU, Vadlamudi S, Bonnycastle LL, Kinnunen L, Saramies J, Sundvall J, Albanus RD, Kiseleva A, Hensley J, Crawford GE, Jiang H, Wen X, Watanabe RM, Lakka TA, Mohlke KL, Laakso M, Tuomilehto J, Koistinen HA, **Boehnke M**, Collins FS, **Parker SC**. The genetic regulatory signature of type 2 diabetes in human skeletal muscle. Nat Commun. 2016 Jun 29;7:11764. doi: 10.1038/ncomms11764. PubMed PMID: 27353450; PubMed Central PMCID: PMC4931250
Type 2 diabetes (T2D) results from the combined effects of genetic and environmental factors on multiple tissues over time. Of the >100 variants associated with T2D and related traits in genome-wide association studies (GWAS), >90% occur in non-coding regions, suggesting a strong regulatory component to T2D risk. To understand how T2D status, metabolic traits and genetic variation influence gene expression, the authors analyzed skeletal muscle biopsies from 271 well-phenotyped Finnish participants with glucose tolerance ranging from normal to newly diagnosed T2D. They performed high-depth strand-specific mRNA-sequencing and dense genotyping. Computational integration of these data with epigenome data, including ATAC-seq on skeletal muscle, and transcriptome data across diverse tissues revealed that the tissue-specific genetic regulatory architecture of skeletal muscle is highly enriched in muscle stretch/super enhancers, including some that overlap T2D GWAS variants. In one such example, T2D risk alleles residing in a muscle stretch/super enhancer are linked to increased expression and alternative splicing of muscle-specific isoforms of ANK1.

In addition to the support for clinical diabetes research by the pilot and feasibility, enrichment program, and the cores (including the clinical core), examples of progress along the clinical spectrum are exemplified in the publications supported by the clinical core, and by Sas, et al., and Scott, et al., above, which identified potential new prognostic biomarkers for DKD and established gene regulatory changes due to epigenetic alterations in human muscle with diabetes, respectively.

Of the 567 publications attributable to the MDRC this reporting period, 189 of them represent collaborations among center members (See bibliography). Similarly, of the 166 new grants awarded during the reporting period, 33 of them represented collaboration, listing two or more MDRC members as key personnel.

For a detailed report of presentations, seminars, symposia, education and training opportunities, please refer to the report of the Enrichment Program.

TABLE A. New Funding Supported by the DRC/CDTR (Awarded 12/01/2016 - 07/31/2018)

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Wellik, Deneen UM Principal Investigator	Title: 54th Annual Midwest Society for Developmental Biology Mechanism: Grant Funding Sources: Private Source	06/01/2016	05/31/2017	$12,000
Gardner, Thomas UM Principal Investigator	Title: Improving the Diagnosis and Treatment of Early Stage Diabetic Retinopathy Mechanism: Grant Funding Sources: Private Source	07/01/2016	06/30/2017	$5,000
Singer, Kanakadurga UM Principal Investigator	Title: Mechanisms of hematopoietic stem cell activation in obesity Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2016	06/30/2019	$1,500
Gregg, Brigid UM Principal Investigator	Title: Programming of beta-cells and Glucose Homeostasis by Maternal Metformin Exposure Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2016	07/31/2020	$1,500
Rui, Liangyou UM Principal Investigator	Title: Hepatic TNF Receptor Associated Factor (TRAF) 3 Promotes Insulin Resistance through the Ubiquitination of Insulin Receptor Substrate (IRS) 1 and 2 Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/01/2016	08/31/2018	$1,800
Boehnke, Michael Participating Investigator with Specified Effort	Title: TOPMed Informatics Resource Center - Data and Working Group Support Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of **Health**	09/29/2016	12/31/2017	$6,894,774
Cone, Roger UM Principal Investigator	Title: Improvement Of Feed Efficiency In A Commercially Relevant Fish Species By Altering Melanocortin-4 Receptor Activity Mechanism: Grant Funding Sources: Agriculture, Department of	10/01/2016	02/28/2019	$249,535
Bridges, David UM Principal Investigator	Title: Regulation of Lipid Storage by mTORC1 Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	11/01/2016	01/31/2021	$1,612,877
Myers Jr, Martin UM Principal Investigator	Title: Michigan Diabetes Research Center (P30)-Administrative Supplement Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/01/2016	11/30/2017	$600,000
Burant, Charles Li, Jun UM Principal Investigators Horowitz, Jeffrey Karnovsky, Alla Participating Investigators with Specified Effort	Title: Michigan MoTrPAC Chemical Analysis Site (MiCAS) Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/08/2016	11/30/2022	$8,238,759
Busui, Rodica UM Principal Investigator	Title: Cardiovascualr autonomic neruopathy in subjects with type 1 diabetes Mechanism: Grant Funding Sources: Private Source	01/01/2017	12/31/2017	$3,000

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Horowitz, Jeffrey UM Principal Investigator	Title: Insulin sensitivity and fatty acid partitioning in skeletal muscle after exercise supplement Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/01/2017	12/31/2017	$513,895
Lumeng, Julie UM Principal Investigator	Title: Maternal Social Modeling and Infant Social Engagement During Feeding as Predictors of Weight Gain Mechanism: Grant Funding Sources: Private Source	01/01/2017	08/01/2018	$102,550
Wu, Jun UM Principal Investigator	Title: Regulation of thermogenesis in subcutaneous fat cells: Crosstalk between PRMT1 and PKA Mechanism: Grant Funding Sources Private Source	01/01/2017	07/19/2018	$98,950
Myers Jr, Martin UM Principal Investigator	Title: Role of the obesity gene, Asb4, in leptin action Mechanism: Grant Funding Sources: Private Source	01/01/2017	12/31/2019	$171,804
Flak, Jonathan UM Sponsor Principal Investigator Myers Jr, Martin UM Principal Investigator	Title: Targeting the VMN to understand Hypoglycemia Pathogenesis Mechanism: Grant Funding Sources: Private Source	01/01/2017	12/31/2023	$1,625,000
Auchus, Richard UM Principal Investigator	Title: Using Molecular Genetics To Establish Etiology for Combined Hypogonadotropic Hypogonadism and Growth Hormone Deficiency Phenotype Mechanism: Grant Funding Sources Private Source	01/01/2017	12/31/2017	$5,000
Ratliff, Briana UM Principal Investigator	Title: Stress, Self-Regulatory Behaviors, and Diabetes Mechanism: Grant Funding Sources: Private Source	01/26/2017	12/31/2018	$472,767
Sandoval, Darleen UM Principal Investigator Olson, David Satin, Leslie Seeley, Randy Participating Investigators with Specified Effort	Title: A novel paracrine role for GLP-1 in the islet Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	02/01/2017	01/31/2021	$1,556,458
Richardson, Caroline Participating Investigator without Specified Effort	Title: A mixed methods pilot randomized controlled trial of a mobile phone-based health program among adults with prediabetes Mechanism: Grant Funding Sources: Private Source Private Source	02/15/2017	08/16/2018	$10,000
Lumeng, Julie Participating Investigator without Specified Effort	Title: Electronic versus print books: Differences in parent-toddler interactions and toddler behavioral regulation Mechanism: Grant Funding Sources Private Source	03/01/2017	10/15/2018	$14,780
Gardner, Thomas Participating Investigator without Specified Effort	Title: Epigenetic Control of Retinal Development Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2017	02/28/2020	$665,733

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Alexander, Neil UM Principal Investigator	Title: Home-based team transitional telecare to optimize mobility and physical activity in recently hospitalized older Veterans Mechanism: Grant Funding Sources: Private Source	03/01/2017	02/28/2019	$499,381
Wellik, Deneen UM Principal Investigator	Title: Hox-Regulated MSCs in Skeletal Development, Growth and Fracture Healing Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2017	02/28/2022	$1,705,000
Burant, Charles Karnovsky, Alla Participating Investigators without Specified Effort	Title: Using metabolomics to identify novel biomarkers for knee osteoarthritis risk Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2017	02/28/2022	$637,569
Holinstat, Michael Participating Investigator without Specified Effort	Title: Role of PIKFyve in platelet-mediated inflammation and thrombosis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/20/2017	03/31/2020	$508,680
Lee, Joyce UM Principal Investigator	Title: Type 1 Diabetes (T1D) E-Health Research Study Mechanism: Grant Funding Sources: Private Source Private Source	03/27/2017	10/05/2017	$25,000
Carter-Su, Christin UM Principal Investigator	Title: Cellular mechanism of action of SH2B1 isoforms implicated in human obesity Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2021	$174,222
Lin, Jiandie UM Principal Investigator	Title: Endocrine regulation of metabolic health during aging Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2019	$426,250
Low, Malcolm UM Principal Investigator Myers Jr, Martin Olson, David Qi, Nathan Sandoval, Darleen Participating Investigators without Specified Effort	Title: Function of the hypothalamic melanocortin system in stimulating counter-regulatory response to hypoglycemia Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2021	$399,756
Lin, Jiandie UM Principal Investigator	Title: Glucose sensing by skeletal myocytes Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2022	$1,946,875
Feldman, Eva UM Principal Investigator Callaghan, Brian Lentz, Stephen, Verhey, Kristen Weisman, Lois Participating Investigators without Specified Effort	Title: Identifying Alterations in Mitochondrial Dynamics Associated with Diabetic Neuropathy Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2018	$57,066

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Shea, Lonnie UM Principal Investigator Cras-Meneur, Corentin Participating Investigator with Specified Effort	Title: Microporous scaffolds for enhancing efficiency of beta-cell progenitor maturation in vitro and in vivo Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	01/31/2019	$399,550
Wang, Xuewei UM Sponsor Principal Investigator	Title: Nitric Oxide Releasing Cannula Integrated with Glucose Electrode for Long Term Single-Port Glycemic Control Mechanism: Grant Funding Sources: Private Source Private Source	04/01/2017	03/31/2020	$285,000
Andjelkovic-Zochowska, Anuska Participating Investigator without Specified Effort	Title: ROLE OF S100A8/A9 IN BLOOD BRAIN BARRIER DYSFUNCTION AFTER SEPSIS Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2022	$977,400
Seeley, Randy Participating Investigator without Specified Effort	Title: R-spondin1-LGR4 Signaling and Ischemia/Reperfusion Injury in Steatotic Liver Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2017	03/31/2022	$2,043,735
Cone, Roger UM Principal Investigator	Title: ALLOSTERIC MODULATORS OF MC4R SIGNALING Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	05/01/2017	04/30/2018	$668,120
Arvan, Peter Participating Investigator without Specified Effort	Title: Clarifying pathogenesis of MIDY - a new form of diabetes mellitus Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	05/01/2017	04/30/2019	$70,968
Weiss, Stephen UM Principal Investigator	Title: Neutrophil extracellular traps (NETs) and innate immune system as novel mediators for mechanotransduction of acute inflammation Mechanism: Grant Funding Sources: Private Source	05/08/2017	05/07/2018	$38,000
Moenter, Suzanne UM Principal Investigator	Title: Coordination of the reproductive neuroendocrine system to produce pulsatile hormone release Mechanism: Grant Funding Sources: Private Source	06/01/2017	05/31/2018	$50,000
Barmada, Sami Participating Investigator without Specified Effort	Title: Determining the role of RNA-based factors in RAN translation of C9ALS/FTD-associated GGGGCC repeats Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	05/31/2020	$122,594
Feldman, Eva Participating Investigator without Specified Effort	Title: Impact of Geospatial Factors and Environmental Pollutants on Amyotrophic Lateral Sclerosis in the State of Michigan Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	05/31/2022	$1,009,261
Shah, Yatrik UM Principal Investigator	Title: MAZ as a Novel Regulator of STAT3 Signaling in Colon Cancer Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	07/31/2018	$42,744

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Ringold, Vicki UM Principal Investigator	Title: Michigan Institute for Clinical and Health Research (MICHR) - KL2 Award Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	02/28/2022	$6,914,295
Holinstat, Michael UM Principal Investigator Ringold, Vicki Participating Investigator with Specified Effort	Title: Michigan Institute for Clinical and Health Research (MICHR) TL1 Award Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	02/28/2022	$2,688,970
Alexander, Neil Lumeng, Julie Ringold, Vicki Participating Investigators with Specified Effort	Title: Michigan Institute for Clinical and Health Research (MICHR) Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2017	02/28/2022	$48,220,260
Boehnke, Michael Participating Investigator with Specified Effort	Title: Statistical Methods for Modeling Polygenic Architecture in Association and Re-sequencing Studies Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/14/2017	04/30/2022	$1,699,264
Kim, Catherine UM Principal Investigator	Title: Anti-Mullerian hormone in men and subclinical measures of cardiovascular disease Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2017	06/30/2022	$1
Kennedy, Robert UM Principal Investigator	Title: Private Source Lecturer in Organic Synthesis Mechanism: Grant Funding Sources: Private Source	07/01/2017	06/30/2018	$3,000
Lumeng, Julie UM Principal Investigator Peterson, Karen Participating Investigator without Specified Effort	Title: Harsh Maternal Restrictive Feeding Practices and Obesity in Early Childhood Mechanism: Grant Funding Sources: Private Source	07/01/2017	06/30/2022	$593,000
Moenter, Suzanne Participating Investigator with Specified Effort	Title: Mechanisms Leading to Adrenal Zonation Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2017	06/30/2021	$1,720,228
Auchus, Richard Participating Investigator with Specified Effort	Title: Molecular Mechanisms of Adrenarche Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2017	06/30/2019	$1,167,500
Newman, Carrie Participating Investigator without Specified Effort	Title: Postdoctoral Training in the Biology of Drug Abuse Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2017	06/30/2022	$1,881,248
Feldman, Eva UM Principal Investigator	Title: Training in Clinical and Basic Neuroscience Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2017	06/30/2022	$1,964,173
Wellik, Deneen UM Principal Investigator	Title: Investigating developmental Hox programs as determinants of sarcomagenesis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/12/2017	05/31/2019	$371,835

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Cipolla, Dana Participating Investigator without Specified Effort	Title: Life Course Determinants of Epigenetic Age Acceleration and Subsequent Dementia Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/15/2017	06/30/2019	$263,486
Elias, Carol UM Principal Investigator Low, Malcolm Moenter, Suzanne Participating Investigators without Specified Effort	Title: Neural basis of leptin action in reproduction Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/15/2017	04/30/2022	$1,870,983
Lumeng, Carey O'Rourke, Robert UM Principal Investigators	Title: Adipose Tissue Macrophage Control of Metabolic Dysfunction in Diabetes Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/18/2017	06/30/2021	$2,340,048
Trievel, Raymond UM Principal Investigator	Title: Collaborative Research: Molecular and Structural Mechanism of histone binding by the epigenetic regulator UHRF2 Mechanism: Grant Funding Sources: National Science Foundation	08/01/2017	07/31/2020	$44,175
Wellik, Deneen Participating Investigator without Specified Effort	Title: Examining the Heterogeneity of Fibroblasts in the Pancreatic Microenvironment Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	07/31/2019	$64,066
Wellik, Deneen UM Principal Investigator	Title: Hox-Expressing Stromal Cells in Muscle Development and Repair Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	07/31/2019	$376,200
Elias, Carol UM Principal Investigator	Title: MCH neurons: the potential link between sleep and the neuroendocrine function Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	07/31/2019	$427,855
Jackson, James UM Principal Investigator	Title: Michigan Center for Urban African American Aging Research-Bridge Funds Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	06/30/2018	$539,441
Rui, Liangyou UM Principal Investigator Cone, Roger Low, Malcolm Myers Jr, Martin Wu, Jun Participating Investigator without Specified Effort	Title: The role of hypothalamic Slug in the regulation of leptin sensitivity, energy balance, and body weight. Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	06/30/2021	$1,782,783
Wellik, Deneen UM Principal Investigator	Title: Training Program in Organogenesis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	04/30/2022	$1,595,565

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Burant, Charles Olson, David Shah, Yatrik Participating Investigators with Specified Effort Myers Jr, Martin Participating Investigator without Specified Effort	Title: University of Michigan Center for Gastrointestinal Research Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2017	05/31/2022	$3,328,114
Lumeng, Julie Participating Investigator without Specified Effort	Title: Technology and Parent-Child Interaction Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/04/2017	05/31/2022	$836,411
Gallagher, Katherine UM Principal Investigator	Title: The Interferon-beta (IFNß)/SETDB2 Epigenetic Axis Regulates Inflammation And Metabolism In Diabetic Wounds Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/09/2017	06/30/2022	$2,428,922
Weisman, Lois UM Principal Investigator Barmada, Sami Participating Investigator with Specified Effort	Title: Phosphoinositide signaling: novel potential targets for Huntington disease Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/15/2017	05/31/2022	$2,270,808
Shea, Lonnie UM Principal Investigator	Title: Measuring Signaling Pathway Dynamics During Tissue Growth in Hydrogels Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/16/2017	07/31/2022	$1,804,927
Ratliff, Briana UM Principal Investigator	Title: A Public Health Approach to Understanding Suicide in Long-Term Care Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/25/2017	07/31/2019	$407,306
Antonetti, David Participating Investigator with Specified Effort	Title: Immune mediated regeneration of retinal ganglion cell axons following optic nerve trauma Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/01/2017	05/31/2021	$1,557,917
Kurabayashi, Katsuo UM Principal Investigator	Title: A Nanotechnology-Based Wearable Biological Sensor for Continuous Monitoring of Inflammatory Immune Diseases Mechanism: Grant Funding Sources: National Science Foundation	09/01/2017	08/31/2020	$360,000
Moenter, Suzanne UM Principal Investigator Schnell, Santiago Participating Investigator with Specified Effort	Title: Cellular and molecular bases for rhythmic GnRH release Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/01/2017	05/31/2022	$2,578,598
Abcouwer, Steven Antonetti, David Lentz, Stephen Puro, Donald Participating Investigators with Specified Effort	Title: Core Grant for Vision Research Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/01/2017	08/31/2022	$2,954,191
Kennedy, Robert Participating Investigator with Specified Effort	Title: Endogenous enkephalins and reward mechanisms Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/01/2017	06/30/2022	$1,612,894

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Kennedy, Robert UM Principal Investigator Myers Jr, Martin Participating Investigator without Specified Effort	Title: In vivo chemical monitoring using capillary separations Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	05/31/2021	$1,317,506
Lumeng, Julie Participating Investigator with Specified Effort	Title: Maternal-Infant Feeding Interaction and Weight Gain Among Infants Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	08/31/2019	$155,583
Shea, Lonnie Participating Investigator with Specified Effort	Title: Stem cell-based biomaterials for spinal cord regeneration in neural tube defects Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	05/31/2022	$1,638,000
Richardson, Caroline Participating Investigator with Specified Effort	Title: Strategies to Enhance Pneumonia Care via Intermediate Intensive Care (STEP-IN) Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	05/31/2022	$3,235,783
Shah, Yatrik Participating Investigator without Specified Effort	Title: Targeting Mitochondrial Iron Metabolism in Inflammatory Bowel Disease Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	01/05/2018	$541,160
Hasson, Rebecca Participating Investigator with Specified Effort	Title: The effect of built and social environments on childhood obesity and racial/ethnic disparities in the national Healthy Communities Study Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	06/30/2021	$3,337,002
Kretzler, Matthias UM Principal Investigator Bitzer, Markus Participating Investigator with Specified Effort	Title: Tissue based integrative biology of diabetic nephropathy in participants of the PERL-study Mechanism: Grant Funding Sources: Private Source Private Source	09/01/2017	08/31/2020	$425,000
Piatt, Gretchen Participating Investigator with Specified Effort	Title: Training to Advance Care Through Implementation Science in Cardiac And Lung Illnesses (TACTICAL) Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	06/30/2022	$3,111,296
Fan, Yanbo UM Principal Investigator	Title: Transcription Factor-EB and Postischemic Angiogenesis Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/01/2017	05/31/2022	$2,138,185
Cipolla, Dana UM Principal Investigator	Title: Perinatal Exposures, Tissue-and Cell-specific Epigenomics, & Lifecourse Outcomes Mechanism: Grant Funding Sources: Health and Human Services, Department of- National Institutes of Health	09/05/2017	04/30/2020	$1,190,918
Ringold, Vicki Participating Investigator without Specified Effort	Title: Psychosocial and physiological mechanisms of cognitive performance in Type 2 diabetes mellitus. Mechanism: Grant Funding Sources: Private Source	09/06/2017	09/05/2018	$17,500

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Rui, Liangyou UM Principal Investigator	Title: Role of NF-¿B-induce kinase (NIK) in liver diseases Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/13/2017	07/31/2021	$1,746,369
Wellik, Deneen Participating Investigator with Specified Effort	Title: Improving Survival in Oral Cancer by Disruption of Tumor Progression Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/14/2017	06/30/2025	$8,086,475
Andjelkovic-Zochowska, Anuska UM Principal Investigator	Title: Claudin Expression Profiles and Blood Brain Barrier in Aging Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/15/2017	06/30/2022	$2,343,371
Alexander, Neil Participating Investigator without Specified Effort	Title: Cumulative and synergistic impact of chronic diseases on physical functioning in older adults: development and validation of a novel measure of multimorbidity Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/15/2017	05/31/2022	$837,000
Dus, Monica UM Principal Investigator	Title: Persistent Neural and Behavioral Reprogramming by the Environment Mechanism: Grant Funding Sources: Private Source	09/15/2017	09/14/2019	$60,000
Kretzler, Matthias UM Principal Investigator Otto, Edgar Participating Investigator with Specified Effort	Title: PREcision Medicine through IntErrogation of Rna in the kidnEy (PREMIERE) Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/15/2017	06/30/2019	$894,696
Boehnke, Michael UM Principal Investigator	Title: Design and Analysis of Human Gene Mapping Studies Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/16/2017	08/30/2018	$400,000
Lee, Jun Hee UM Principal Investigator	Title: Role of Sestrin and autophagy signaling pathways in attenuation of aging and age-associated pathologies Mechanism: Grant Funding Sources: Private Source	09/18/2017	09/17/2019	$60,000
Weiss, Stephen Participating Investigator without Specified Effort	Title: Wiskott-Aldrich syndrome protein (WASp) signaling in the oncogenesis of T cell lymphomas Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/25/2017	08/31/2020	$319,593
Peterson, Karen UM Principal Investigator Burant, Charles Cipolla, Dana Participating Investigators without Specified Effort	Title: E3Gen: Multigenerational Effects of Toxicant Exposures on Life Course Health and Neurocognitive Outcomes in the ELEMENT Birth Cohorts Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/30/2017	06/30/2022	$1,684,369
Shah, Yatrik UM Principal Investigator	Title: Integration of Hepatic Hepcidin and Intestinal HIF-2 alpha in Systemic Iron Metabolism Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/30/2017	09/29/2020	$106,812

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Shea, Lonnie Participating Investigator with Specified Effort	Title: Interrupting Cellular Crosstalk in the Immunosuppressive Microenvironment of Pancreas Cancer Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/30/2017	08/31/2020	$1,497,616
Fort, Patrice UM Principal Investigator Antonetti, David Gardner, Thomas Participating Investigators without Specified Effort	Title: Progressive Impact of Diabetes on Retinal Neuroprotection by a-Crystallins Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	09/30/2017	08/31/2020	$1,167,921
Kennedy, Robert Participating Investigator without Specified Effort	Title: A microfluidic platform for discovery and optimization of photoredox reactions Mechanism: Grant Funding Sources: Private Source	10/01/2017	09/30/2018	$50,000
Weiss, Stephen UM Principal Investigator	Title: Breast Cancer EMT Programs Private Source Mechanism: Grant Funding Sources Private Source	10/01/2017	09/30/2018	$250,000
Li, Jun Participating Investigator with Specified Effort	Title: Comprehensive mapping of mouse testis cell types and spermatogenic stages by single-cell RNA sequencing Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/01/2017	11/30/2019	$443,790
Schnell, Santiago Participating Investigator with Specified Effort	Title: Small molecule stabilizers of Hsp70 for treatment of spinal and bulbar muscular atrophy Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/01/2017	11/30/2018	$388,542
Singer, Kanakadurga UM Principal Investigator Gregg, Brigid Lumeng, Carey MacDougald, Ormond Participating Investigators without Specified Effort	Title: The programming effect of maternal obesity on metabolism and metabolic inflammation Mechanism: Grant Funding Sources Private Source	12/01/2017	11/30/2018	$5,000
Holinstat, Michael UM Principal Investigator	Title: The racial disparity in platelet PAR4 signaling enhances thrombus formation Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/15/2017	11/30/2019	$201,534
Wellik, Deneen Participating Investigator without Specified Effort	Title: Regulation and function of HOX genes in Ewing sarcoma pathogenesis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/18/2017	11/30/2022	$1,886,070
Richardson, Caroline Participating Investigator with Specified Effort	Title: Improving Outcomes in Kidney Disease Using Systems-Driven Education and Coaching Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	12/26/2017	11/30/2022	$2,516,557
Auchus, Richard UM Principal Investigator	Title: Sex-Steroids in Aging Women: the Role of the Adrenal Gland Mechanism: Grant Funding Sources Private Source	12/31/2017	12/30/2018	$58,500

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Gallagher, Katherine UM Principal Investigator	Title: Epigenetic Alterations in Macrophages Influence Chronic Inflammation in Abdominal Aortic Aneurysms Mechanism: Grant Funding Sources: Private Source	01/01/2018	12/31/2018	$12,500
Li, Jun Participating Investigator with Specified Effort	Title: Genetic and Genomic Analysis of Arterial Dysplasia Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/01/2018	12/31/2021	$2,923,371
MacDougald, Ormond UM Principal Investigator	Title: Investigating the role of SFRP5 and Wnt signaling in adipocyte metabolism Mechanism: Grant Funding Sources: Private Source	01/01/2018	12/31/2020	$58,438
Kennedy, Robert Participating Investigator with Specified Effort	Title: Neurochemical mechanisms of sedative effects on sleep homeostasis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/01/2018	11/30/2022	$1,492,979
Boehnke, Michael Participating Investigator with Specified Effort	Title: TOPMed Informatics Resource Center Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/05/2018	12/31/2018	$723,702
Shea, Lonnie UM Principal Investigator	Title: Heterogeneity of early metastatic tumor cells Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/09/2018	01/08/2020	$73,440
Longworth, Zora Participating Investigator with Specified Effort	Title: Identification of Microbiome Based Markers to Improve Colorectal Cancer Detection Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	01/15/2018	12/31/2020	$1,430,379
Arvan, Peter UM Principal Investigator	Title: Role of the Ventral Hippocampus in Emotional Behavior After Sepsis Mechanism: Grant Funding Sources: Private Source	01/15/2018	01/14/2020	$70,000
Burant, Charles Participating Investigator without Specified Effort	Title: The Role of Airway Microbiota in Nontuberculous Mycobacterial Infection in Cystic Fibrosis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	02/04/2018	01/31/2021	$499,910
Myers Jr, Martin UM Principal Investigator Antonetti, David Carter-Su, Christin Cras-Meneur, Corentin Elias, Carol Goforth, Paula Herman, William Lentz, Stephen Olson, David Qi, Nathan Sandoval, Darleen Tan, Meng Ye, Wen Participating Investigators with Specified Effort	Title: Michigan Diabetes Research Center Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	02/27/2018	11/30/2022	$8,697,693

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Weisman, Lois UM Principal Investigator	Title: Mechanisms for the Termination of Myosin V-Mediated Transport Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	02/28/2018	02/27/2020	$71,992
Cone, Roger UM Principal Investigator Elias, Carol Moenter, Suzanne Participating Investigators without Specified Effort	Title: A role for hypothalamic melanocortin 3 receptors in integrating energy state with reproductive physiology Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2018	02/28/2021	$170,094
Lumeng, Julie Participating Investigator without Specified Effort	Title: Developmental Trajectories of Late Preterm Infants Using an Ecological Framework Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2018	02/28/2019	$69,335
Lin, Jiandie UM Principal Investigator Weiss, Stephen Participating Investigator without Specified Effort	Title: Neuregulin-4 Signaling in Hepatocytes Defines an Endocrine Checkpoint for NASH and HCC Progression Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2018	02/28/2021	$114,577
Li, Jun Participating Investigator with Specified Effort	Title: The Molecular Genetics of Venous Thromboembolic Disease Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	03/01/2018	02/28/2023	$1,949,167
Antonetti, David Participating Investigator with Specified Effort	Title: A novel inflammatory cell with neuroprotective and neuroregenerative properties Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2023	$1,559,503
Lee, Jun Hee UM Principal Investigator Schnell, Santiago Participating Investigator without Specified Effort	Title: Defining the Sestrin2-AKT signaling pathway, a novel mechanism in the insulin signaling network Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2020	$36,398
Shea, Lonnie UM Principal Investigator	Title: Engineering Natural Killer Cell Homing and Activation at the Metastatic Niche Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2021	$186,426
Wellik, Deneen UM Principal Investigator	Title: Hox genes regulate functionally distinct, regionally restricted MSC populations Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2020	$772,433
Arvan, Peter UM Principal Investigator	Title: Neural and Molecular Mechanisms of Emotional Dysfunction after Sepsis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2022	$785,367
Haus, Jacob UM Principal Investigator	Title: Strategies and functional outcomes of enhancing in vivo production of soluble rage isoforms Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	05/31/2021	$2,103,419

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Elias, Carol UM Principal Investigator Olson, David Participating Investigator without Specified Effort	Title: Transcriptome analysis of hypothalamic neurons during pubertal transition Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/01/2018	03/31/2020	$155,875
Feldman, Eva UM Principal Investigator	Title: The Role of NK Cells in ALS Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/15/2018	03/31/2020	$388,437
Boehnke, Michael UM Principal Investigator	Title: Whole Genome Sequencing for Schizophrenia and Bipolar Disorder in the GPC Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/16/2018	05/31/2019	$469,745
Feldman, Eva UM Principal Investigator	Title: Training in Clinical and Basic Neuroscience [T32 Meeting - Travel Supplement Request] Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	04/24/2018	06/30/2018	$648
Burant, Charles Participating Investigator without Specified Effort	Title: Targeting Epithelial-Immune Cell Crosstalk to Improve Therapy in Pancreatic Cancer Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	05/01/2018	07/31/2020	$133,692
Cartee, Gregory UM Principal Investigator	Title: Skeletal Muscle Glucose Uptake: Exercise and Insulin Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	05/05/2018	04/30/2021	$1,577,867
Hussain, Mehboob UM Principal Investigator	Title: Hepatic endocrine suppression of the pancreatic beta-cell Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	05/07/2018	08/31/2018	$366,265
Weiss, Stephen UM Principal Investigator	Title: Neutrophil extracellular traps (NETs) and innate immune system as novel mediators for mechanotransduction of acute inflammation Mechanism: Grant Funding Sources: Private Source	06/01/2018	05/31/2019	$38,000
Chun, Tae-Hwa Participating Investigator without Specified Effort	Title: CAREER: Probing Mechanisms of Beta Cell Dysfunction via Quantitative Droplet Molecular Transport Mechanism: Grant Funding Sources: National Science Foundation	06/01/2018	05/31/2023	$500,000
Wellik, Deneen UM Principal Investigator	Title: Characterization of the role of mesenchymal Hox5 genes in alveologenesis Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2018	05/31/2021	$177,222
Holinstat, Michael Participating Investigator with Specified Effort	Title: Interference of blood coagulation by Acinetobacter baumannii Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2018	06/02/2018	$428,895
Gardner, Thomas UM Principal Investigator	Title: Michigan Vision Clinician Scientist Development Program Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2018	04/30/2023	$2,345,985

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Brook, Robert Participating Investigator without Specified Effort	Title: Multi-scale systems analysis of blood pressure control and hypertension Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	06/01/2018	02/28/2022	$1,986,689
Lee, Joyce UM Principal Investigator	Title: T1D Exchange Quality Improvement Initiative Mechanism: Grant Funding Sources: Private Source Private Source	06/01/2018	03/31/2020	$17,500
Kurabayashi, Katsuo UM Principal Investigator	Title: A Nanotechnology-Based Wearable Biological Sensor for Continuous Monitoring of Inflammatory Immune Diseases Mechanism: Grant Funding Sources: National Science Foundation	06/18/2018	08/31/2020	$50,000
Auchus, Richard UM Principal Investigator	Title: Activation of androgen biosynthesis and drug metabolism by cytochrome b5 Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	04/30/2022	$1,591,219
Wellik, Deneen Participating Investigator without Specified Effort	Title: Anabolic Mechanisms of PTH Action in Bone Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2019	$156,000
Kennedy, Robert UM Principal Investigator	Title: Private Source Lecturer in Organic Synthesis 2018 Mechanism: Grant Funding Sources: Private Source	07/01/2018	06/30/2019	$3,000
Newman, Carrie UM Principal Investigator	Title: Exploring the link between reactive oxygen species and CP-AMPAR up-regulation in addiction Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2020	$380,868
Kennedy, Robert Participating Investigator without Specified Effort	Title: Identification of Neurochemical Antecedents and Consequences of Distinct Learning Processes Relevant to Addiction Liability Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2020	$442,398
Stuenkel, Edward UM Principal Investigator	Title: Increasing URM Diversity: Targeting Transitions in the Neuroscience Education Continuum Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2023	$1,231,394
Kretzler, Matthias Participating Investigator without Specified Effort	Title: Integrative Molecular Epidemiology Approach to Identify Nephrotic Syndrome Subgroups Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	04/30/2022	$678,423
Barmada, Sami Participating Investigator without Specified Effort	Title: Investigating the Role of Proteostasis Regulator, Ubiquilin 2, in Synucleinopathies and Tauopathies Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2020	$120,576

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Singer, Kanakadurga UM Principal Investigator Burant, Charles Carter-Su, Christin Lumeng, Carey Participating Investigators without Specified Effort	Title: Mechanisms of hematopoietic stem cell activation in obesity. Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2019	$21,134
Gallagher, Katherine UM Principal Investigator	Title: Palmitate Regulates JMJD2 Epigenetic Alterations in Macrophages and Directs Wound Healing Mechanism: Grant Funding Sources: Private Source	07/01/2018	06/30/2020	$60,000
Gallagher, Katherine Participating Investigator without Specified Effort	Title: Palmitate Regulates JMJD3 Epigenetic Alterations in Macrophages and Directs Wound Healing Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/01/2018	06/30/2020	$121,632
Sandoval, Darleen UM Principal Investigator	Title: Sex differences in the diet-dependent metabolic effects of bariatric surgery Mechanism: Grant Funding Sources: Private Source	07/01/2018	06/30/2021	$179,722
Lumeng, Julie Participating Investigator with Specified Effort	Title: Training Leaders in Developmental Behavioral Pediatrics Mechanism: Grant Funding Sources: Health and Human Services, Department of-Health Resources and Services Administration	07/01/2018	06/30/2023	$935,131
Lee, Jun Hee UM Principal Investigator	Title: Unraveling genetic, environmental and cell-to-cell variations in fatty liver transcriptome Mechanism: Grant Funding Sources: Private Source Private Source	07/01/2018	06/30/2019	$50,000
Callaghan, Brian UM Principal Investigator Busui, Rodica Feldman, Eva Horowitz, Jeffrey O'Rourke, Robert Sandoval, Darleen Seeley, Randy Participating Investigators without Specified Effort	Title: The effect of high intensity interval training and surgical weight loss on distal symmetric polyneuropathy outcomes Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/06/2018	05/31/2023	$3,127,881
Singer, Kanakadurga UM Principal Investigator Sandoval, Darleen Participating Investigator with Specified Effort MacDougald, Ormond Moenter, Suzanne Participating Investigators without Specified Effort	Title: The Role of Androgens in Obesity Induced Meta-Inflammation Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/11/2018	04/30/2023	$2,185,904
Newman, Carrie UM Principal Investigator	Title: Motivation in females; interactions between gonadal hormones and striatal glutamatergic plasticity. Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	07/31/2018	07/30/2020	$74,046

P.I./s	Funding	Project Start Date	Project End Date	Award Sponsor Total
Wellik, Deneen Participating Investigator without Specified Effort	Title: Elucidating residential mesenchymal stromal cells in an adult lung and their role in bronchiolitis obliterans syndrome Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2018	07/31/2019	$69,658
Duan, Cunming UM Principal Investigator	Title: Nuclear action of a novel fish kisspeptin receptor isoform Mechanism: Grant Funding Sources: National Science Foundation	08/01/2018	07/31/2022	$862,034
Herman, William UM Principal Investigator Ye, Wen Participating Investigator with Specified Effort	Title: Treatment for TIA to manage cardiovascular disease and diabetes in older adults Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2018	04/30/2020	$429,000
Pennathur, Subramaniam UM Principal Investigator Bitzer, Markus Ju, Wenjun Kretzler, Matthias Participating Investigators with Specified Effort	Title: University of Michigan O'Brien Kidney Translational Core Center Mechanism: Grant Funding Sources: Health and Human Services, Department of-National Institutes of Health	08/01/2018	07/31/2023	$2,906,848

# of New Awards:	166	Awards Total:	$221,790,276
# of NIH Awards:	126	NIH Awards Total:	$214,295,140
# of Collaborations	33		

B.4 What opportunities for training and professional development has the project provided?

See Enrichment report and Reports from Individual Core for Training and Development activities.

C. OVERALL PRODUCTS

C.1 PUBLICATIONS

Are there publications or manuscripts accepted for publication in a journal or other publication (e.g., book, one-time publication, monograph) during the reporting period resulting directly from this award?

Yes

Publications Reported for this Reporting Period

Public Access Compliance	Citation
Complete	Ge C, Cawthorn WP, Li Y, Zhao G, Macdougald OA, Franceschi RT. Reciprocal Control of Osteogenic and Adipogenic Differentiation by ERK/MAP Kinase Phosphorylation of Runx2 and PPARγ Transcription Factors. Journal of cellular physiology. 2016 March;231(3):587-96. PubMed PMID: 26206105; PubMed Central PMCID: PMC4745986.
Complete	Chakravarthy H, Navitskaya S, O'Reilly S, Gallimore J, Mize H, Beli E, Wang Q, Kady N, Huang C, Blanchard GJ, Grant MB, Busik JV. Role of Acid Sphingomyelinase in Shifting the Balance Between Proinflammatory and Reparative Bone Marrow Cells in Diabetic Retinopathy. Stem cells (Dayton, Ohio). 2016 April;34(4):972-83. PubMed PMID: 26676316; PubMed Central PMCID: PMC5088619.
Complete	Cheng Y, Kerppola RE, Kerppola TK. ATR-101 disrupts mitochondrial functions in adrenocortical carcinoma cells and in vivo. Endocrine-related cancer. 2016 April;23(4):1-19. PubMed PMID: 26843528; PubMed Central PMCID: PMC4887102.
Complete	Karvonen-Gutierrez CA, Zheng H, Mancuso P, Harlow SD. Higher Leptin and Adiponectin Concentrations Predict Poorer Performance-based Physical Functioning in Midlife Women: the Michigan Study of Women's Health Across the Nation. The journals of gerontology. Series A, Biological sciences and medical sciences. 2016 April;71(4):508-14. PubMed PMID: 26302979; PubMed Central PMCID: PMC5014187.
Complete	Lumeng JC. Promoting young children's engagement in organized extracurricular activities: 'Tiger parenting' or obesity prevention?. Obesity (Silver Spring, Md.). 2016 April;24(4):793. PubMed PMID: 27028281; PubMed Central PMCID: PMC5088494.
Complete	Karuppagounder V, Giridharan VV, Arumugam S, Sreedhar R, Palaniyandi SS, Krishnamurthy P, Quevedo J, Watanabe K, Konishi T, Thandavarayan RA. Modulation of Macrophage Polarization and HMGB1-TLR2/TLR4 Cascade Plays a Crucial Role for Cardiac Remodeling in Senescence-Accelerated Prone Mice. PloS one. 2016 April 12;11(4):e0152922. PubMed PMID: 27070323; PubMed Central PMCID: PMC4829159.
Complete	Zheng Z, Wang G, Li L, Tseng J, Sun F, Chen X, Chang L, Heng H, Zhang K. Transcriptional signatures of unfolded protein response implicate the limitation of animal models in pathophysiological studies. Environmental disease. 2016 April 14;1(1):24-30. PubMed PMID: 28265594; PubMed Central PMCID: PMC5336312.
Complete	Adhikari R, D'Souza J, Soliman EZ, Burke GL, Daviglus ML, Jacobs DR Jr, Park SK, Sheppard L, Thorne PS, Kaufman JD, Larson TV, Adar SD. Long-term Coarse Particulate Matter Exposure and Heart Rate Variability in the Multi-ethnic Study of Atherosclerosis. Epidemiology (Cambridge, Mass.). 2016 May;27(3):405-13. PubMed PMID: 27035690; PubMed Central PMCID: PMC5472334.
Complete	Fan Y, Lu H, Guo Y, Zhu T, Garcia-Barrio MT, Jiang Z, Willer CJ, Zhang J, Chen YE. Hepatic Transmembrane 6 Superfamily Member 2 Regulates Cholesterol Metabolism in Mice. Gastroenterology. 2016 May;150(5):1208-1218. PubMed PMID: 26774178; PubMed Central PMCID: PMC4842105.
Complete	Lu C, Cardoso RC, Puttabyatappa M, Padmanabhan V. Developmental Programming: Prenatal Testosterone Excess and Insulin Signaling Disruptions in Female Sheep. Biology of reproduction. 2016 May;94(5):113. PubMed PMID: 27053365; PubMed Central PMCID: PMC4939741.
Complete	Barbetti F, Colombo C, Haataja L, Cras-Méneur C, Bernardini S, Arvan P. Hyperglucagonemia in an animal model of insulin- deficient diabetes: what therapy can

	improve it?. Clinical diabetes and endocrinology. 2016 May 2;2:11. PubMed PMID: 28702245; PubMed Central PMCID: PMC5471666.
Complete	Chen YS, Wu R, Yang X, Kou S, MacDougald OA, Yu L, Shi H, Xue B. Inhibiting DNA methylation switches adipogenesis to osteoblastogenesis by activating Wnt10a. Scientific reports. 2016 May 3;6:25283. PubMed PMID: 27136753; PubMed Central PMCID: PMC4853709.
Complete	Smarr CB, Yap WT, Neef TP, Pearson RM, Hunter ZN, Ifergan I, Getts DR, Bryce PJ, Shea LD, Miller SD. Biodegradable antigen-associated PLG nanoparticles tolerize Th2-mediated allergic airway inflammation pre- and postsensitization. Proceedings of the National Academy of Sciences of the United States of America. 2016 May 3;113(18):5059-64. PubMed PMID: 27091976; PubMed Central PMCID: PMC4983813.
Complete	Mancuso P. The role of adipokines in chronic inflammation. ImmunoTargets and therapy. 2016 May 23;5:47-56. PubMed PMID: 27529061; PubMed Central PMCID: PMC4970637.
Complete	Herman WH, Kalyani RR, Wexler DJ, Matthews DR, Inzucchi SE. Response to Comment on American Diabetes Association. Approaches to Glycemic Treatment. Sec. 7. In Standards of Medical Care in Diabetes-2016. Diabetes Care 2016;39(Suppl. 1):S52-S59. Diabetes care. 2016 June;39(6):e88-9. PubMed PMID: 27222560; PubMed Central PMCID: PMC5864133.
Complete	Rubin JK, Hinrichs-Krapels S, Hesketh R, Martin A, Herman WH, Rubino F. Identifying Barriers to Appropriate Use of Metabolic/Bariatric Surgery for Type 2 Diabetes Treatment: Policy Lab Results. Diabetes care. 2016 June;39(6):954-63. PubMed PMID: 27222554; PubMed Central PMCID: PMC5864132.
Complete	Scheller EL, Cawthorn WP, Burr AA, Horowitz MC, MacDougald OA. Marrow Adipose Tissue: Trimming the Fat. Trends in endocrinology and metabolism: TEM. 2016 June;27(6):392-403. PubMed PMID: 27094502; PubMed Central PMCID: PMC4875855.
Complete	Scott RA, Freitag DF, Li L, Chu AY, Surendran P, Young R, Grarup N, Stancáková A, Chen Y, Varga TV, Yaghootkar H, Luan J, Zhao JH, Willems SM, Wessel J, Wang S, Maruthur N, Michailidou K, Pirie A, van der Lee SJ, Gillson C, Al Olama AA, Amouyel P, Arriola L, Arveiler D, Aviles-Olmos I, Balkau B, Barricarte A, Barroso I, Garcia SB, Bis JC, Blankenberg S, Boehnke M, Boeing H, Boerwinkle E, Borecki IB, Bork-Jensen J, Bowden S, Caldas C, Caslake M, Cupples LA, Cruchaga C, Czajkowski J, den Hoed M, Dunn JA, Earl HM, Ehret GB, Ferrannini E, Ferrieres J, Foltynie T, Ford I, Forouhi NG, Gianfagna F, Gonzalez C, Grioni S, Hiller L, Jansson JH, Jørgensen ME, Jukema JW, Kaaks R, Kee F, Kerrison ND, Key TJ, Kontto J, Kote-Jarai Z, Kraja AT, Kuulasmaa K, Kuusisto J, Linneberg A, Liu C, Marenne G, Mohlke KL, Morris AP, Muir K, Müller-Nurasyid M, Munroe PB, Navarro C, Nielsen SF, Nilsson PM, Nordestgaard BG, Packard CJ, Palli D, Panico S, Peloso GM, Perola M, Peters A, Poole CJ, Quirós JR, Rolandsson O, Sacerdote C, Salomaa V, Sánchez MJ, Sattar N, Sharp SJ, Sims R, Slimani N, Smith JA, Thompson DJ, Trompet S, Tumino R, van der A DL, van der Schouw YT, Virtamo J, Walker M, Walter K, Abraham JE, Amundadottir LT, Aponte JL, Butterworth AS, Dupuis J, Easton DF, Eeles RA, Erdmann J, Franks PW, Frayling TM, Hansen T, Howson JM, Jørgensen T, Kooner J, Laakso M, Langenberg C, McCarthy MI, Pankow JS, Pedersen O, Riboli E, Rotter JI, Saleheen D, Samani NJ, Schunkert H, Vollenweider P, O'Rahilly S, Deloukas P, Danesh J, Goodarzi MO, Kathiresan S, Meigs JB, Ehm MG, Wareham NJ, Waterworth DM. A genomic approach to therapeutic target validation identifies a glucose-lowering GLP1R variant protective for coronary heart disease. Science translational medicine. 2016 June 1;8(341):341ra76. PubMed PMID: 27252175; PubMed Central PMCID: PMC5219001.
Complete	Walden P, Jiang Q, Jackson EA, Oral EA, Weintraub MS, Rubenfire M. Assessing the incremental benefit of an extended duration lifestyle intervention for the components of the metabolic syndrome. Diabetes, metabolic syndrome and obesity : targets and therapy. 2016 June 1;9:177-84. PubMed PMID: 27330320; PubMed Central PMCID: PMC4898037.
Complete	Wu J, Wen XW, Faulk C, Boehnke K, Zhang H, Dolinoy DC, Xi C. Perinatal Lead Exposure Alters Gut Microbiota Composition and Results in Sex-specific Bodyweight Increases in Adult Mice. Toxicological sciences : an official journal of the Society of Toxicology. 2016 June;151(2):324-33. PubMed PMID: 26962054; PubMed Central PMCID: PMC4880136.

Complete	Zhang J, Qiao C, Chang L, Guo Y, Fan Y, Villacorta L, Chen YE, Zhang J. Cardiomyocyte Overexpression of FABP4 Aggravates Pressure Overload-Induced Heart Hypertrophy. PloS one. 2016 June 13;11(6):e0157372. PubMed PMID: 27294862; PubMed Central PMCID: PMC4905683.
Complete	Cartee GD, Hepple RT, Bamman MM, Zierath JR. Exercise Promotes Healthy Aging of Skeletal Muscle. Cell metabolism. 2016 June 14;23(6):1034-1047. PubMed PMID: 27304505; PubMed Central PMCID: PMC5045036.
Complete	Vincent M, Schnell S. A collection of intrinsic disorder characterizations from eukaryotic proteomes. Scientific data. 2016 June 21;3:160045. PubMed PMID: 27326998; PubMed Central PMCID: PMC4915274.
Complete	Chan JL, Koda J, Heilig JS, Cochran EK, Gorden P, Oral EA, Brown RJ. Immunogenicity associated with metreleptin treatment in patients with obesity or lipodystrophy. Clinical endocrinology. 2016 July;85(1):137-49. PubMed PMID: 26589105; PubMed Central PMCID: PMC4875885.
Complete	Coogan PF, White LF, Yu J, Burnett RT, Marshall JD, Seto E, Brook RD, Palmer JR, Rosenberg L, Jerrett M. Long term exposure to NO2 and diabetes incidence in the Black Women's Health Study. Environmental research. 2016 July;148:360-366. PubMed PMID: 27124624; PubMed Central PMCID: PMC4874900.
Complete	Luo Z, Chen Q, Annis AM, Piatt G, Green LA, Tao M, Holtrop JS. A Comparison of Health Plan- and Provider-Delivered Chronic Care Management Models on Patient Clinical Outcomes. Journal of general internal medicine. 2016 July;31(7):762-70. PubMed PMID: 26951287; PubMed Central PMCID: PMC4907946.
Complete	Riahi Y, Wikstrom JD, Bachar-Wikstrom E, Polin N, Zucker H, Lee MS, Quan W, Haataja L, Liu M, Arvan P, Cerasi E, Leibowitz G. Autophagy is a major regulator of beta cell insulin homeostasis. Diabetologia. 2016 July;59(7):1480-1491. PubMed PMID: 26831301; PubMed Central PMCID: PMC5912938.
Complete	Scheller EL, Burr AA, MacDougald OA, Cawthorn WP. Inside out: Bone marrow adipose tissue as a source of circulating adiponectin. Adipocyte. 2016 July;5(3):251-69. PubMed PMID: 27617171; PubMed Central PMCID: PMC5014002.
Complete	Weinhouse C, Sartor MA, Faulk C, Anderson OS, Sant KE, Harris C, Dolinoy DC. Epigenome-wide DNA methylation analysis implicates neuronal and inflammatory signaling pathways in adult murine hepatic tumorigenesis following perinatal exposure to bisphenol A. Environmental and molecular mutagenesis. 2016 July;57(6):435-46. PubMed PMID: 27334623; PubMed Central PMCID: PMC4945497.
Complete	Faulk C, Kim JH, Anderson OS, Nahar MS, Jones TR, Sartor MA, Dolinoy DC. Detection of differential DNA methylation in repetitive DNA of mice and humans perinatally exposed to bisphenol A. Epigenetics. 2016 July 2;11(7):489-500. PubMed PMID: 27267941; PubMed Central PMCID: PMC4939917.
Complete	Jin S, Furtaw MD, Chen H, Lamb DT, Ferguson SA, Arvin NE, Dawod M, Kennedy RT. Multiplexed Western Blotting Using Microchip Electrophoresis. Analytical chemistry. 2016 July 5;88(13):6703-10. PubMed PMID: 27270033; PubMed Central PMCID: PMC5113996.
Complete	Luo X, Miller SD, Shea LD. Immune Tolerance for Autoimmune Disease and Cell Transplantation. Annual review of biomedical engineering. 2016 July 11;18:181-205. PubMed PMID: 26928211; PubMed Central PMCID: PMC4947009.
Complete	Mottillo EP, Desjardins EM, Crane JD, Smith BK, Green AE, Ducommun S, Henriksen TI, Rebalka IA, Razi A, Sakamoto K, Scheele C, Kemp BE, Hawke TJ, Ortega J, Granneman JG, Steinberg GR. Lack of Adipocyte AMPK Exacerbates Insulin Resistance and Hepatic Steatosis through Brown and Beige Adipose Tissue Function. Cell metabolism. 2016 July 12;24(1):118-29. PubMed PMID: 27411013; PubMed Central PMCID: PMC5239668.
Complete	Oh BR, Chen P, Nidetz R, McHugh W, Fu J, Shanley TP, Cornell TT, Kurabayashi K. Multiplexed Nanoplasmonic Temporal Profiling of T-Cell Response under Immunomodulatory Agent Exposure. ACS sensors. 2016 July 22;1(7):941-948. PubMed PMID: 27478873; PubMed Central PMCID: PMC4960639.
Complete	Wareham NJ, Herman WH. The Clinical and Public Health Challenges of Diabetes

	Prevention: A Search for Sustainable Solutions. PLoS medicine. 2016 July 26;13(7):e1002097. PubMed PMID: 27458730; PubMed Central PMCID: PMC4961419.
Complete	Scheller EL, Khoury B, Moller KL, Wee NK, Khandaker S, Kozloff KM, Abrishami SH, Zamarron BF, Singer K. Changes in Skeletal Integrity and Marrow Adiposity during High-Fat Diet and after Weight Loss. Frontiers in endocrinology. 2016 July 27;7:102. PubMed PMID: 27512386; PubMed Central PMCID: PMC4961699.
Complete	Berger EA, Carion TW, Jiang Y, Liu L, Chahine A, Walker RJ, Steinle JJ. β-Adrenergic receptor agonist, compound 49b, inhibits TLR4 signaling pathway in diabetic retina. Immunology and cell biology. 2016 August;94(7):656-61. PubMed PMID: 26888251; PubMed Central PMCID: PMC4980247.
Complete	Kasper N, Mandell C, Ball S, Miller AL, Lumeng J, Peterson KE. The Healthy Meal Index: A tool for measuring the healthfulness of meals served to children. Appetite. 2016 August 1;103:54-63. PubMed PMID: 26994739; PubMed Central PMCID: PMC5433522.
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Complete	Kimball A, Schaller M, Joshi A, Davis FM, denDekker A, Boniakowski A, Bermick J, Obi A, Moore B, Henke PK, Kunkel SL, Gallagher KA. Ly6C^{Hi} Blood Monocyte/Macrophage Drive Chronic Inflammation and Impair Wound Healing in Diabetes Mellitus. Arteriosclerosis, thrombosis, and vascular biology. 2018 May;38(5):1102-1114. PubMed PMID: 29496661; PubMed Central PMCID: PMC5920725.
Complete	Prasad S, Neef T, Xu D, Podojil JR, Getts DR, Shea LD, Miller SD. Tolerogenic Ag-PLG nanoparticles induce tregs to suppress activated diabetogenic CD4 and CD8 T cells. Journal of autoimmunity. 2018 May;89:112-124. PubMed PMID: 29258717; PubMed Central PMCID: PMC5902637.
Complete	Rodriquez EJ, Livaudais-Toman J, Gregorich SE, Jackson JS, Nápoles AM, Pérez-Stable EJ. Relationships between allostatic load, unhealthy behaviors, and depressive disorder in U.S. adults, 2005-2012 NHANES. Preventive medicine. 2018 May;110:9-15. PubMed PMID: 29421445; PubMed Central PMCID: PMC5845838.
Complete	Teslovich TM, Kim DS, Yin X, Stancáková A, Jackson AU, Wielscher M, Naj A, Perry JRB, Huyghe JR, Stringham HM, Davis JP, Raulerson CK, Welch RP, Fuchsberger C, Locke AE, Sim X, Chines PS, Narisu N, Kangas AJ, Soininen P, Ala-Korpela M, Gudnason V, Musani SK, Jarvelin MR, Schellenberg GD, Speliotes EK, Kuusisto J, Collins FS, Boehnke M, Laakso M, Mohlke KL. Identification of seven novel loci associated with amino acid levels using single-variant and gene-based tests in 8545

	Finnish men from the METSIM study. Human molecular genetics. 2018 May 1;27(9):1664-1674. PubMed PMID: 29481666; PubMed Central PMCID: PMC5905595.
Complete	Wood L, Roelofs K, Koch LG, Britton SL, Sandoval DA. Vertical sleeve gastrectomy corrects metabolic perturbations in a low-exercise capacity rat model. Molecular metabolism. 2018 May;11:189-196. PubMed PMID: 29519582; PubMed Central PMCID: PMC6001357.
Complete	Ammari Z, Pak SC, Ruzieh M, Dasa O, Tiwari A, Jaume JC, Alfonso-Jaume MA. Posttransplant Tacrolimus-Induced Diabetic Ketoacidosis: Review of the Literature. Case reports in endocrinology. 2018 May 9;2018:4606491. PubMed PMID: 29854487; PubMed Central PMCID: PMC5966672.
Complete	Zeng L, Mathew AV, Byun J, Atkins KB, Brosius FC 3rd, Pennathur S. Myeloperoxidase-derived oxidants damage artery wall proteins in an animal model of chronic kidney disease-accelerated atherosclerosis. The Journal of biological chemistry. 2018 May 11;293(19):7238-7249. PubMed PMID: 29581235; PubMed Central PMCID: PMC5949994.
Complete	Hussain SS, Harris MT, Kreutzberger AJB, Inouye CM, Doyle CA, Castle AM, Arvan P, Castle JD. Control of insulin granule formation and function by the ABC transporters ABCG1 and ABCA1 and by oxysterol binding protein OSBP. Molecular biology of the cell. 2018 May 15;29(10):1238-1257. PubMed PMID: 29540530; PubMed Central PMCID: PMC5935073.
Complete	Orozco LD, Farrell C, Hale C, Rubbi L, Rinaldi A, Civelek M, Pan C, Lam L, Montoya D, Edillor C, Seldin M, Boehnke M, Mohlke KL, Jacobsen S, Kuusisto J, Laakso M, Lusis AJ, Pellegrini M. Epigenome-wide association in adipose tissue from the METSIM cohort. Human molecular genetics. 2018 May 15;27(10):1830-1846. PubMed PMID: 29566149; PubMed Central PMCID: PMC5932563.
Complete	Wang JM, Qiu Y, Yang Z, Kim H, Qian Q, Sun Q, Zhang C, Yin L, Fang D, Back SH, Kaufman RJ, Yang L, Zhang K. IRE1α prevents hepatic steatosis by processing and promoting the degradation of select microRNAs. Science signaling. 2018 May 15;11(530). PubMed PMID: 29764990; PubMed Central PMCID: PMC6075656.
Complete	Allison MB, Pan W, MacKenzie A, Patterson C, Shah K, Barnes T, Cheng W, Rupp A, Olson DP, Myers MG Jr. Defining the Transcriptional Targets of Leptin Reveals a Role for <i>Atf3</i> in Leptin Action. Diabetes. 2018 June;67(6):1093-1104. PubMed PMID: 29535089; PubMed Central PMCID: PMC5961413.
Complete	Brown RJ, Oral EA, Cochran E, Araújo-Vilar D, Savage DB, Long A, Fine G, Salinardi T, Gorden P. Long-term effectiveness and safety of metreleptin in the treatment of patients with generalized lipodystrophy. Endocrine. 2018 June;60(3):479-489. PubMed PMID: 29644599; PubMed Central PMCID: PMC5936645.
Complete	Harvey I, Stephenson EJ, Redd JR, Tran QT, Hochberg I, Qi N, Bridges D. Glucocorticoid-Induced Metabolic Disturbances Are Exacerbated in Obese Male Mice. Endocrinology. 2018 June 1;159(6):2275-2287. PubMed PMID: 29659785; PubMed Central PMCID: PMC5946848.
Complete	Jaiswal M, Divers J, Urbina EM, Dabelea D, Bell RA, Pettitt DJ, Imperatore G, Pihoker C, Dolan LM, Liese AD, Marcovina S, Linder B, Feldman EL, Pop-Busui R. Cardiovascular autonomic neuropathy in adolescents and young adults with type 1 and type 2 diabetes: The SEARCH for Diabetes in Youth Cohort Study. Pediatric diabetes. 2018 June;19(4):680-689. PubMed PMID: 29292558; PubMed Central PMCID: PMC5938122.
Complete	Jun H, Yu H, Gong J, Jiang J, Qiao X, Perkey E, Kim DI, Emont MP, Zestos AG, Cho JS, Liu J, Kennedy RT, Maillard I, Xu XZS, Wu J. An immune-beige adipocyte communication via nicotinic acetylcholine receptor signaling. Nature medicine. 2018 June;24(6):814-822. PubMed PMID: 29785025; PubMed Central PMCID: PMC5992032.
Complete	Ward KM, Yeoman L, McHugh C, Kraal AZ, Flowers SA, Rothberg AE, Karnovsky A, Das AK, Ellingrod VL, Stringer KA. Atypical Antipsychotic Exposure May Not Differentiate Metabolic Phenotypes of Patients with Schizophrenia. Pharmacotherapy. 2018 June;38(6):638-650. PubMed PMID: 29722909; PubMed Central PMCID: PMC6014920.

Complete	Rupp AC, Allison MB, Jones JC, Patterson CM, Faber CL, Bozadjieva N, Heisler LK, Seeley RJ, Olson DP, Myers MG Jr. Specific subpopulations of hypothalamic leptin receptor-expressing neurons mediate the effects of early developmental leptin receptor deletion on energy balance. Molecular metabolism. 2018 June 6. PubMed PMID: 29914853; PubMed Central PMCID: PMC6034096.
Complete	Griffin C, Eter L, Lanzetta N, Abrishami S, Varghese M, McKernan K, Muir L, Lane J, Lumeng CN, Singer K. TLR4, TRIF, and MyD88 are essential for myelopoiesis and CD11c⁺ adipose tissue macrophage production in obese mice. The Journal of biological chemistry. 2018 June 8;293(23):8775-8786. PubMed PMID: 29636416; PubMed Central PMCID: PMC5995515.
Complete	Zhao XY, Li S, DelProposto JL, Liu T, Mi L, Porsche C, Peng X, Lumeng CN, Lin JD. The long noncoding RNA Blnc1 orchestrates homeostatic adipose tissue remodeling to preserve metabolic health. Molecular metabolism. 2018 June 8. PubMed PMID: 29934059; PubMed Central PMCID: PMC6034069.
Complete	Hinder LM, Murdock BJ, Park M, Bender DE, O'Brien PD, Rumora AE, Hur J, Feldman EL. Transcriptional networks of progressive diabetic peripheral neuropathy in the db/db mouse model of type 2 diabetes: An inflammatory story. Experimental neurology. 2018 July;305:33-43. PubMed PMID: 29550371; PubMed Central PMCID: PMC5955815.
Complete	Mancuso P, Curtis JL, Freeman CM, Peters-Golden M, Weinberg JB, Myers MG Jr. Ablation of the leptin receptor in myeloid cells impairs pulmonary clearance of Streptococcus pneumoniae and alveolar macrophage bactericidal function. American journal of physiology. Lung cellular and molecular physiology. 2018 July 1;315(1):L78-L86. PubMed PMID: 29565180; PubMed Central PMCID: PMC6087898.
Complete	Spencer MS, Kieffer EC, Sinco B, Piatt G, Palmisano G, Hawkins J, Lebron A, Espitia N, Tang T, Funnell M, Heisler M. Outcomes at 18 Months From a Community Health Worker and Peer Leader Diabetes Self-Management Program for Latino Adults. Diabetes care. 2018 July;41(7):1414-1422. PubMed PMID: 29703724; PubMed Central PMCID: PMC6014532.
Complete	Adams JM, Pei H, Sandoval DA, Seeley RJ, Chang RB, Liberles SD, Olson DP. Liraglutide Modulates Appetite and Body Weight Through Glucagon-Like Peptide 1 Receptor-Expressing Glutamatergic Neurons. Diabetes. 2018 August;67(8):1538-1548. PubMed PMID: 29776968; PubMed Central PMCID: PMC6054439.
Complete	Douros JD, Lewis AG, Smith EP, Niu J, Capozzi M, Wittmann A, Campbell J, Tong J, Wagner C, Mahbod P, Seeley R, D'Alessio DA. Enhanced Glucose Control Following Vertical Sleeve Gastrectomy Does Not Require a β-Cell Glucagon-Like Peptide 1 Receptor. Diabetes. 2018 August;67(8):1504-1511. PubMed PMID: 29759973; PubMed Central PMCID: PMC6054432.
Complete	Fernandez C, DeJesus JM, Miller AL, Appugliese DP, Rosenblum KL, Lumeng JC, Pesch MH. Selective eating behaviors in children: An observational validation of parental report measures. Appetite. 2018 August 1;127:163-170. PubMed PMID: 29729326; PubMed Central PMCID: PMC5994375.
Complete	Headen DM, Woodward KB, Coronel MM, Shrestha P, Weaver JD, Zhao H, Tan M, Hunckler MD, Bowen WS, Johnson CT, Shea L, Yolcu ES, García AJ, Shirwan H. Local immunomodulation with Fas ligand-engineered biomaterials achieves allogeneic islet graft acceptance. Nature materials. 2018 August;17(8):732-739. PubMed PMID: 29867165; PubMed Central PMCID: PMC6060019.
Complete	Huang C, Fisher KP, Hammer SS, Navitskaya S, Blanchard GJ, Busik JV. Plasma Exosomes Contribute to Microvascular Damage in Diabetic Retinopathy by Activating the Classical Complement Pathway. Diabetes. 2018 August;67(8):1639-1649. PubMed PMID: 29866771; PubMed Central PMCID: PMC6054433.
Complete	Kowluru A, Kowluru RA. RACking up ceramide-induced islet β-cell dysfunction. Biochemical pharmacology. 2018 August;154:161-169. PubMed PMID: 29715450; PubMed Central PMCID: PMC6051906.

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Category	Explanation
Other	http://diabetesresearch.med.umich.edu

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Have inventions, patent applications and/or licenses resulted from the award during the reporting period? No

If yes, has this information been previously provided to the PHS or to the official responsible for patent matters at the grantee organization?

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. OVERALL PARTICIPANTS

D.1 WHAT INDIVIDUALS HAVE WORKED ON THE PROJECT?

Commons ID (eRA Commons User Name)	S/K	Name	Degree(s)	Role	Cal EFFORT	Aca	Sum	Foreign Org	Component(s)	Country	SS
	Y	Myers, Martin G	BA,PHD, MD	PD/PI					Admin Core-6954 (Administration Core)		NA
	N	Garcia-Galiano, David		Technician					Core-6976 (Microscopy Imaging and Cel… Core (MICPC))		NA
	N	Kopera, Huira		Technician					Core-6977 (Molecular Genetics Core (MGC))		NA
	N	Larkin, Dennis		Technician					Core-6977 (Molecular Genetics Core (MGC))		NA
	N	Schuster, Kristen		Technician					Core-6955 (Animal Studies Core)		NA
	N	Whalen, Jason		Technician					Core-6975 (Clinical Core)		NA
	N	White, Julianna		Technician					Core-6977 (Molecular Genetics Core (MGC))		NA
	N	Whitesall, Steve		Technician					Core-6955 (Animal Studies Core)		NA
	N	Zhu, Qing		Technician					Core-6977 (Molecular Genetics Core (MGC))		NA
	Y	Lanigan, Thomas M		Co-Investigator					Core-6977 (Molecular Genetics Core (MGC))		NA
	Y	Tan, Meng Hee	MD	Co-Investigator					Core-6975 (Clinical Core)		NA
	Y	Ye, Wen	PHD	Co-Investigator					Core-6975 (Clinical Core)		NA
	N	Cain, Sarah		Administrative Assistant					Project-6978 (Enrichment Program), Project-6979 (Pilot and Feasibility Program), Project-6980		NA

									(Expanded Pilot and Feasibility Program)		
	N	Campbell, Pamela		Administrative Assistant					Admin Core-6954 (Administration Core)		NA
	N	Malec, Mary		Director of Administration					Admin Core-6954 (Administration Core)		NA
	N	Wylie, Robin		Programmer					Admin Core-6954 (Administration Core)		NA
eRA Commons User Name	Y	CARTER-SU, CHRISTIN	PHD,BS, MS	Core Director					Project-6978 (Enrichment Program), Project-6979 (Pilot and Feasibility Program), Project-6980 (Expanded Pilot and Feasibility Program)		NA
	Y	Elias, Carol Fuzeti	PHD	Lab Dir - In Situ Hybridization (ISH) Module					Core-6976 (Microscopy Imaging and Cel… Core (MICPC))		NA
	Y	Cras-Meneur, Corentin	PHD	Lab Dir - Islet Lab					Core-6955 (Animal Studies Core)		NA
	Y	Antonetti, David	PHD	Core Director					Core-6976 (Microscopy Imaging and Cel… Core (MICPC))		NA
	Y	Giacherio, Donald Allen	PHD,BS,PHD	Lab Dir - Chem Lab					Core-6975 (Clinical Core)		NA
	Y	Michele, Daniel E	BS,PHD	Lab Dir - CGM Lab					Core-6955 (Animal Studies Core)		NA
	Y	OLSON, DAVID P	BS,MD,PHD,BA	Core Director					Core-6977 (Molecular Genetics Core (MGC))		NA
	Y	Lentz, Stephen Ignatius	PHD,BS	Lab Dir - Imaging Lab					Core-6976 (Microscopy Imaging and Cel… Core (MICPC))		NA
	Y	Qi, Nathan R.		Lab Dir -					Core-6955		NA

EFFORT

eRA Commons User Name					EFFORT						
				RMP & BP Labs					(Animal Studies Core)		
	Y	Goforth, Paulette B.	BA,PHD	Lab Dir - Cellular Physiology Lab					Core-6976 (Microscopy Imaging and Cel… Core (MICPC))		NA
	Y	Sandoval, Paul		Core Director					Core-6955 (Animal Studies Core)		NA
	Y	HERMAN, WILLIAM H	BS,MD,MPH	Core Director					Core-6975 (Clinical Core)		NA

Glossary of acronyms:
S/K - Senior/Key
DOB - Date of Birth
Cal - Person Months (Calendar)
Aca - Person Months (Academic)
Sum - Person Months (Summer)
Foreign Org - Foreign Organization Affiliation
SS - Supplement Support
RE - Reentry Supplement
DI - Diversity Supplement
OT - Other
NA - Not Applicable

D.2 PERSONNEL UPDATES

D.2.a Level of Effort

Will there be, in the next budget period, either (1) a reduction of 25% or more in the level of effort from what was approved by the agency for the PD/PI(s) or other senior/key personnel designated in the Notice of Award, or (2) a reduction in the level of effort below the minimum amount of effort required by the Notice of Award?

No

D.2.b New Senior/Key Personnel

Are there, or will there be, new senior/key personnel?

No

D.2.c Changes in Other Support

Has there been a change in the active other support of senior/key personnel since the last reporting period?

Yes

File uploaded: D.2.c_OtherSupport-ALL.pdf

D.2.d New Other Significant Contributors

Are there, or will there be, new other significant contributors?

No

D.2.e Multi-PI (MPI) Leadership Plan

Will there be a change in the MPI Leadership Plan for the next budget period?

NA

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MYERS, MARTIN G. JR.

ACTIVE

(THIS AWARD)
P30 DK020572 2/27/18–11/30/22 EFFORT
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Principal Investigator

R01DK104999 (Olson) 4/1/16-3/31/21 EFFORT
NIH/NIDDK $306,836
Unique Roles for Defined PVH Neurons in the Control
Of Energy Balance
The goal of this project is to test the hypothesis that discrete subsets of PVH neurons play unique roles in metabolic regulation. We focus on analyzing the neural circuitry, physiologic function and transcriptional profile of insulin receptor substrate-4 neurons located within the PVH.
Role: Co-Investigator

R01 DK056731 9/1/18– 6/30/22 EFFORT
NIH/NIDDK $270,012
Molecular Mechanisms of Leptin receptor/Jak2 action
This proposal continues the study of LepRb signaling pathways and their roles in the regulation of physiology and neuronal function in vivo.
Role: Principal Investigator

Private Source (Seeley PI) 9/8/14-6/30/20 EFFORT
MOA of Liraglutide $0 (grant in NCTX)
This project uses genetic mouse models to manipulate Glp1R neurons to examine the site and mechanism of action of liraglutide.
Role: Co-Investigator

R01 DK099359 (Rhodes PI) 7/1/15-5/31/19 EFFORT
SubK with Chicago, prime NIH/NIDDK $12,516
Central Control of Pancreatic Islet Function
This project uses tract tracing and neuronal manipulations of glucose sensing enzymes in the brain to understand the pathways by which the brain controls islet function.
Role: PI of subcontract

R01 DK054222 (Carter-Su) 4/1/16-3/31/21 EFFORT
NIH/NIDDK $299,809
Cellular mechanism of action of SH2B1 isoforms
implicated in human obesity
The long-term goal of this project is to delineate cellular and molecular mechanisms by which SH2B1 isoforms influence neuronal function, neural circuitry and regulate body weight, thereby providing a molecular basis for new therapeutic strategies.
Role: Co-Investigator

R01 DK107730 (Carter-Su) 7/1/16-4/30/21 EFFORT
NIH/NIDDK $293,004
Cellular and molecular mechanisms of SH2B1 mutations that cause profound childhood obesity
The specific aims of this grant are to: 1) determine neurotrophic ligand signaling pathways and proteins that are enhanced by SH2B1 and impaired by human mutations; 2) determine how nuclear SH2B1, which is required for neurite outgrowth, enhances gene expression and how the human mutations impair that enhancement; and 3) define the role for SH2B1 in the control of circuit formation and transcription in neurons involved in energy balance.
Role: Co-Investigator

Private Source 7/1/16-12/31/19 EFFORT
$53,263
Dr. Myers will serve as the Editor in Private Source overseeing the peer review and direction of editorial content of the journal, with the primary objective of enhancing the position of Diabetes as the leading source of original research on diabetes and its complications.
Role: Principal Investigator

Private Source 1/1/17-12/31/19 EFFORT
Enhanced screening of potential therapeutic targets of obesity and diabetes $258,065
The long-term goal of the UM team is to develop a robust research program synergistic with and complimentary to the Private Source pipeline of potential therapeutic agents for the prevention and treatment of diabetes, obesity and related metabolic disorders.
Role: Principal Investigator

(NEW)
Private Source 1/1/18-12/3/20 EFFORT
Mechanisms of Anorectic PRLH Action $128,616
The goal of this project is to dissect and understand the function of PRLH and the CNS systems by which PRLH mediates its effects on food intake and body weight using genetic mouse models, together with PRLH (and PRLH-related peptides).
Role: Principal Investigator

(NEW)
Private Source 4/1/18-3/31/19 EFFORT
Generation and Validation of a Humanized Lepr $64,205
Mouse Line
The goal of this project is to design and generate all appropriate materials necessary for the generation of the genetically modified mouse models.
Role: Principal Investigator

INACTIVE

R01 DK098853 12/17/13-11/30/17 EFFORT
NIH/NIDDK $195,750
A leptin-regulated brainstem circuit that controls glucose and energy homeostasis
This proposal examines the regulation and function of midbrain and hindbrain LepRb neurons, including those that express CCK. This award does not encompass the electrophysiologic examination of these neurons.
Role: Principal Investigator

R01 DK078056 4/1/14– 3/31/18 EFFORT
NIH/NIDDK $216,688
Role of the Lateral Hypothalamic Area in Leptin action
This proposal examines the regulation, action in the mesolimbic dopamine system and physiologic function of LHA LepRb neurons.
Role: Principal Investigator

Private Source (Seeley PI) 11/1/15-12/31/17 EFFORT
Elucidating the Mechanisms by which GDF-15 Reduces Food Intake and Lowers Body Weight $206,431
This project will focus on starting a comprehensive program to better understand the MIC-1 system and its relationship to potential beneficial effects on metabolism and the purpose of this proposal is to laying out how this might be done as a collaboration with Private Source
Role: Co-Investigator

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

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ANTONETTI, DAVID A

ACTIVE

R01 EY 012021 (Antonetti) 01/01/2015-12/31/2019
NIH/NEI $276,961
Mechanisms of Retinal Vascular Permeability in Diabetes

EFFORT

The overall goal of this project is to understand how diabetes alters the blood retinal barrier and contributes to macular edema. The project focuses on signaling events that alter the tight junction complex changing retinal vascular permeability and also how these changes impact angiogenesis. This research will identify new targets for therapeutic intervention that are effective against both growth factors and inflammatory cytokines.

R24 EY 024864 (Kern) 04/01/2016-03/31/2020
Case Western University/NIH $112,360
Novel Therapies to Inhibit Diabetic Retinopathy

EFFORT

The goal of this project will be to test novel proprietary compounds for their effect on retinal vascular permeability in models of diabetic retinopathy.

P30 EY007003 (Hughes) 09/01/2017-08/31/2022
NIH/NEI $379,147
Core Grant for Vision Research

EFFORT

The specific aims of the Core Grant for Vision Research at the University of Michigan are to enhance the research environment for vision scientists, facilitate collaborative studies of the visual system and its diseases, and expand vision research on this campus to bring the skills and perspectives of non-vision scientists to bear upon research issues of the visual system.

U2C DK110768 (Low) 08/02/2016-06/30/2021
NIH/NIDDK $731,243
Michigan Mouse Metabolic Phenotyping Center

EFFORT

The goal of this project is to provide comprehensive and state of the art services internally, while expanding their availability to researchers on a national level and continuing the development of more sensitive and more specific tools to probe the pathogenesis and biochemical consequences of diabetes and obesity in mouse models.

(THIS AWARD)
P30 DK020572 (Myers) 02/27/2018-11/30/2022
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center

EFFORT

The Microscopy Imaging and Cell Physiology core provides state-of-the-art protein and RNA imaging and cell physiological analysis to enhance the diabetes-related research of members of the Michigan Diabetes Research Center. MICP core services include standard fluorescence microscopy, live cell imaging, calcium imaging, RNA in situ hybridization and image analysis. The core also provides electrophysiological analysis in combination with optogenetic techniques to assess neuronal cell signaling.

(NEW)
R01 EY028350 (Segal) 09/01/2017-05/31/2021
NIH $250,000
EFFORT
Immune mediated regeneration of retinal ganglion cell axons following optic nerve trauma

The major goals of this project are to elucidate the factors that drive the differentiation of reparative neutrophils and develop protocols to generate them in vitro for therapeutic application.

(NEW)
R01 (Segal) 04/01/2018-03/31/2023
NIH $200,000
EFFORT
A Novel Inflammatory Cell with Neuroprotective and Neuroregenerative Properties

The studies proposed here stem from our discovery of a novel subset of pro-regenerative neutrophils, characterized by the cell surface phenotype Ly6GlowCD14+, that accumulate in the posterior chamber of the eye following intraocular administration of the yeast cell wall extract, zymosan.

(NEW)
(Lee) 01/01/2018-12/31/2022
Research to Prevent Blindness $115,000
EFFORT
Private Source

The goal of this project is to elucidate the processes that affect vision and to translate this knowledge to improve the vision and lives of all people.

(NEW)
(Abcouwer) 04/08/2018-04/07/2021
Private Source $198,865
EFFORT
Mouse Retinal Ischemia/Reperfusion Model for Drug and Biomarker Discovery

The overall objectives of this study modality is to utilize retinal ischemia-reperfusion (IR) injury models in mice to test the efficacy of various biologic compounds (herein referred to as monoFabs) delivered by intravitreal (ivt) injections for the ability to prevent retinal vascular permeability, neurodegeneration, and inflammatory gene expression responses and to test the ability of these biologics to promote restoration of the blood-retinal barrier and promote resolution of retinal inflammation.

(NEW)
(Antonetti) 05/31/2018-05/31/2019
Private Source $125,793
EFFORT
Collaboration 2018

(NEW)
R01 (Abcouwer/Antonetti) 09/01/2018-07/31/2023
NIH $306,366
EFFORT
Inflammatory Resolution and Vascular Restoration in Diabetic Retinopathy

The current application represents what is, in our opinion, a novel approach to understanding disease pathology in diabetic retinopathy. Here we propose to explore the mechanisms by which the retina restores normal blood-retinal barrier properties after an ischemic challenge and understand the process of inflammatory resolution.

The overall goal of this project is to test novel aldose reductase inhibitors for Applied Therapeutics Inc.

INACTIVE

R01 EY 023725 (Antonetti) 04/01/2014-03/31/2018
NIH/NEI $396,830
EFFORT
Discovering Novel Atypical PKC Inhibitors as in vivo Chemical Probes
The goals of this project are to provide a robust chemical pharmacophore, pharmacokinetic analysis, mechanism of action and in vivo effectiveness for atypical protein kinase C inhibitors to treat macular edema with specific leads available for clinical trials.
Role: Principal Investigator

(Antonetti) 02/28/2017-11/27/2017
Private Source $136,692
EFFORT
Protective effects of ATXi in IR mouse model
The goal of this project is to build on a successful I/R study in rats with protective efficacy of one of the Roche compounds on ERG b-wave and RGC counts and extent with additional readouts that are considered relevant for the neuropathy in glaucoma.
Role: Principal Investigator

(Antonetti) 02/12/2016-12/31/2017
Private Source $40,964
EFFORT
Testing in mDia1 Knockout for Retinal Pathology in Diabetes and Ischemia Reperfusion
The goal of the studies is to determine if deletion of Diaph1 is protective against multiple indices of retinopathic changes in the diabetic retina. Wild type and Diaph1 KO mice will be rendered T1D with streptozotocin.
Role: Co-Investigator

R01 GM094526 (Flanagan) 01/01/2013-12/31/2017
NIH/Pennsylvania State University $89,273
EFFORT
Structural Studies of Tight Junction Proteins
The goal of this project is to utilize structural biological approaches to examine the organization of the tight junction complex that will inform cellular and molecular biological experiments to test specific hypotheses within the cellular environment.
Role: Co-Investigator

(Abcouwer and Antonetti) 05/16/2016-12/31/2017
Private Source $50,468
EFFORT
Examining the Effect of a Senolytic Drug Compound on Retinal Ganglion Cell Senescence and Retinal Pathology Following Ischemia-Reperfusion Injury
Using C57BL/6J mice, a senolytic drug compound provided by Unity Biotechnology (herein referred to as UBC1) will be tested for the ability to eliminate senescent retinal ganglion cells (RGC) and improve pathological outcomes following retinal ischemia reperfusion (IR) injury.
Role: Principal Investigator

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

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CARTER-SU, C

ACTIVE

R01 DK54222 (PI: Carter-Su) 4/1/2016 - 3/31/2021
NIH/NIDDK $299,809 Annual direct costs
EFFORT
Cellular mechanism of action of SH2B1 isoforms implicated in human obesity
The specific aims of this grant are to: 1) use novel in vivo mouse models to determine how the unique C-terminal tails of SH2B1 isoforms impact the function of LepRb-expressing neurons in the hypothalamus; 2) determine the cellular and molecular mechanism by which the C-terminal tails of SH2B1 isoforms regulate the function of SH2B1; and 3) define the role for SH2B1 isoforms in the regulation of body weight and insulin sensitivity.

R01 DK107730 (PI: Carter-Su) 7/1/2016 - 6/30/2021
NIH/NIDDK $293,004 Annual direct costs
EFFORT
Cellular and molecular mechanisms of SH2B1 mutations that cause profound childhood obesity
The specific aims of this grant are to: 1) determine neurotrophic ligand signaling pathways and proteins that are enhanced by SH2B1 and impaired by human mutations; 2) determine how nuclear SH2B1, which is required for neurite outgrowth, enhances gene expression and how the human mutations impair that enhancement; and 3) define the role for SH2B1 in the control of circuit formation and transcription in neurons involved in energy balance.

(THIS AWARD)

P30 DK020572 (Myers, PI; Carter-Su, Co-I) 02/27/2018 – 11/30/2022
NIH/NIDDK $1,115,804 Annual direct costs
EFFORT
Michigan Diabetes Research Center
Dr. Carter-Su is the Associate Director and Director of the Pilot and Feasibility Study and Enrichment Programs. The Center grant provides salary money only and does not fund research in the PI's laboratory.

INACTIVE:

R13 DK095665 (PI: Carter-Su) 06/01/12 - 05/31/17 (nc extension to 6/31/18)
NIH/NIDDK/NICHD $8,000 annual direct costs for 3 yrs of 5 yr period (monies awarded every other year)
EFFORT
FASEB Science Research Conference on The Growth Hormone/Prolactin Family in Biology and Disease. Funds travel costs for speakers and travel awards for young investigators to attend meeting.

P30 DK020572 (PI: Myers) (this grant) 12/1/12 - 11/30/17
NIH/NIDDK $927,424 Annual direct costs
EFFORT
Michigan Diabetes Research and Training Center
Dr. Carter-Su was the Associate Director and Director of the Pilot and Feasibility Study and Enrichment Programs. The Center grant provided salary money only and did not fund research in the PI's laboratory.

Center (MDRC) provides leadership, infrastructure, and resources to support and enhance diabetes research, including the translation of scientific discoveries from bench to bedside.
Role: Associate Director (Center); Director (P/F and Enrichment Programs)

OVERLAP

There is no scientific or administrative overlap between the DRTC grant and any other active support.

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CRAS-MENEUR, CORENTIN

ACTIVE

(THIS AWARD)
P30 DK020572 (Myers) 2/27/17–11/30/22
NIH/NIDDK $101,403
Michigan Diabetes Research Center $1,115,804 (Total Project)
Animal Studies Core
EFFORT
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Lab Director

(NEW)
Private Source (Qi) 9/1/17-8/31/19
Beta cell endoplasmic reticulum-mitochondrial crosstalk $227,273
in the pathogenesis of T1D.
EFFORT
In this multi-P.I. R-01 proposal, the applicants' central hypothesis is that normally, the amount of misfolded proinsulin is kept at sub-threshold levels by active ER-associated degradation (ERAD) of proinsulin that prevents excessive accumulation of misfolded proinsulin forms. Failure of efficient ERAD allows the low-level misfolded proinsulin to accumulate and trigger many of the same phenotypes seen in MIDY. Thus,efficient ERAD of proinsulin (in one subset of molecules) is actually coupled to proper folding of proinsulin (in another subset of molecules). Thus, β--cell secretory capacity depends on the efficiency of ERAD. If correct, then if proinsulin ERAD should become impaired, misfolded proinsulin may accumulate, triggering pancreatic β-cell dysfunction.
Role: Research Investigator

R21 EB024410
NIH (Shea PI) 4/1/17-3/31/19
Microporous scaffolds for enhancing efficiency of beta-cell $150,000
progenitor maturation in vitro and in vivo
EFFORT
In this project,we propose that microporous scaffolds can provide cues that promotes differentiation and supports the cellular organization into islet-like structures.
Role: Co-Investigator

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

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ELIAS, CF

ACTIVE

(THIS AWARD)
P30 DK020572 2/27/18–11/30/22
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Lab Director

EFFORT

(NEW)
2R01HD069702-07 (PI: Elias) 7/15/2017 – 4/30/2022
NIH/NICHD 240,229
Neural basis of leptin action in reproduction
The major goal of this project is to determine the neural network and mechanisms associated with leptin action in the ventral premammillary nucleus to control reproduction.

EFFORT

(NEW)
1R21HD090567-01 (MPI: Elias, Vanini) 8/01/2017 – 7/31/2019
NIH/ NICHD $150,000
MCH neurons: the potential link between sleep and the neuroendocrine function
The major goal of this application is to assess if activation of a specific population of MCH neurons drives sleep and alters the pulsatile release of LH.

EFFORT

(NEW)
1R03 HD092855-01 (PI: Elias) 4/01/2018 – 3/31/2020
NIH/NICHD 50,000
Transcriptome analysis of hypothalamic neurons during pubertal transition
The major goal of this application is to perform a screening of transcript changes in hypothalamic neurons during pubertal transition.

EFFORT

INACTIVE
None

OVERLAP
None

OMB No. 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

PHS 2590RPPR OTHER SUPPORT FORMAT PAGE

GIACHERIO, D

ACTIVE

(THIS AWARD)
P30 DK20572 (Myers PI) 2/27/18–11/30/22
NIH/NIDDK $1,115,804
EFFORT
Michigan Diabetes Research Center
The goal is to promote new discoveries and enhance scientific progress through the support of cutting-edge basic and clinical research by its highly interactive research base.
Role: Lab Director

OVERLAP

There is no scientific, budgetary, or committed effort overlap with this submission.

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Goforth, P

ACTIVE

EFFORT

NIH (Seeley, PI) 07/01/15-06/30/20
P30 DK089503 $32,842 Annual direct costs
Michigan Nutrition and Obesity Research Center.
The goal of this project is to provide infrastructure, expertise, training and pilot and feasibility grants in the areas of obesity and obesity-related diseases.
Role: Director, Cellular Physiology Laboratory

(THIS AWARD)
EFFORT

NIH (Myers, PI) 2/27/18-11/30/22
P30 DK020572 $1,115,804 Annual direct costs
Michigan Diabetes Research Center.
The mission of the MDRC is to promote new discoveries and enhance scientific progress through the support of cutting-edge basic and clinical research by its highly interactive research base.
Role: Lab Director, Cellular Physiology Laboratory

EFFORT

NIH (Olson, PI) 04/01/2016-3/31/2021
R01 DK104999 $32,852 Annual direct costs
Unique Roles for Defined PVH Neurons in the control of Energy Balance
This proposal aims to test the hypothesis that discrete subsets of PVH neurons play unique roles in metabolic regulation. We focus on analyzing the neural circuitry, physiologic function and transcriptional profile of insulin receptor substrate-4 neurons located within the PVH.
Role: Co-Investigator

Private Source
EFFORT

(Myers, PI) 09/16/2016-8/31/2019
$10,948 Annual direct costs
Control of glucose homeostasis and energy expenditure by the dmVMN
This proposal focuses on identifying secreted proteins/peptides from a specific cell population in the VMH that are known to be involved in the regulation blood glucose.
Role: Co-Investigator

(NEW)
Private Source
EFFORT

Myers, PI) 01/01/2018-12/03/2020
Mechanisms of anorectic PRLH action $8,377 Annual direct costs
The UM team proposes to leverage its knowledge, expertise and technology to dissect and understand the function of PRLH and the CNS systems by which PRLH mediates its effects on food intake and body weight. Using genetic mouse models, together with PRLH (and PRLH-related peptides).
Role: Co-Investigator

Private Source

09/01/2016-08/31/2019

EFFORT

Fellows Training Program $23,647 Annual direct costs

The goals of the collaboration are for the University, with its expertise in the areas of 1) CNS mechanisms regulating appetite and energy expenditure, 2) mechanisms regulating weight loss after bariatric surgery, and 3) clinical research on obesity to work with Private Source to select and support postdoctoral fellows to work with faculty researchers in the area of obesity research.
Role: Collaborator

OVERLAP

There is no overlap among these projects.

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HERMAN, W.H.

ACTIVE

P30 DK092926 — 9/20/16-7/31/21 — EFFORT
NIH/NIDDK — $405,969
Michigan Center for Diabetes Translational Research
The Michigan Center for Diabetes Translational Research (MCDTR) supports type 2 translational research in diabetes among the faculty of the University of Michigan and regional, national, and international institutions.
Role: Principal Investigator

(THIS AWARD)
P30 DK20572 (Myers PI) — 2/27/18–11/30/22 — EFFORT
NIH/NIDDK — $1,115,804
Michigan Diabetes Research Center
The goals of the Center for Diabetes Research are to meet the needs of investigators and thereby support and strengthen the University's interdepartmental activities in research, training and outreach in the field of diabetes, its complications, and related endocrine and metabolic disorders.
Role: Clinical Core Director

R01 DK109995 — 7/7/16-4/30/20 — EFFORT
NIH/NIDDK — $331,072
Population health impact of a self-insured employer's policy change to cover weight reduction and diabetes prevention interventions for employees, dependents, and retirees with prediabetes
This project will evaluate the impact of recent policy changes on population health by first comparing the yield of four strategies being used to identify nondiabetic employees, dependents, and retirees with prediabetes. These include using claims, HbA1c, and BMI levels available in the U of M's self-funded health insurance database to identify prediabetic individuals.
Role: Principal Investigator

U01 DK094157 — 3/1/00–6/30/19 — EFFORT
Case Western University (NIH/NIDDK prime) — $120,000
Epidemiology of Diabetes Intervention and Complications
A prospective observational study of the DCCT cohort designed to determine the long-term course of atherosclerotic cardiovascular disease in type 1 diabetes.
Role: Principal Investigator

U01 DK094157 — 3/1/00–6/30/19 — EFFORT
Case Western University (NIH/NIDDK prime) — $24,670
Epidemiology of Diabetes Skeletel Substudy
A prospective observational study of the DCCT cohort designed to determine the long-term course of atherosclerotic cardiovascular disease in type 1 diabetes.
Role: Principal Investigator

U01 DK098246 1/1/13-7/31/19
George Washington University (NIH/NIDDK prime) $468,428
EFFORT
Glycemia Reduction Approaches for Diabetes: A comparative effectiveness study
To assess the comparative efficacy, safety, and tolerability of five antidiabetic medications with different glucose lowering mechanisms when used in conjunction with metformin, and to assess the relative benefits and risks of two treatment strategies (the early introduction of combination therapy versus the use of sequential therapy) to determine which strategy best improves glycemic control over time.
Role: Principal Investigator

HHSN2762014 00001C (Saran PI) 2/8/14–2/07/19
NIH/NIDDK $1,498,792
EFFORT
United State Renal Data System (USRDS) Coordinating Center
The USRDS performs surveillance for chronic kidney disease and end-stage renal disease in the U.S.
Role: Co-Investigator

R01 HD074559 (J, Lee PI) 5/1/14 – 2/28/19
NIH $332,050
EFFORT
Conventional and Metabolomic Predictors of Pediatric Prediabetes & Insulin Resistance
The proposed study will evaluate the longitudinal test performance of an array of conventional biomarkers of glycemia, including Hemoglobin A1c (HbA1c), and novel metabolomic biomarkers for identifying progression of glucose tolerance (normal to prediabetes or prediabetes to diabetes) in an overweight and obese pediatric cohort.
Role: Co-Investigator

George Washington University (NIH/NIDDK prime) 8/1/16-7/31/21
Glycemia Reduction Approaches in Diabetes: A $161,291
EFFORT
comparative effectiveness study (GRADE) - Economic Analysis Expansion
The main goal of this project is to describe the resource utilization and cost of diabetes management, quality of life experienced, and determine the within trial cost utility for participants in four treatment groups.
Role: Principal Investigator SubK

R01 ES026578 (Park PI) 8/1/16-4/30/21
NIH/NIEHS $335,639
EFFORT
Exposure to Multipollutants and Obesity, Type-2 Diabetes
and Metabolic Syndrome
This new epidemiologic study in a multi-ethnic cohort of women seeks to address research gaps and improve our understanding of how exposure to multiple pollutants affects the risks of developing T2DM, obesity and MetS.
Role: Co-Investigator

(NEW)
R01 DK112930 (Ye PI) 10/1/17-6/30/22
Ohio State University (NIH prime) $11,681
EFFORT
Impact of Augmented Care at the Worksite for
Diabetes Prevention
In this project, we will assess the effectiveness and cost-effectiveness of a group-based diabetes prevention intervention.
Role: Co-Investigator

(NEW)
R21 AG060277 8/1/18-4/30/20
NIH/NIA $125,000
EFFORT
Treatment for TIA to manage cardiovascular disease and diabetes in older adults
The goal of this project is to develop a model of transient ischemic attack (TIA) incidence and its sequeli, integrate the TIA model into a unified model of cardiovascular disease in persons with diabetes, and use this model to assess the cost-effectiveness of carotid endarterectomy in individuals with TIA under modern standards of care.
Role: Principal Investigator

INACTIVE

R18 DK 092765 (subcontract with Indiana University Program ACTIVE II: Behavioral Depression Treatment for Type 2 Diabetes 2/1/17-6/30/17
$9,299
EFFORT
The goal of this project is to assess comparative cost-effectiveness of each of three intervention arms (i.e., cognitive behavioral therapy and exercise (CBT+EXER), CBT alone, or EXER alone) against usual care in terms of predicted incidence of diabetes complications (e.g., coronary heart disease) and quality-adjusted life-years (QALYs).
Role: Principal Investigator

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

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LANIGAN, THOMAS

ACTIVE

(THIS AWARD)
P30 DK020572 2/27/18–11/30/22 EFFORT
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center (MDRC)
The Vector Core provides a core laboratory to the MDRC for the construction, purification and characterization of recombinant vectors containing genes relevant to the study of diabetes for use as *in vitro* and *in vivo* gene transfer and gene editing agents with a focus on AAV vectors and CRISPR technologies.
Role: Co-Investigator

(NEW)
P01 DK034933 08/01/2017 - 07/31/2022 EFFORT
NIH/NIDDK $750,000
University of Michigan Center for Gastrointestinal Research
The Vector Core provides a core laboratory to the UMCGR for the construction, purification and characterization of recombinant vectors containing genes relevant to the study of gastrointestinal research for use as *in vitro* and *in vivo* gene transfer and gene editing agents.
Role: Co-Investigator

INACTIVE

None

OVERLAP

None

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MICHELE, D

ACTIVE

R01 AR068428-01A1 (Michele, PI) 08/15/2016-06/30/2021 EFFORT
NIH $220,000
Mechanosignaling functions of the dystrophin glycoprotein complex in muscular dystrophy
Summary: The goal of this project is to understand the mechanisms by which the dystrophin glycoprotein complex acts as a mechanosensor in muscle to regulate nitric oxide synthesis and muscle blood flow
Role: PI

P30-AR069620 (Jepsen, PI; Michele, Core D Director) 08/01/2016-07/31/2021 EFFORT
NIH/NIAMS $499,295
Michigan Integrative Musculoskeletal Health Core Center
The goal of this project is to create a integrated musculoskeletal research core to provide core research services to the musculoskeletal research community. Core D is the Phenotyping and Functional Assessment Core which is focused on phenotyping small animal models and providing physiological testing on bone, tendon and muscle in vivo and in vitro.
Role: Core D Director

Private Source (Michele, PI) 10/01/2014-09/30/2018 EFFORT
Private Source $20,543
iPSC-derived cardiomyocytes from patients with inherited cardiomyopathies
Summary: The goal of this project is to develop patient specific iPS cells for studying the mechanisms of dystrophic cardiomyopathy.
Role: PI

T32 HL125242 (Jalife, PI) 07/01/2015-06/30/2020 EFFORT
NIH/NHLBI $188,911
Training Program in Translational Cardiovascular Research and Entrepreneurship
Summary: The goal of this predoctoral training program is to prepare the next generation of scientists for diverse scientific careers by training them in both state of the art translational cardiovascular research but also to expose them to the principles of research entrepreneurship.
Role: Associate Director

Private Source (Michele, PI) 02/01/2017-01/01/2020 EFFORT
Private Source $20,000
Frankel Cardiovascular Center Summer Undergraduate Fellowship Program
The overall goal of the Frankel Cardiovascular Summer Fellowship Program is to provide undergraduate student fellows an opportunity to perform full-time, mentored research experience in the state of the art cardiovascular research laboratories at the University of Michigan Frankel Cardiovascular Center.

Private Source (Michele, PI) 06/26/2017-12/25/2018 EFFORT
$33,663
Effects of edasalonexent on dystrophic cardiomyocyte signaling and function
The goal of this project is to test whether edasolonexent, an NF-Kb inhibitor, has any additional effect on dystrophin deficient cardiac myocyte membrane stability or cell signaling. The project uses isolated cardiac myocytes treated acutely in vitro or adult cardiomyocytes treated for 7 days in vitro.
Role: PI

(THIS AWARD)
P30 DK020572 (Myers, PI) 02/27/18-11/30/2022
NIH/NIDDK $1,115,804/yr
Michigan Diabetes Research Center (MDRC)
Summary: This P30 supports the Michigan Diabetes Research Center focused on supporting basic research cores to support NIH funded diabetes research. Dr.Michele is participating as a part of the Animal Phenotyping Core and oversight of continuous glucose monitoring laboratory for monitoring animal blood glucose by telemetry.
Role: Participating Investigator

EFFORT

(new)
R01 HL139813 (Beard, PI) 06/01/2018-02/28/2022
NIH NHLBI $313,382/yr
Multi-scale systems analysis of blood pressure control and hypertension
Summary: This proposed project investigates the mechanisms underlying 'essential' (or 'primary') hypertension by undertaking a systems investigation of pathway interactions in cardiovascular phenotypes (in animal models and patients). Data will be analyzed using multi-scale computational models to construct and test new hypotheses on cause-and-effect relationships in hypertension and hypertensive heart disease.
Role: Co-I
Overlap: none

EFFORT

(new)
R01 HL144657 (Beard, PI) 09/01/2018-08/31/2022
NIH NHLBI $343,852/yr
Computational systems analysis of cardiac mechanical-energetic coupling in heart disease
Summary: The goal is to utilize rat models and human patients with HF and develop computer models to explain how the depletion of cytoplasmic metabolite pools in the myocardium affects energetic state and contractile function in heart failure
Role: Co-I
*Fundable Score, awaiting NOA.
Overlap: none

EFFORT

INACTIVE

K26 OD016502 (Michele, PI) 06/15/2013 – 3/31/2018
NIH $72,472
Mentored training in comprehensive mouse phenotyping
Summary: The goal of this award is to provide mentored training opportunities through developed short courses in comprehensive cardiovascular mouse phenotyping through the Physiology Phenotyping Core.

EFFORT

R21AR066213-01 (Michele, PI) 08/01/15-07/31/18
NIH/NIAMS $110,000
In vivo molecular probes for the membrane repair pathway in muscle
The goal of this project is to develop and utilize in vivo GFP based biosensors to study the membrane repair pathway in normal and dystrophic muscle
Role: PI

EFFORT

OVERLAP

There is no scientific, budgetary, or committed effort overlap with this submission.

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OLSON, DAVID P

ACTIVE

(THIS AWARD)
P30 DK020572 2/27/18–11/30/22
NIH/NIDDK $1,115,804
EFFORT
Michigan Diabetes Research Center
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Core Director

R01 DK104999-01-A1 (Olson, PI) 4/1/2016 - 3/31/2021
NIH/NIDDK $297,836
EFFORT
"Unique Roles for Defined PVH Neurons in the Control of Energy Balance"
This proposal aims to test the hypothesis that discrete subsets of PVH neurons play unique roles in metabolic regulation. We focus on analyzing the neural circuitry, physiologic function and transcriptional profile of insulin receptor substrate-4 neurons located within the PVH. Elucidation of the anatomic and cellular mechanisms through which the PVH regulates metabolism and endocrine function will yield new insights and potential targets for the treatment of obesity and diabetes.

R01-DK-078056-06-A1 (Martin Myers, PI) 4/1/2014 - 3/31/2019
NIH/NIDDK $240,764
EFFORT
"Role of the Lateral Hypothalamic Area in Leptin Action"
This study will analyze leptin-regulated neural pathways in the lateral hypothalamic area (LHA) that contribute to body energy homeostasis, incentive, and activity.
Role: Co-Investigator

Private Source (Seeley, PI) 8/1/2014 – 12/31/2019 (NCE)
"Mechanism of Action of Liraglutide" $618,105
EFFORT
This study will determine the neurobiological basis of the actions of liraglutide on appetite suppression by cell selective manipulation of GLP1R within the central nervous system.
Role: Co-Investigator

(NEW)
Private Source (Myers, PI) 1/1/2017 - 12/31/2019
$258,065
EFFORT
"Enhanced screening of potential therapeutic targets of obesity and diabetes"
Goal: Determine MOA of therapeutic agents that target Calcr, Gcgr, or Npy2r for diabetes, obesity and metabolic disorders.
Role: Co-investigator

1 R01 DK107282-01-A1 (Sandoval, PI) 2/1/2017 - 1/31/2021
NIH/NIDDK $250,000
EFFORT
"A novel paracrine role for GLP-1 in the islet"
Goal: To explore the physiological role for paracrine action of GLP-1.
Role: Co-Investigator

(NEW)
2 P30 DK034933-31-A1 (Owyang, PI) 8/1/2017 - 5/31/2022
EFFORT
NIH/NIDDK $630,567
"University of Michigan Center for Gastrointestinal Research"
The overreaching goal is to investigate signal transduction mechanisms regulating homeostasis and GI disorders.
Role: Core Faculty Member: Manager, Genome Editing Program, Molecular Biology Core

INACTIVE

Private Source Olson, PI) 12/1/2014-11/30/2017
"Functional assessment of melanocortin-3 receptor expressing neurons in feeding and energy balance"
The goals of this project are to map the neural connections to and from Mc3R neurons in the lateral hypothalamus and understand their functional role in energy balance.

R01-HD041469 (Moenter, PI) 4/1/2013-03/31/2018
NIH/NIAID
"Central Actions of Estrogens: Effects on GnRH neurons"
These studies will identify the mechanisms by which an acute stress blocks the LH surge in intact mice and test the neurobiological mechanisms blocked by stress. In related efforts, we will study kisspeptin neurons in the anteroventral periventricular (AVPV) and arcuate region and determine how their inputs and intrinsic properties change with estradiol and time of day to affect the reproductive axis.
Role: Co-I

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

OMB No. 0925-0002 (Rev. 07/18 Approved Through 03/31/2020)

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SANDOVAL, DARLEEN

ACTIVE

(THIS AWARD)
P30 DK020572 2/27/18–11/30/22 EFFORT
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Core Director

(NEW)
NIH R01DK115583-01 (Singer) 07/01/18-06/30/23 EFFORT
The Role of Androgens in Obesity Induced Meta-Inflammation $9,633
Project goals are to determine the impact of androgens on myelopoiesis and the generation of activated tissue macrophages during obesity, the direct impact of androgens on impairments of adipocyte fatty acid storage and function, and the impact of androgens on systemic energy balance and insulin sensitivity.
Role: Co-Investigator

(NEW)
Private Source 01/01/18-12/31/18 EFFORT
Wayne State University, Private Source $8,525
Hypothalamic GHR neurons in glucose homeostasis and lipid metabolism
This collaboration with Wayne State University will study the role of LepR/GHR neuronal populations within the ARC in regulation of glucose and lipid metabolism.

NIH R01DK107282-02 (Sandoval) 02/01/17 – 01/31/21 EFFORT
A novel paracrine role for GLP-1 in the islet $250,000
In this proposal, we will use our unique genetic models combined with pharmacological and surgical interventions in order to advance the understanding of the in vivo role of pancreatic GLP-1 and in the process will help elucidate many controversies surrounding this source of GLP-1.
Role: Principal Investigator

NIH R01DK107652-02 (Seeley) 07/01/16 – 06/30/19 EFFORT
Molecular mechanism for bariatric surgery on obesity and diabetes $309,000
The specific goal of this proposal is to test several hypotheses directed at uncovering the key populations of FXR and the FXR-target genes that mediate the diverse effects of VSG.
Role: Co-Investigator

Private Source (Seeley) 09/08/14 – 06/30/20 EFFORT
Mechanisms of Action (MOA) of Liraglutide $309,053
This grant is to explore the effects of liraglutide on a number of circuits in the CNS.
Role: Co-Investigator

(NEW)
Private Source (Myers) 01/01/18 - 12/03/20 EFFORT
"Mechanisms of anorectic PRLH action" $128,616

The UM team proposes to leverage its knowledge, expertise and technology to dissect and understand the function of PRLH and the CNS systems by which PRLH mediates its effects on food intake and body weight. Using genetic mouse models, together with PRLH (and PRLH-related peptides).

(NEW)
Private Source (Seeley) 03/17/18 - 03/26/20 EFFORT $150,125
Three tests will be performed fo Private Source nder this agreement using already established mouse models.

INACTIVE
Private Source (Seeley) 01/01/18 – 08/31/18 EFFORT $193,237
Elucidating the mechanisms by which GDF-15 reduces food intake and lowers body weight
Our laboratories our committed to starting a comprehensive program to better understand the MIC-1 system and its relationship to potential beneficial effects on metabolism and the purpose of this proposal is to laying out how this might be done as a collaboration with Private Source
Role: Co-Investigator

OVERLAP
There is no scientific, budgetary, or committed effort overlap with this submission.

OMB No. 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

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TAN, MENG

ACTIVE

(THIS AWARD)
P30 DK020572 (Myers) 2/27/18–11/30/22 EFFORT
NIH/NIDDK $1,115,804
Michigan Diabetes Research Center
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.
Role: Co-Investigator

U01 DK098246 (Herman) 1/1/13-7/31/19 EFFORT
George Washington University (NIH/NIDDK prime) $471,151
Glycemia Reduction Approaches for Diabetes: A comparative effectiveness study
To assess the comparative efficacy, safety, and tolerability of five antidiabetic medications with different glucose lowering mechanisms when used in conjunction with metformin, and to assess the relative benefits and risks of two treatment strategies (the early introduction of combination therapy versus the use of sequential therapy) to determine which strategy best improves glycemic control over time.
Role: Co-Investigator

INACTIVE

R01 DK062370 (Boehnke) 6/1/14-5/30/18 EFFORT
NIH/NIDDK $496,836
Identifying Genes for Type 2 Diabetes: FUSION
The project builds on a longstanding and productive collaboration between researchers in the USA and Finland to understand the genetic basis of type 2 diabetes, and to use this information to reveal disease mechanisms. In this proposal, we will continue to identify genetic loci that influence risk to type 2 diabetes and variability in diabetes-related quantitative traits, and increasingly focus on identifying the causal variants, genes and other functional units, and the mechanisms by which they act.
Role: Co-Investigator

OVERLAP

There is no scientific, budgetary, or committed effort overlap with this submission.

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OMB No. 0925-0002 (Rev. 07/18 Approved Through 03/31/2020)

PHS 2590/RPPR OTHER SUPPORT FORMAT PAGE

Ye, W

ACTIVE

P30-DK092926 (Herman) 9/20/2016-7/30/2021
Pilot and Feasibility Grant (Ye and Lisabeth) 12/01/2016-4/30//2018
NIDDK $100,000
EFFORT
Development and Validation of a Stroke Simulation Model for Evaluating Stroke Prevention and Treatment Policies in Type 2 Diabetes Patients

P30-DK-092926 (Herman) 9/20/2016 - 7/30/2021
NIH/NIDDK $405,969
EFFORT
Michigan Center for Diabetes Translational Research (P30)
The Michigan Center for Diabetes Translational Research (MCDTR) supports MCDTR members and regional, national, and international collaborators to conduct research to translate diabetes interventions with proven efficacy from the bedside into clinical and community practice (type 2 translational research). The specific aims of the MCDTR are to: raise awareness of, and interest in, type 2 translational research in diabetes and create an environment that supports such research, identify, develop, and support researchers engaged in research to translate interventions with proven efficacy into real world health care settings, communities, and populations at risk, administer cores that provide services critical to type 2 translational research in diabetes for new and established investigators, foster interdisciplinary collaborations to advance type 2 translational research in diabetes, provide education and training opportunities in diabetes translational research and to administer a Pilot and Feasibility Study Grants Program to attract new investigators to the field and to enable them to generate preliminary data for successful grant applications.

U01-DK-062456 (Magee) 08/20/14-05/31/19
NIH $2,262,129
EFFORT
Childhood Liver Disease Research & Education Network Data Coordinating Center
The primary goal of this proposal is to continue clinical and translational research on rare pediatric liver diseases that include: biliary atresia; Alagille syndrome, alpha-1-antitrypsin deficiency, progressive familial intrahepatic cholestasis syndromes, bile acid synthesis defects, mitochondrial hepatopathies, idiopathic neonatal hepatitis, and cystic fibrosis liver disease. It is anticipated that the network will consist of up to 15 clinical sites and a single data coordinating center (DCC).

R01 DK104733 (Piatt) 04/01/15-03/31/20
NIH $499,129
EFFORT
Ongoing Diabetes Self-Management Support in Church-Based Settings
The goal of this proposal is to examine the effectiveness of three DSMS approaches compared to enhanced usual care within the context of churches. A cluster randomized, practical behavioral trial with three parallel intervention groups will be implemented. Twenty-one churches in metro-Detroit will be randomized to either 1) Parish Nurse+Peer Leader DSMS 2) Parish Nurse DSMS, or 3) Peer Leader DSMS.
Role: Co-Investigator

(THIS AWARD)
P30-DK-020572 (Myers) 2/27/18-11/30/22
NIH/NIDDK $1,115,804
EFFORT
Michigan Diabetes Research Center (MDRC)
The goal of the MDRC is to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among member investigators studying diabetes, its complications, and related endocrine and metabolic disorders.

U01-HL128952 (Han) 09/09/15-07/31/19
NIH $241,661
EFFORT
Redefining Therapy In Early COPD: RETHINC
The goal of this project is to perform a double blind, randomized controlled parallel group 12 week trial of bronchodilator therapy versus placebo in subjects who have symptoms (defined as CAT≥10) despite "normal" spirometry (FEV1/FVC>0.7) to determine the proportion of patients with a ≥ 4 point improvement in SGRQ.

R01-DK109995 (Herman) 7/7/2016 to 4/30/2020
NIDDK $332,066
EFFORT
Population health impact of a self-insured employer's policy change to cover weight reduction and diabetes prevention interventions for employees, dependents, and retirees with prediabetes

In September 2015, the University of Michigan changed its healthcare benefits to cover interventions for diabetes prevention at no out-of-pocket cost for the ~20,000 overweight or obese employees, dependents, and retirees with prediabetes among its ~85,000 employees, dependents, and retirees. This project will evaluate the impact of this large-scale policy change on population health.

U01-DK-098246 (Herman) 8/1/2016 to 7/31/2018
NIDDK $161,291
EFFORT
Glycemia Reduction Approaches in Diabetes: A comparative effectiveness study (GRADE) - Economic Analysis Expansion
The main goal of this project is to describe the resource utilization and cost of diabetes management, quality of life experienced, and determine the within trial cost utility for participants in four treatment groups.
Role: Co-I

(NEW)
R01-DK112930 (Ye) 10/1/2017 to 6/30/2022
OSU / NIH $18,106
EFFORT
Impact of Augmented Care at the Worksite for Diabetes Prevention
The subcontract will cover work conducted by Dr. Wen Ye at the University of Michigan, School of Public Health and William H. Herman, MD, MPH at the University of Michigan Medical School associated with the above-referenced research study designed to assess the effectiveness and cost-effectiveness of a group-based diabetes prevention intervention.

(NEW)
R21-AG060277 (Herman) 8/1/2018 to 7/31/2020
NIDDK $193,958
EFFORT
Cost-effectiveness of carotid endarterectomy to manage cardiovascular disease in older adults with diabetes, following a transient ischemic attack (R21)
We will develop a model of transient ischemic attack (TIA) incidence and its sequeli, integrate the TIA model into a unified model of cardiovascular disease in persons with diabetes, and use this model to assess the cost-effectiveness of carotid endarterectomy in individuals with TIA under modern standards of care.

INACTIVE

None

OVERLAP

There is no expectation of overlap at this time. If overlap occurs, Dr. Ye will adjust her effort as needed.

E. OVERALL IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES? Not Applicable
E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE? NOTHING TO REPORT
E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER? Not Applicable
E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)? NOTHING TO REPORT

F. OVERALL CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. OVERALL SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

File(s) uploaded:
MYERS_HUM00042036 thru 2-20-2019.pdf

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Report Attached: Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes

Report Attached: The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes

Report Attached: Development of blood biomarkers for clinical management of diabetic foot ulcers

G.4.c ClinicalTrials.gov

Does this project include one or more applicable clinical trials that must be registered in ClinicalTrials.gov under FDAAA?

No

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Are there personnel on this project who are newly involved in the design or conduct of human subjects research?

Yes

Ulrike Klueh, PhD, Wayne State University
CITI Program
CITI Health Information Privacy and Security (HIPS) for Clinical Investigators

The following P/F awardees completed PEERRS Certifications in Human Subjects Biomedical & Health Sciences Module & Certification Test
PEERRS is the U. Michigan's online Program for Education & Evaluation in Responsible Research and Scholarship
Robert O'Rourke, MD, U.Michigan
Lonnie Shea, PhD, U.Michigan
Amy Rothberg, MD, U.Michigan
Andrew Schrepf, PhD, U.Michigan

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH

funded research)?

No

G.7 VERTEBRATE ANIMALS

Does this project involve vertebrate animals?

Yes

G.8 PROJECT/PERFORMANCE SITES

Organization Name:	DUNS	Congressional District	Address
Primary: REGENTS OF THE UNIVERSITY OF MICHIGAN - ANN ARBOR	073133571	MI-012	3003 SOUTH STATE STREET 1st Floor Wolverine Tower ANN ARBOR MI 481091274

G.9 FOREIGN COMPONENT

No foreign component

G.10 ESTIMATED UNOBLIGATED BALANCE

G.10.a Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25% of the current year's total approved budget?

Yes

Estimated unobligated balance: 1002000

G.10.b Provide an explanation for unobligated balance:
The majority of the unobligated balance is from carry-forward and is dedicated to the Administrative Supplement for Jodee Allen (see section B.3) and Year 40 P/F awardees. The Administrative supplement award is $600k and was awarded in late 2017 with carry-forward authorization. No expenses had incurred at the end of Yr40.
$77k is dedicated to Yr40 P/F awardees that requested nctx. $300k is dedicated to Yr41 P/F awardees, as they did not received funding until February 2018.
Yr 41 balance is approx $245k and the majority is dedicated to the Yr41 Awardees.

G.10.c If authorized to carryover the balance, provide a general description of how it is anticipated that the funds will be spent
The majority of the carryover balance will be dedicated to the Administrative Supplement -$600k and Yr40 and Yr41 P/F awardees - approximately $400k

G.11 PROGRAM INCOME

Is program income anticipated during the next budget period?

No

G.12 F&A COSTS

Not Applicable

UNIVERSITY OF MICHIGAN
eResearch.umich.edu
Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Road, Building 520, Suite 3214, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Dr. Martin Myers

Cc:

Martin	Myers
Mary	Malec

Subject: Scheduled Continuing Review [CR00067268] Approved for [HUM00042036]

SUBMISSION INFORMATION:
Study Title: Michigan Diabetes Research Center
Full Study Title (if applicable): Michigan Diabetes Research Center IRBMED# 1989-545
Study eResearch ID: HUM00042036
SCR eResearch ID: CR00067268
SCR Title: HUM00042036_Continuing Review - Mon Feb 19 08:02:26 EST 2018
Date of this Notification from IRB: 2/21/2018
Date of Approval for this SCR: 2/21/2018
Review: Expedited
Current IRB Approval Period: 2/21/2018 - 2/20/2019
Expiration Date: Approval for this expires **at 11:59 p.m. on 2/20/2019**
UM Federalwide Assurance: FWA00004969 (For the current FWA expiration date, please visit the UM HRPP Webpage)
OHRP IRB Registration Number(s): IRB00001995

NOTICE OF CONTINUING IRB APPROVAL FOR A PROJECT LACKING IMMEDIATE PLANS FOR INVOLVEMENT OF HUMAN SUBJECTS, THEIR DATA, AND/OR THEIR SPECIMENS:
The IRBMED has reviewed and approved the scheduled continuing review for the scope of activities described in study referenced above in accordance with 45 C.F.R. §46.118, **Applications and proposals lacking definite plans for involvement of human subjects:**

> Certain types of applications for grants, cooperative agreements, or contracts are submitted to departments or agencies with the knowledge that subjects may be involved within the period of support, but definite plans would not normally be set forth in the application or proposal. These include activities such as institutional type grants when selection of specific projects is the institution's responsibility; research training grants in which the activities involving subjects remain to be selected; and projects in which human subjects' involvement will depend upon completion of instruments, prior animal studies, or purification of compounds. These applications need not be reviewed by an IRB before an award may be made. However, except for research exempted or waived under §46.101(b) or (i), **no human subjects may be involved in any project supported by these awards until the project has been reviewed and approved by the IRB**, as provided in this policy, and certification submitted, by the institution, to the department or agency.

The IRB determined that the proposed research conforms to applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS).

At such time as you are ready to begin research activities with human subjects, their data, and/or specimens, you **must submit an amendment or new IRB application. No work with human subjects, including subject recruitment, may be conducted under this approval.**

APPROVAL PERIOD AND EXPIRATION:
The approval period for this study is listed above. Please note the expiration date. If the approval lapses, you may not conduct work on this study until appropriate approval has been re-established.

RENEWAL/TERMINATION:
At least two months prior to the expiration date, you should submit a continuing review application either to renew or terminate the study. Failure to allow sufficient time for IRB review may result in a lapse of approval that may also affect any funding associated with the study.

AMENDMENTS:
All proposed changes to the study (e.g., personnel or documents), must be approved in advance by the IRB through the amendment process.

SUBMITTING VIA eRESEARCH:
You can access the online forms for continuing review, amendments, and AEs/ORIOs in the eResearch workspace for this approved study.

MORE INFORMATION:
You can find additional information about UM's Human Research Protection Program (HRPP) in the Operations Manual and other documents available at: http://research-compliance.umich.edu/human-subjects/

Michael Geisser
Co-chair, IRBMED

Alan Sugar
Co-chair, IRBMED

Inclusion Enrollment Report

Inclusion Data Record (IDR) #: 253790

Using an Existing Dataset or Resource: Yes

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial:

Study Title: Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					0
Asian	0	0		0	0					0
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	10	1		0	0					11
White	26	7		0	0					33
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	**36**	**8**		**0**	**0**					**44**

Cumulative Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	10	1	0	0	0	0	0	0	0	11
White	26	7	0	0	0	0	0	0	0	33
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	**36**	**8**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**44**

Inclusion Data Record (IDR) #: 253791

Using an Existing Dataset or Resource: Yes

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial:

Study Title: The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					0
Asian	0	0		0	0					0
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	0	0		0	0					0
White	2	0		0	0					2
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	**2**	**0**		**0**	**0**					**2**

Cumulative Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	2	0	0	0	0	0	0	0	0	2
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	**2**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**2**

Inclusion Data Record (IDR) #: 253792

Using an Existing Dataset or Resource: Yes

Delayed Onset Study ?: No

Clinical Trial: No

Enrollment Location: Domestic

NIH Defined Phase III Clinical Trial:

Study Title: Development of blood biomarkers for clinical management of diabetic foot ulcers

Planned Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0		0	0					0
Asian	0	0		0	0					0
Native Hawaiian or Other Pacific Islander	0	0		0	0					0
Black or African American	40	40		0	0					80
White	40	40		0	0					80
More than One Race	0	0		0	0					0
Unknown or Not Reported										
Total	**80**	**80**		**0**	**0**					**160**

Cumulative Enrollment

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	40	40	0	0	0	0	0	0	0	80
White	40	40	0	0	0	0	0	0	0	80
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	**80**	**80**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**160**

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Withheld pursuant to exemption

Budget ; Redacted by agreement

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A. COMPONENT COVER PAGE

Project Title: Administration Core
Component Project Lead Information: Myers, Martin G

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Now entering its 40th year, the Michigan Diabetes Research Center (MDRC) continues to establish, promote, and enhance multidisciplinary and collaborative basic biomedical and clinical research among investigators addressing diabetes, its complications, and related endocrine and metabolic disorders. The Administration Core of the MDRC provides leadership, infrastructure, and resources to support and enhance diabetes research, including the translation of scientific discoveries from bench to bedside. To accomplish this, the Administration Core will:
•Organize, coordinate, integrate, and administer all MDRC components and their activities.
•Identify and recruit new investigators to diabetes research and the MDRC, maintain and curate the MDRC membership roster, and support new and established investigators in diabetes research.
•Raise awareness of, interest in, and support for research in diabetes, its complications and related endocrine and metabolic disorders and create an environment that facilitates such research.
•Assess the productivity, effectiveness, and appropriateness of MDRC activities
•Assess scientific opportunities, and areas for collaboration among MDRC members
•Recruit, organize and utilize Internal and External Advisory Committees.
•Keep records, including regarding the use of MDRC facilities and services; publications; pilot and feasibility awards; and new grant applications resulting from preliminary data enabled by the MDRC.
•Effect interactions with and reporting to other Diabetes Research Centers, the NIDDK, and other appropriate individuals, groups, or organizations.
•Maintain the MDRC website, including curating and overseeing the site and ensuring the proper and seamless integration of the MDRC website with the NIDDK Diabetes Research Center program website.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Accomplishments-AdminCore.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The Administration Core will seek to enhance its outreach to members and new potential members. To do this, the Core will seek to more regularly update the MDRC website, will advertise MDRC services at MDRC enrichment events, and establish a newsletter for members. The Administration Core will direct the Enrichment Core to initiate awards for trainee presentations at the annual symposium. The MDRC will hold an external/internal advisory meeting in March, 2019, with Jean Schaffer, MD, Virginia Minnich Distinguished Professor of Medicine and Director, Diabetes Research Center, Washington University School of Medicine as our external advisor.

B.2 What was accomplished under these goals?

The Administration Core oversees and organizes the entire center. As part of this function, the administration core convenes advisory and oversight committees for the Center. The Administration Core conferred with the internal Core Advisory Committees plus external advisors Mitch Lazar, MD, PhD (Director, Penn DRC, University of Pennsylvania) in 2017 and Ruth Loos, PhD (Director, Genetics of Obesity and Related Metabolic Traits Program, Icahn School of Medicine at Mt. Sinai) in 2018 to review the MDRC and its Cores and Programs. While the advisors thought that the cores and programs were strong, they enumerated a number of issues/suggestions:

Overall- Consider requiring Core use for all P/F awardees. Need to improve outreach/advertising of core services for MDRC members.

Animal Studies- monitor usage and cost of Continuous Glucose Monitoring service. Collaborating with MMPC on an S10 to purchase new shared equipment.

Clinical Core- Research registry doing well; Chem lab utilization ebbs and flows and may need some new equipment.

Molecular Genetics Core- The genotyping/analysis to identify ideal founders is not always straightforward (can take 1 week to 4 months). The core may need additional space and equipment. Recharge rates need to be updated yearly, as the methods are evolving very rapidly. Some Regional MDRC members may not know about the availability of the core.

Enrichment and P/F- suggest offering awards for trainees for posters/presentations at the symposium.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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A. COMPONENT COVER PAGE

Project Title: Animal Studies Core
Component Project Lead Information: Sandoval, Darleen A

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

As it has for over a decade, the fee-for-service MDRC Animal Studies Core (ASC) (previously, the Animal Phenotyping Core- APC) provides state-of-the art equipment, services, training, and consultation regarding the detailed metabolic phenotyping of mouse and rat models of metabolic disease. To address the previously unmet needs of MDRC members, the MDRC has invested in new technology and established a host of new services over the past five years. The ASC will continue to support these technologies and services, providing access to crucial equipment, expertise and training to empower specialized studies of rodent models of diabetes and related diseases. The ASC consists of four labs:
1)The Rat Metabolic Phenotyping Lab: includes the assessment of glucose homeostasis, whole animal metabolic assessment, body composition, and other specialized metabolic assessments in rats.
2)The Optogenetics and Behavioral Phenotyping Lab: provides training and access to optogenetic equipment to examine physiologic and behavioral responses to neural circuit manipulation, as well as with equipment to measure relevant behaviors, such as homeostatic and non-homeostatic feeding, activity, reward, and other behaviors that impact and/or are regulated by metabolic parameters in rodents.
3)The Continuous Glucose Monitoring Lab: provides continuous assessment of blood glucose concentrations in conscious, unrestrained rodents by radiotelemetry. This technology minimizes the stress of handling rodents and permits a detailed analysis of glucose fluctuations within normal feeding patterns and across extended time-frames.
4)The Islet Lab: provides islet isolation from mice and rats and ex vivo studies (including perifusion) of islets and other endocrine tissues.

The ASC directly supports the goals of the MDRC. The services that the ASC provide are unique and are an important means to study rodent models of diabetes and related diseases, without which crucial aspects of diabetes-related research could not be accomplished. This core provides the necessary infrastructure to perform advanced, standardized, metabolic phenotyping of animal models of diabetes and related disorders that arise from genetic, pharmacologic, dietary, or other perturbations. The centralized equipment and services expedites research for many MDRC investigators in a cost-effective manner and provides access to complex metabolic techniques that they may not have otherwise.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Animal Studies Core.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The CGM laboratory performed a pilot project with DSI to study the use of continuous glucose monitoring in mice. We shared the probe performance data and made suggested modifications of the surgical protocol for implanting the HDXG in mice. DSI incorporated those suggestions into their mouse HD-XG surgical protocol that is disseminated to DSI users.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will continue to evaluate usage and needs by our members or modify existing services. We have some specific plans for the CGM and Islet laboratories.

Continuous glucose monitoring laboratory: we are investigating the possibility of using subcutaneously implanted continuous glucose monitoring probes that are Blue-tooth enabled. This would allow us to offer a less-invasive strategy for continuous glucose monitoring.

Islet laboratory: We are developing additional islet staining (eg. proliferation and/or apoptosis) based on user needs. We are also assessing the use of fluorescent reporters for in vitro and in vivo real time insulin secretion measurements. Lastly, we are working on collaborations to develop new imaging and morphometric measurement approaches.

Rat metabolic and behavioral phenotyping laboratory: We have purchased a new laser for the Optogenetic and Behavioral laboratory. This replaces an outdated and poorly functioning unit allowing for our members to access to state-of-the art equipment for these studies.

B.2 What was accomplished under these goals?

New services or changes in existing services:

Islet isolation laboratory: Discussions with current users and other members of the MDRC has led to the addition of alpha- and beta-cell staining, imaging, and quantification of cell mass to the list of services we off. We have purchased the necessary equipment to upgrade a shared microscope between the Arvan Lab and the Core in order for us to do triple staining for beta-cells, alpha-cells, and nuclei (DAPI). We are currently sharing expenses for consumables with the Arvan lab.

Significant accomplishments

The following publications exemplify progress made during the current funding period (center members listed in Bold):

Kim GH, Shi G, Somlo DR, Haataja L, Song S, Long Q, Nillni EA, **Low MJ**, **Arvan P, Myers MG Jr, Qi L.** Hypothalamic ER-associated degradation regulates POMC maturation, feeding, and age-associated obesity. J Clin Invest. 2018 Mar 1;128(3):1125-1140. doi: 10.1172/JCI96420. Epub 2018 Feb 19. PubMed PMID: 29457782; PubMed Central PMCID: PMC5824855.

This paper from the Qi lab in collaboration with multiple MDRC members, focuses on the role of endoplasmic reticulum (ER) with pro-opiomelanocortin (POMC) neurons. POMC neurons function as key regulators of metabolism and physiology by releasing prohormone-derived neuropeptides with distinct biological activities. However, our understanding of early events in prohormone maturation in the ER remains incomplete. Highlighting the significance of this gap in knowledge, a single POMC cysteine-to-phenylalanine mutation at position 28 (POMC-C28F) is defective for ER processing and causes early onset obesity in a dominant-negative manner in humans through an unclear mechanism. This manuscript reports a pathologically important role of Sel1L-Hrd1, the protein complex of ER-associated degradation (ERAD), within POMC neurons. Mice with POMC neuron-specific Sel1L deficiency developed age-associated obesity due, at least in part, to the ER retention of POMC that led to hyperphagia. The Sel1L-Hrd1 complex targets a fraction of nascent POMC molecules for ubiquitination and proteasomal degradation, preventing accumulation of misfolded and aggregated POMC, thereby ensuring that another fraction of POMC can undergo normal posttranslational processing and trafficking for secretion. Moreover, the authors report that the disease-associated POMC-C28F mutant evades ERAD and becomes aggregated due to the presence of a highly reactive unpaired cysteine thiol at position 50. Thus, this study not only identifies ERAD as an important mechanism regulating POMC maturation within the ER, but also provides insights into the pathogenesis of monogenic obesity associated with defective prohormone folding.

Zamarron BF, Mergian TA, Cho KW, Martinez-Santibanez G, Luan D, **Singer K**, DelProposto JL, Geletka LM, Muir LA, **Lumeng CN**. Macrophage Proliferation Sustains Adipose Tissue Inflammation in Formerly Obese Mice. Diabetes. 2017 Feb;66(2):392-406. doi: 10.2337/db16-0500. Epub 2016 Nov 8. PubMed PMID: 28108608; PubMed Central PMCID: PMC5248991.

This manuscript by Carey Lumeng's laboratory focuses on the inflammatory state of adipose tissue after weight loss. Obesity causes dramatic proinflammatory changes in the adipose tissue immune environment, but relatively little is known regarding how this inflammation responds to weight loss (WL). To understand the mechanisms by which meta-inflammation resolves during WL, the Lumen lab examined adipose tissue leukocytes in mice after withdrawal of a high-fat diet. After 8 weeks of WL, mice achieved similar weights and glucose tolerance values as age-matched lean controls but showed abnormal insulin tolerance. Despite fat mass normalization, total and $CD11c^{+}$adipose tissue macrophage (ATM) content remained elevated in WL mice for up to 6 months and was associated with persistent fibrosis in adipose tissue. ATMs in formerly obese mice demonstrated a proinflammatory profile, including elevated expression of interferon-γ, tumor necrosis factor-α, and interleukin-1β. T-cell-deficient $Rag1^{-/-}$ mice showed a degree of ATM persistence similar to that in WT mice, but with reduced inflammatory gene expression. ATM proliferation was identified as the predominant mechanism by which ATMs are retained in adipose tissue with WL. Thus, this study suggests that WL does not

completely resolve obesity-induced ATM activation, which may contribute to the persistent adipose tissue damage and reduced insulin sensitivity observed in formerly obese mice.

Zhang K, Kim H, Fu Z, Qiu Y, Yang Z, Wang J, Zhang D, Tong X, **Yin L, Li J, Wu J, Qi NR**, Houten SM, **Zhang R**. Deficiency of the Mitochondrial NAD Kinase Causes Stress-Induced Hepatic Steatosis in Mice. Gastroenterology. 2018 Jan;154(1):224-237. doi: 10.1053/j.gastro.2017.09.010. Epub 2017 Sep 18. PubMed PMID: 28923496; PubMed Central PMCID: PMC5742027.

This manuscript from one of our Wayne State University members, Ren Zang, focuses on the mitochondrial nicotinamide adenine dinucleotide (NAD) kinase (NADK2, also called MNADK) which catalyzes phosphorylation of NAD to yield NADP. Little is known about the functions of mitochondrial NADP and MNADK in liver physiology and pathology. In this manuscript they investigated the effects of reduced mitochondrial NADP by deleting MNADK in mice. They generated MNADK knockout (KO) mice on a C57BL/6NTac background; mice with a wild-type Mnadk gene were used as controls. Some mice were placed on an atherogenic high-fat diet (16% fat, 41% carbohydrate, and 1.25% cholesterol supplemented with 0.5% sodium cholate) or given methotrexate intraperitoneally. The KO mice had metabolic features of MNADK-deficient patients, such as increased serum concentrations of lysine and C10:2 carnitine. When placed on the atherogenic high-fat diet, the KO mice developed features of nonalcoholic fatty liver disease and had increased levels of reactive oxygen species in livers and primary hepatocytes, compared with control mice. During fasting, the KO mice had a defect in fatty acid oxidation. MNADK deficiency reduced the activation of cAMP-responsive element binding protein-hepatocyte specific and peroxisome proliferator-activated receptor alpha, which are transcriptional activators that mediate the fasting response. The activity of mitochondrial sirtuins was reduced in livers of the KO mice. Methotrexate inhibited the catalytic activity of MNADK in hepatocytes and in livers in mice with methotrexate injection. In mice given injections of methotrexate, supplementation of a diet with nicotinamide riboside, an NAD precursor, replenished hepatic NADP and protected the mice from hepatotoxicity, based on markers such as increased level of serum alanine aminotransferase. The authors conclude that MNADK facilitates fatty acid oxidation, counteracts oxidative damage, maintains mitochondrial sirtuin activity, and prevents metabolic stress-induced non-alcoholic fatty liver disease in mice.

Number of users (see attached form)

21 different investigators utilized the core since the last progress report period from (12/1/2016 to 07/31/18). 19 of these investigators are MDRC members (details are provided in the accompanying **table B.2**) and 2 were investigators external to UM. There were 41 different tests performed and all 3 laboratories were utilized, even our newest Islet laboratory. These numbers of users are similar to the previous period.

There were approximately 20 publications citing Animal Studies Core. It is a little difficult to compare this to previous years as this core used to include mouse metabolic phenotyping which is now covered through the MMPC.

Table B.2: Use of Core Facilities - period December 2016 - July 2018

CORE: Animal Studies Core

Determinations/Services Rendered

A	Surgeries (catheterization, pancreatectomy, etc)
B	Glucose Clamps (hyperinsulinemic-euglycemic, hyperglycemic, hypoglycemic)
C	Glucose, Insulin, and fatty tolerance tests
D	Energy expenditure (VO2 max, temperature-controlled, metabolic measurements) and body composition
E	Blood sampling, tissue and organ dissections
F	Manual measurement of body weight, food intake, and compound dosing via multiple pathways
G	Miscellaneous (including glucose and insulin assays, rectal/IP/subcutaneous temperature testing, etc)
H	Ethovision
I	Locomotor activity
J	Operant conditioning
K	Optogenetics
L	Training
M	Data analysis
N	Fiberoptic Cannulas
O	ICV surgeries
P	Continuous Glucose Monitoring (CGM)
Q	Islet preparation and analysis
R	Pancreas IHC for alpha and beta-cell mass

Core User	Funded Project	Period of Core Use	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	Actual use and comments
Center Members																					
Sandoval	R01DK 107282	12/1/2016-01/01/2017																x			16 rats; 1 month of data collection
Sandoval	R01DK 107282	06/06/2017-07/06/2017																x			12 rats; 1 month of data collection
Sandoval	internal funding	03/30/2018-04/30/2018																x			14 rats; 1 month of data collection
Myers/Flak	R01 DK098853	01/16/2017-02/16/2017																x			12 mice; 1 month of data collection
Flak	R01 DK098853	1/16/2017																x			training: calibration methods
Sandoval	internal funding	11/01/2017-12/26/2017																x			training: 8 surgeries
Soleinampour	DK108921	01/2018-02/2018																	x		Q. 11 mice for islet isolation
Gregg	internal funding	02/2018-04/2018																	x		Q. 14 mice for islet isolation
Seeley	Private Source	01/2018-07/2018																	x		Q. 8 mice for islet isolation Q. 8 mice for β-cell staining (40 slides) Q. 8 mice for β-cell Imaging (40 slides) Q. 8 mice for β-cell quantification (40 slides)
Low	pilot project	5/1/2018																	x		Q. 2 mice for Islet isolation

Core User	Funded Project	Period of Core Use	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	Actual use and comments
Myers	non-federal funding	03/2018-ongoing																	x		Q. 26 mice for β-cell staining (130 slides) Q. 26 mice for β-cell Imaging (130 slides) Q. 26 mice for β-cell quantification (130 slides)
Sandoval	R01DK 107282	03/2018-08/2018																	x		Q. 8 mice for islet Isolation Q. 2 mice for β-cell staining (10 slides)
Qi	(billing ongoing)	08/2018-ongoing																	x		Q. 3 islets perifusion Q. 9 mice for β-cell staining (45 slides) Q. 8 mice for β-cell Imaging (40 slides) Q. 8 mice for β-cell quantification (40 slides)
Hussain	(billing ongoing)	08/2018																	x		Q. 2 mice for β-cell staining (10 slides)
Burant	Private Source	7/11/2016-7/13/2016				x	x	x													D. Energy Expenditure (VO2max) 13 rats E. Tissue Dissection 25 Rats F. Manual Body Weight Recording 25 Rats
Cartee	1) 5 R01 AG010026-25 2) Project Grant U010306	1/16/2017-3/29/2017	x	x	x	x	x														A. Dual Catheterization Surgery 1 rat B. Hyperinsulinemic-euglycemic clamp 23 rats C. Glucose Tolerance Test 24 rats D. Body Composition 48 rats D. Energy Expenditure (CLAMS) 24 rats E. Tissue Dissection 24 rats
Evans	5 P30 DK089503-09	10/27/2017-11/10/2017				x															D. Body Composition 126 rats
Ferrario	5 R01 DK106188- 03	7/5/2016-5/9/2017				x															D. Body Composition 138 Rats
Myers	1) 5 R01 DK078056-09 2) 5 R37 DK056731-19 3) Private Source 4) 5 P30 DK020572-40 5) 5 R01 DK098853-04 Private Source	7/5/2016-6/29/2018								x											H. Ethovision (Open Field Test) 23 mice H. Ethovision (Elevated Plus Maze) 23 mice
Non- Center Members																					
Atherton -Koch	Private Source	9/8/2017-10/5/2017				x	x	x													D. Exercise Training 16 rats E. Tissue Dissection 16 rats F. Orgastric Gavage Dosing 32 rats
Seo	Start Up Fund	11/14/2016-11/18/2016								x											H. Ethovision (Open Field Test) 20 mice H. Ethovision (Elevated Plus Maze) 20 mice

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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Withheld pursuant to exemption

Budget ; Redacted by agreement

of the Freedom of Information and Privacy Act

A. COMPONENT COVER PAGE

Project Title: Clinical Core
Component Project Lead Information: HERMAN, WILLIAM H

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Clinical Core of the Michigan Diabetes Research Center (MDRC) provides resources and expertise to enhance the effectiveness, efficiency, and multidisciplinary nature of clinical research performed by MDRC investigators. Specifically, the Clinical Core provides resources and expertise to support type 1 translational research that focuses on moving basic science discovery and preclinical development into people with diabetes in order to enhance human health and well-being. This bench-to-bedside process may involve testing new drugs, devices, or treatment programs for patients at risk for or with diabetes and its complications and comorbidities or with related metabolic and endocrine disorders. The MDRC Clinical Core provides MDRC clinical investigators:

•Well–equipped and accessible clinical research space for diabetes-related studies,
•Expertise and resources to facilitate the recruitment of diabetic subjects into clinical studies,
•A chemistry laboratory to provide expertise and state-of-the-art laboratory analytical services, and
•Biostatistical services to address experimental design, data management, and data analysis.

Since its creation five years ago, the Clinical Core has adapted to the changing University of Michigan (UM) research environment and the evolving needs of MDRC investigators to provide ready access to well-equipped research space and to expand access to potential research subjects using tools made possible by the implementation of the new UM electronic medical record. In addition, the Clinical Core has rolled out new laboratory services with excellent quality control and low cost. It has also brought on new staff to assist with study design, data management, and data analysis. All of these services are designed to facilitate diabetes-related clinical research and collaboration. Discoveries made at a molecular or whole animal level can be tested in human subjects using the resources of the Clinical Core. Similarly, observations made using Clinical Core resources can be understood at a more detailed and mechanistic level using resources provided by MDRC biomedical research cores.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Clinical Core.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We will continue to address the changing needs of MDRC clinical investigators by aligning core resources to address their needs. In the next year, we will continue to promote the Clinical Research Unit to clinical investigators and to streamline on-line registration and scheduling to improve efficiency and simplify utilization management. We will also periodically reevaluate the need for and feasibility of providing CRU staffing. We will continue to promote the services of the Diabetes Research Registry by revising the website and conducting an analysis to assess the accuracy of the data fields being collected by self-report. Moving forward, we will perform validation only for data fields which cannot be obtained accurately through the self-report. The Chemistry Laboratory will continue to promote its services to MDRC investigators and to add new assays to serve the needs of its members. Biostatistical Services will continue to be offered to MDRC investigators and additional efforts will be made to extend services from clinical investigators to basic biomedical researchers.

B.2 What was accomplished under these goals?

Clinical Research Unit

To address changing needs and to facilitate clinical research by MDRC investigators, the Clinical Core of the MDRC acquired dedicated clinical research space in three locations. The first location shares space with the Michigan Institute for Clinical and Health Research Clinical Research Unit at Domino's Farms, Lobby M. This MDRC Clinical Research Unit (CRU) offers a waiting room, shared intake space, staff work space with two desks, and three examination rooms equipped with wall-mounted sphygmomanometers, exam tables, desks, and chairs. MDRC investigators also have access to shared laboratory space equipped with a refrigerated centrifuge, a small specimen refrigerator for short-term sample storage, and a shuttle service to transport samples to the U-M hospital laboratory. The second location is the MDRC CRU at the Metabolism, Endocrinology, and Diabetes (MEND) Outpatient Clinic located at Domino's Farms, Lobby C. This facility offers a waiting area, one fully equipped exam room, and access to the Endocrine Testing Unit laboratory for specimen processing and short-term sample storage. The third facility is the MDRC CRU at the Kellogg Eye Center/Brehm Diabetes Research Center. One fully equipped examination room is located off the Kellogg Eye Center main lobby next to the Kellogg Eye Center Blood Drawing Station.

MDRC investigators apply to use the MDRC Clinical Research Units online and if approved, are given access to the scheduling calendars. Approved researchers agree to acknowledge the MDRC grant and provide the Clinical Core with information concerning publications and other research funding arising from use of the MDRC CRU. Please see (Table B.1)

Diabetes Research Registry

Over the past 3 years, the number of registrants in the Diabetes Research Registry has grown, from 6,376 in 2017 to 7,134 in 2017 to 7,984 in July 2018. Since December 2016, the DRR has addressed 28 requests for services. Please see (Table B.2)

Chemistry Laboratory

Over the past 20 months, the Chemistry Laboratory has analyzed 36,694 samples from 39 different investigators working on 47 unique projects inside the University as well as 2 investigators from the University of Toledo and 1 investigator from Kansas State University (Table B.3). The Chemistry Laboratory performed 28 different assays and utilized 20 different multiplex assay panels and 5 different ELISA panels –

- Human Adipokine Magnetic Bead Panel 2 (IL-6, Insulin, TNF-α)
- Human Cytokine/Chemokine Magnetic Bead Panel (GM-CSF, IFNγ, MCP-3, IL-17A, IL-1β, IL-6, IL-8, MCP-1, MIP-1α, MIP-1β, TNF-α, VEGF-A)
- Human Cytokine/Chemokine Magnetic Bead Panel (IFNγ, IL-10, IL-17A, IL-1rα, IL-1β, IL-4, IL-6, IL-8, MCP-1, MIP-1α, TNF-α, VEGF)
- Human Cytokine/Chemokine Magnetic Bead Panel (IFNγ, IL-10, IL-1rα, IL-1β, IL-4, IL-6, IL-8, TNF-α)
- Human Neurodegenerative Disease Magnetic Bead Panel 3 (BDNF)
- Mouse Adipokine Magnetic Bead Panel (IL-6, Insulin, Leptin, MCP-1, PAI-1 (total), Resistin, TNF-a)
- Mouse Adipokine Magnetic Bead Panel (Insulin, MCP-1, TNF-a)
- Mouse Angiogenesis/Growth Factor Magnetic Bead Panel (G-CSF, sFasL, Amphiregulin, Leptin, IL-1β, EGF, IL-6, Endoglin, Endothelin-1, FGF-2, Follistatin, HGF, IL-17A, PLGF-2, KC, MCP-1, Prolactin, MIP-1α, TNF-α)
- Mouse Bone Magnetic Bead Panel (ACTH, IL-6, Osteoprotegerin, DKK1, Sclerostin, TNF-α, FGF-23)
- Mouse Cytokine/Chemokine Magnetic Bead Panel (IL-1β, IL-6, IL-10, MCP-1)
- Mouse Cytokine/Chemokine Magnetic Bead Panel (pre-mixed 32-plex)
- Mouse Cytokine/Chemokine Magnetic Bead Panel (IFN-y, IL-1β, IL-2, IL-10, IL-13, IL-17A, MCP-1, TNF-α)
- Mouse Cytokine/Chemokine Magnetic Bead Panel (IL-1β, IL-6, IL-10, MCP-1, TNF-α)
- Mouse Cytokine/Chemokine Magnetic Bead Panel (IFN-y, IL-1β, IL-2, IL-10, IL-13, IL-17A, MCP-1, MIG, RANTES, TNF-α)
- Mouse Metabolic Magnetic Bead Panel (IL-6, Leptin, MCP-1, Resistin, TNF-α)

- Mouse Metabolic Magnetic Bead Panel (Ghrelin (active), GIP, GLP-1 (active), Glucagon, Leptin, PYY)
- Mouse Myokine Magnetic Bead Panel (FGF-21)
- Rat Cytokine/Chemokine Magnetic Bead Panel (IL-1β, TNF-α)
- Rat Metabolic Magnetic Bead Panel (IL-6, Leptin, TNF-α)
- TGF-B1 Single Plex Magnetic Bead Panel (TGF-1B)
- Human Leptin ELISA (1)
- Mouse Insulin ELISA (15)
- Mouse Leptin ELISA (15)
- Rat Leptin ELISA (3)
- Human Salivary Cortisol (34)

Over the past 20 months, the Chemistry Lab accepted and approved 27 new applications and has added three new assays: Cystatin C, Bile Acids (total), and 1,5-Anhydrogluctiol. Please see (Table B.3)

Biostatistical Services

Since December 2016, biostatistical services have been provided for 17 discrete projects. Please see (Table B.4)

Publications

The Clinical Core provided support or consultation that directly led to 48 publications. These publications are included in the Overall Component Section C.

Three papers that highlight representative scientific advances supported by the Clinical Core Clinical Research Unit, Chemistry Lab, and Biostatistical Services are listed below (center members listed in Bold).

1. ***Rothberg AE***, *McEwen LN, Kraftson AT, Ajluni N, Fowler CE, Nay CK, Miller NM,* ***Burant CF, Herman WH****. Impact of weight loss on waist circumference and the components of the metabolic syndrome. BMJ Open Diabetes Res Care. 2017 Feb 20;5(1):e000341. doi: 10.1136/bmjdrc-2016-000341. eCollection 2017. PubMed PMID: 28316795; PubMed Central PMCID: PMC5337678.*

The MDRC CRU was used by these investigators to perform detailed clinical phenotyping.

OBJECTIVE:
Central adiposity is a component of the metabolic syndrome (MetS). Little is known about the impact of medical weight loss and decreased waist circumference (WC) on the MetS. Our objective was to assess the impact of changes in WC on blood pressure, lipids and glycemia.

RESEARCH DESIGN AND METHODS:
We studied 430 obese patients enrolled in a 2-year, intensive, behavioral, weight management program. We report results for participants who completed 6-month and 2-year follow-up.

RESULTS:
Participants were 49±9 years of age (mean±SD), 56% were women and 85% were white. Baseline body mass index (BMI) was 41±6 kg/m^2 and baseline WC was 120±14 cm. At 6 months, BMI decreased by 6±3 kg/m^2 and WC by 14±9 cm. Relative change in WC was defined as the 6-month or 2-year WC minus the baseline WC divided by the baseline WC. Systolic blood pressure decreased by 8 mm Hg for the tertile of participants with the largest relative decrease in WC and by 2 mm Hg for those with the smallest relative decrease in WC (p=0.025). Similar patterns of improvement were observed in total cholesterol (-29 vs -12 mg/dL, p=0.017), low-density lipoprotein-cholesterol (-19 vs -4 mg/dL, p=0.033), and glycated hemoglobin (-1.2 vs -0.3%, p=0.006). At 2 years, BMI decreased by 5±4 kg/m^2 and WC by 11±11 cm and similar patterns of improvements were seen in components of the MetS. At both 6 months and 2 years, larger relative decreases in WC were associated with greater improvements in lipids and glycemia independent of sex.

CONCLUSIONS:
In obese people, greater relative decreases in WC with medical weight loss are associated with greater improvements in components of the MetS independent of sex.

2. ***Flak JN**, Arble D, Pan W, Patterson C, Lanigan T, **Goforth PB**, Sacksner J, Joosten M, Morgan DA, Allison MB, Hayes J, **Feldman E, Seeley RJ, Olson DP**, Rahmouni K, **Myers MG Jr**. A leptin-regulated circuit controls glucose mobilization during noxious stimuli. J Clin Invest. 2017 Aug 1;127(8):3103-3113. doi:10.1172/JCI90147. Epub 2017 Jul 17. PubMed PMID: 28714862; PubMed Central PMCID: PMC5531403.*

This high visibility manuscript published in JCI used the Chemistry Laboratory to measure insulin, leptin, and glucocorticoid levels.

Abstract

Adipocytes secrete the hormone leptin to signal the sufficiency of energy stores. Reductions in circulating leptin concentrations reflect a negative energy balance, which augments sympathetic nervous system (SNS) activation in response to metabolically demanding emergencies. This process ensures adequate glucose mobilization despite low energy stores. We report that leptin receptor-expressing neurons (LepRb neurons) in the periaqueductal gray (PAG), the largest population of LepRb neurons in the brain stem, mediate this process. Application of noxious stimuli, which often signal the need to mobilize glucose to support an appropriate response, activated PAG LepRb neurons, which project to and activate parabrachial nucleus (PBN) neurons that control SNS activation and glucose mobilization. Furthermore, activating PAG LepRb neurons increased SNS activity and blood glucose concentrations, while ablating LepRb in PAG neurons augmented glucose mobilization in response to noxious stimuli. Thus, decreased leptin action on PAG LepRb neurons augments the autonomic response to noxious stimuli, ensuring sufficient glucose mobilization during periods of acute demand in the face of diminished energy stores.

3. ***Herman WH**, Pan Q, Edelstein SL, Mather KJ, Perreault L, Barrett-Connor E, Dabelea DM, Horton E, Kahn SE, Knowler WC, Lorenzo C, Pi-Sunyer X, Venditti E, **Ye W**; Diabetes Prevention Program Research Group. Impact of Lifestyle and Metformin Interventions on the Risk of Progression to Diabetes and Regression to Normal Glucose Regulation in Overweight or Obese People With Impaired Glucose Regulation. Diabetes Care. 2017 Dec;40(12):1668-1677. doi: 10.2337/dc17-1116. Epub 2017 Oct 11. Erratum in: Diabetes Care. 2018 Feb 23;:. PubMed PMID: 29021207; PubMed Central PMCID: PMC5711336.*

The Clinical Core provided biostatistical services including assistance with study design and data analysis for this secondary analysis of DPP data. Core staff member Wen Ye is as a co-author of the manuscript.

OBJECTIVE:

Both lifestyle and metformin interventions can delay or prevent progression to type 2 diabetes mellitus (DM) in people with impaired glucose regulation, but there is considerable interindividual variation in the likelihood of receiving benefit. Understanding an individual's 3-year risk of progressing to DM and regressing to normal glucose regulation (NGR) might facilitate benefit-based tailored treatment.

RESEARCH DESIGN AND METHODS:

We used the values of 19 clinical variables measured at the Diabetes Prevention Program (DPP) baseline evaluation and Cox proportional hazards models to assess the 3-year risk of progression to DM and regression to NGR separately for DPP lifestyle, metformin, and placebo participants who were adherent to the interventions. Lifestyle participants who lost ≥5% of their initial body weight at 6 months and metformin and placebo participants who reported taking ≥80% of their prescribed medication at the 6-month follow-up were defined as adherent.

RESULTS:

Eleven of 19 clinical variables measured at baseline predicted progression to DM, and 6 of 19 predicted regression to NGR. Compared with adherent placebo participants at lowest risk of developing diabetes, participants at lowest risk of developing diabetes who adhered to a lifestyle intervention had an 8% absolute risk reduction (ARR) of developing diabetes and a 35% greater absolute likelihood of reverting to NGR. Participants at lowest risk of developing diabetes who adhered to a metformin intervention had no reduction in

their risk of developing diabetes and a 17% greater absolute likelihood of reverting to NGR. Participants at highest risk of developing DM who adhered to a lifestyle intervention had a 39% ARR of developing diabetes and a 24% greater absolute likelihood of reverting to NGR, whereas those who adhered to the metformin intervention had a 25% ARR of developing diabetes and an 11% greater absolute likelihood of reverting to NGR.

CONCLUSIONS:
Unlike our previous analyses that sought to explain population risk, these analyses evaluate individual risk. The models can be used by overweight and obese adults with fasting hyperglycemia and impaired glucose tolerance to facilitate personalized decision-making by allowing them to explicitly weigh the benefits and feasibility of the lifestyle and metformin interventions.

Table B.1: Use of Core Facilities - period December 2016 - July 2018

CORE: Clinical Core: Clinical Research Unit (CRU)

Determinations/Services Rendered

A. CRU@Domino's Farms
B. CRU@MEND Clinic
C. CRU@Kellogg Eye Center

Core User	Funded Project	Period of Core Use	A	B	C	Actual use and comments (Visits per month)
Barkan	Private Source	2/2016 - 08/2018		X		<1
Feldman	TINSAL R01-DK107956	12/2016 - 12/2017			X	5
Herman	EDIC U01-DK0945157	12/2016 - 08/2018			X	2
Herman	EDIC-Hypoglycemia U01-DK0945157	07/2017 - 08/2018			X	2
Herman	GRADE U01-DK098246	12/2016 - 08/2018	X			50
Herman	GRADE U01-DK098246	12/2016 - 08/2018			X	1
Oral	Private Source	08/2017 - 08/2018		X		1
Oral		12/2016 - 08/2018		X		<1
Oral		05/2018 - 08/2018		X		1
Pop-Busui		12/2016 - 08/2018		X		12
Pop-Busui		12/2016 - 08/2018		X		8
Pop-Busui	PERL UC4-DK101108	12/2016 - 08/2018		X		5
Pop-Busui	Private Source	02/2018 - 08/2018		X		2
Pop-Busui		11/2017 - 08/2018		X		4
Rothberg		04/2018 - 08/2018		X		4
Thomas	TRIALNet NCT00097292	12/2016 - 08/2018	X			1

* Non-member

Table B.2: Use of Core Facilities - period December 2016 - July 2018

CORE: Clinical Core - Diabetes Research Registry

Determinations/Services Rendered

Core User	Funded Project	Period of Core Use	Actual use and comments
Members			
Boehnke M/Burant C	NIH	12/2016	N=459 94 recruited for study
Boehnke M/ Burant C	NIH	01/2017	N=491 120 recruited for study
Zhang P	NIDDK	01/25/2017	N=1841
Boehnke M/ Burant C	NIH	02/2017	N=503 100 recruited for study
Simeone D	Private Source	02/08/2017	N=1072 females; N=1269 males
Tan M/Patel M	N/A	2/9/2017	
Boehnke M/ Burant C	NIH	03/2017	N=581 114 recruited for study
Boehnke M/ Burant C	NIH	04/2017	N=436 87 recruited for study
Boehnke M/ Burant C	NIH	05/2017	N=461 90 recruited for study
Boehnke M/ Burant C	NIH	06/2017	N=393 83 recruited for study
Boehnke M/ Burant C	NIH	07/2017	N=406 85 recruited for study
Ang L	Private Source	07/11/2017	N=622
Ojeda L		07/19/2017	N=345
Boehnke M/ Burant C	NIH	08/2017	N=313 79 recruited for study
Boehnke M/ Burant C	NIH	09/2017	N=385 52 recruited for study
Boehnke M/ Burant C	NIH	10/2017	N=130 22 recruited for study
Boehnke M/ Burant C	NIH	11/2017	N=180 38 recruited for study

Core User	Funded Project	Period of Core Use	Actual use and comments
Burant C & Tan MH	NIH	12/05/2017	N=2164 with known BMI.
Pop-Busui R	Private (external)	12/20/2017	N=569
Boehnke M/ Burant C	NIH	12/2018	N=137 23 recruited in study
Boehnke M/ Burant C	NIH	01/2018	N=330 88 recruited for study
Boehnke M/ Burant C	NIH	02/2018	N=285 60 recruited for study
Boehnke M/ Burant C	NIH	03/2018	N=495 81 recruited for study
Boehnke M / Burant C	NIH	04/2018	N=540 86 recruited for study
Boehnke M / Burant C	NIH	05/2018	N=560 102 recruited for study
Burant C	NIH	06/2018	N=397 80 recruited for study
Oral E/ Tan MH	NIH	06/03/2018	Total n = 4656 T1D = 1555 T2D = 3101
Burant C	NIH	07/2018	N=78 11 recruited for study

Non-Members

Table B.3: Use of Core Facilities - period December 2016 - July 2018

CORE: Chemistry Laboratory

Determinations/Services Rendered

A	ACTH
B	Adiponectin
C	1,5-Anhydroglucitol
D	Bile Acids
E	Cholesterol, Total
F	Cholesterol, HDL
G	Cholesterol, LDL
H	Corticosterone (mouse)
I	Cortisol
J	C-Peptide
K	C-Reactive Protein
L	Creatinine (serum or urine)

M	Cystatin C
N	DHEA-SO4
O	Free Fatty Acids
P	Fructosamine
Q	Ghrelin (total)
R	Glucagon
S	Glucose
T	Growth Hormone
U	Hemoglobin A1c (human)
V	Hemoglobin A1c (mouse)
W	IGF-1
X	IL-6

Y	Insulin (human)
Z	Insulin (rodent)
AA	ELISA - Multiplex Labor Charge
AB	Leptin
AC	Lipid Profile
AD	Microalbumin - Urine
AE	Parathyroid Hormone
AF	Pro-Insulin
AG	TNF-α
AH	Total Protein - Urine
AI	Triglycerides
AJ	Vitamin D, 25-Hydroxy

*** Non-member**

Core User	Funded Project	Period of Core Use	Services Requested + Samples Submitted																																	Total Actual Usage
			A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	
Akil, Huda	F039212	12/1/16 - 7/31/2018	1824								1824																		798										4446
Barkan, Ariel	N018876	12/1/16 - 7/31/2018																		319	319						319												957
Berent-Spillson	F041217	12/1/16 - 7/31/2018																			76		5				76				5								162
* Bridges, Dave	F045750	12/1/16 - 7/31/2018																			16						16				16								48
Brosius, Frank	C274070	12/1/16 - 7/31/2018																			22								38										60
Burant-Halter	G005310	12/1/16 - 7/31/2018										22								50	29						29												130
* Colacino, Justin	U045211	12/1/16 - 7/31/2018												31																									31
Cras-Meneur, Corentin	F041238	12/1/16 - 7/31/2018																										192											192
Dolinoy, Dana (K.Neier)	F034447	12/1/16 - 7/31/2018																											152										152
Ellingrod, Vicki	F043182	12/1/16 - 7/31/2018							42		61		30								42		44				42		38	12	42			89					442
Ferrario, Carrie	F040723	12/1/16 - 7/31/2018																											114										114
* Gheidi, Ali	F047524	12/1/16 - 7/31/2018																											76										76
* Gipson, Debbie	F042907	12/1/16 - 7/31/2018												966																						469			1435
Harlow, Sioban	F036649	12/1/16 - 7/31/2018																					203																203
Hassan, Rebecca	N017349	12/1/16 - 7/31/2018																			1498						1498												2996
Jackson, James	U057760	12/1/16 - 7/31/2018																													438								438
Kim, Catherine	F047759	12/1/16 - 7/31/2018												881	440																	441							1762
* Kirkpatrick (Ext. - KSU)	External PO	12/1/16 - 7/31/2018																			36							128											164
Kretzler, Matthias	C035484	12/1/16 - 7/31/2018													891																								891
Kretzler, Matthias	N020325	12/1/16 - 7/31/2018													891																								891
Kretzler, Matthias	N020343	12/1/16 - 7/31/2018													891																								891
Kretzler, Matthias	N023060	12/1/16 - 7/31/2018													891																								891
Kretzler, Matthias	F037374	12/1/16 - 7/31/2018												846																	846							1692
Kumasaramy (Ext. UT)	External PO	12/1/16 - 7/31/2018												27			56				27							56				56							222
Lecka-Cznernik (Ext. UT)	External PO	12/1/16 - 7/31/2018																										32											32

Core User	Funded Project	Period of Core Use	Services Requested + Samples Submitted																																		Total Actual Usage
			A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ	
Lee, Joyce	F036144	12/1/16 - 7/31/2018			273				180				286					126			2392		314				2392				180								6143
Lee, Pearl	F039731	12/1/16 - 7/31/2018																					14																14
Lumeng, Casey	F042208	12/1/16 - 7/31/2018																											190										190
MacDougald, Ormond	F040415	12/1/16 - 7/31/2018																											38										38
Mathew, Anna	F044337	12/1/16 - 7/31/2018																													99								99
* Meeker, John	F042878	12/1/16 - 7/31/2018														200																							200
* Meeker, John	F034444	12/1/16 - 7/31/2018														200																							200
* Muller, Martijn	F037963	12/1/16 - 7/31/2018									162		228	228		162					228								380		228							163	1779
Myers, Martin	F035632	12/1/16 - 7/31/2018																											456										456
Myers, Martin	F042854	12/1/16 - 7/31/2018																											76										76
Myers, Martin	N022567	12/1/16 - 7/31/2018								171																			570										741
Oral, Elif	G016875	12/1/16 - 7/31/2018																											38	99									137
Padmanabhan, Vasantha	F042884	12/1/16 - 7/31/2018																											152										152
Peterson, Karen	U025123	12/1/16 - 7/31/2018		200					200			200									200				200		200			200									1400
Peterson, Karen	F042881	12/1/16 - 7/31/2018		200					200			200									200				200		200			200									1400
* Rosania, Gustavo	N023621	12/1/16 - 7/31/2018																											38										38
* Schmidt, Thomas	F047244	12/1/16 - 7/31/2018																											38										38
* Schwendeman, Anna	N024429	12/1/16 - 7/31/2018																																			12		12
Seeley, Randy	N019965	12/1/16 - 7/31/2018															60														60								120
Seeley, Randy	F043505	12/1/16 - 7/31/2018																			18							18			18								54
Seeley, Randy	U045388	12/1/16 - 7/31/2018				44																									106								150
Seeley, Randy	N020050	12/1/16 - 7/31/2018																											76										76
Somers, Emily	F043795	12/1/16 - 7/31/2018												987																	99					495			1581
* Sutton, Nadia	G020912	12/1/16 - 7/31/2018																											38										38
* Swanson, Leslie	F039303	12/1/16 - 7/31/2018																											418										418
* Yung, Raymond	N020616	12/1/16 - 7/31/2018											100	100									100								100								400
* Zhang, Jifeng	F041827	12/1/16 - 7/31/2018							477																			18	38		477								1010
* Zhang, Jifeng (Oren Rom)	F038817	12/1/16 - 7/31/2018							75																				190		75								340
* Zick, Suzie	U018791	12/1/16 - 7/31/2018																											76										76

Table B.4. Biostatistical Services Use by MDRC Members

	User	Services	Grant/study Title	Grant #
*	Jaber, Linda	Design	Utilizing family support in Arabs for diabetes self-management	Not funded
	Lee, Joyce	Design and data analysis	Utilization, Costs, and Patient Out-of-Pocket Costs for Type 1 Diabetes in the Era of the High Deductible Health Plan	Pending
	Oral, Elif	Design and data analysis	A new paradigm for treatment of Type 2 diabetes: targeting the repression of energy expenditure	Pending
	Piatt, Gretchen	Design and data analysis	Ongoing Diabetes Self-Management Support in Church-Based Settings	5-R01-DK-104733-03
	Piatt, Gretchen	Data analysis	Cost-Effectiveness of Diabetes Self-Management Education and Support in the Community: Projections from a Randomized Controlled Trial	Manuscript in progress
	Pop-Busui, Rodica and Eva Feldman	Design and data analysis	Targeting Inflammation using Salsalate in Type 1 Diabetic Neuropathy (TINSAL-T1DN)	R03DK094499
*	Toby E. Jayaratne	Consulting on data analysis	Genetic Explanations for Type 2 Diabetes	None
	Sari Priesand and Mike Munson	Data analysis	Plantar Fasciitis in Patients with Type 1 and Type 2 Diabetes Mellitus: A Prevalence Study	Manuscript in process
*	Brian Schmidt	Data analysis	Role of Podiatry in Preventing Severe Diabetic Foot Complications	Manuscript submitted
	Meng Tan	Consultation	Meta-analysis using individual data	None
	Herman, William	Design and data analysis	Population health impact of a self-insured employer's policy change to cover weight reduction and diabetes prevention interventions for employees, dependents, and retirees with prediabetes	R01DK09513
	Herman, William	Design and data analysis	Diabetes Prevention Program Outcomes Study manuscript EOS109	George Washington University / S-DPP1415-JB04
	Herman, William	Design and data analysis	Glycemia Reduction Approaches in Diabetes:	George Washington University /

User	Services	Grant/study Title	Grant #
		A comparative effectiveness study (GRADE) – Economic Analysis Expansion	Private Source
Herman, William	Design and data analysis	Treatment for TIA to manage cardiovascular disease and diabetes in older adults	R21-AG-060277-01
Nathan Qi/Bill Herman	Design and power calculation		Pending
* Ariel Barkan	Design and analysis	Stimulation of sst-2 and sst-5 as pathophysiological mechanism(s) in hyperglycemia	
Matthew DiMagno	Analysis	Chronic Pancreatitis: Effect of Pioglitazone on Endocrine Function, Quality of Life and Exocrine Function & Structure	

*Non-members

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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Withheld pursuant to exemption

Budget ; Redacted by agreement

of the Freedom of Information and Privacy Act

A. COMPONENT COVER PAGE

Project Title: Microscopy Imaging and Cellular Physiology Core (MICPC)
Component Project Lead Information: Antonetti, David

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Microscopy Imaging and Cellular Physiology (MICP) Core provides members of the Michigan Diabetes Research Center access to state of the art microscopy imaging, in situ hybridization, and electrophysiologic (including optogenetics) analysis, along with expert analysis and support. For over 20 years, the MICPC has provided researchers use of confocal and wide-field microscopes to allow a wide array of cellular and tissue imaging techniques including; imaging of fixed tissues and cells, quantification, co-localization, and live cell imaging including FRET and FRAP experiments. We have now added in situ hybridization analysis with fluorescent or radioisotope or chromogenic substrates for localization and/or quantification of mRNA. The core also has also developed an electrophysiology laboratory that enables the analysis of electrical and ionic changes in neurons, islets, or other relevant tissues, including optogentic activation of these tissues. Core personnel provide extensive expertise in imaging, in situ hybridization and electrophysiology, enabling MDRC investigators to rapidly develop novel experimental ideas and obtain high quality results with expert analysis. Core personnel provide structured service, maintenance and expertise in imaging and cell physiology and related experiments to support diabetes research at Michigan

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 MICP Core.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: B.4 MICP Core.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The MICP Core has contributed to 49 publications in this reporting period.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The Microscopy, Imaging and Cellular Physiology Core (MICPC) provides state-of-the-art protein and RNA imaging and cell physiological analysis to enhance the diabetes-related research of members of the MDRC. We plan to continue our service with no changes to the initial goals.

B.2 What was accomplished under these goals?

The MICPC continues to support MDRC members with access to confocal microscopy and image analysis software and recently expanded the core to include services in the Cellular Physiology and *in situ* Hybridization Laboratories. The Core has been located in the Brehm Center for Diabetes Research since April 2010. The Diabetes Research Center continues a synergistic relationship with the Kellogg Eye Center Vision Core. Dr. Lentz supports both groups to maintain, train and educate investigators and staff on the use of the three confocal microscopes and image processing/analysis software that are available. The core is extensively used for microscopy and image analysis and contributes to a wide range of manuscripts addressing issues relating to diabetes and its complications. Further, the newly added core services in cellular physiology and *in situ* hybridization have been established and are providing services to a variety of investigators in the MDRC.

Research and Development in Microscopy: The core's Nikon A1 confocal was enhanced to support live cell microscopy by adding a wide field Photometrics 95B cMOS camera and Sutter motorized filter sets to collect a variety of fluores ent proteins/signals including Cyan Fluorescent Protein (CFP), Yellow Fluorescent Protein (YFP), Green Fluorescent Protein (GFP) and mCherry. A Nikon Elements Förster/Fluorescence Resonance Energy Transfer (FRET) module was also purchased and used to capture data of a Rho FRET-Biosensor, which was a vast improvement over using the confocal portion of the microscope to collect this type of data. Many MDRC investigators and the Imaging Laboratory Director have direct experience with live cell microscopy and the ability to capture wide-field images of live cells on our sophisticated Nikon system will greatly improve the core's capabilities to serve the needs of MDRC investigators. There are 10 MDRC members that would take advantage of this added technology including: Drs. Antonetti, Carter-Su, Feldman, MacDougald, Myers, Olson, Qi, Satin, Stuenkel, and Verhey.

Research and Development in Image Analysis The MICPC recently built a high-end Windows 10-64bit workstation that has a 16-core with 32 threads 3.4 GHz processor, 64-GB RAM, 8-GB graphics card and multiple solid state hard drives. The core also recently renewed licenses for several software packages to support image analysis, including Imaris v9.2.1 4D visualization/quantification, MetaMorph v7.10, Autoquant vX3 2D/3D deconvolution, and MATLAB vR2018b. These were done in collaborative support from the Vision Core. Image Analysis is the second most used service of the core and 60% of the core investigators used this service for almost 1000 hours over the 1.5 years. Many of these investigators use the Imaris 3D image analysis software to quantify their confocal images. There are 21 MDRC members that use image analysis in their studies including Drs. Abcouwer, Antonetti, Arvan, Carter-Su, Feldman, Fort, Goforth, Inoue, Kahana, Kennedy, Lentz, Low, MacDougald, Omary, Pennathur, Puro, Satin, Shtein, Stuenkel, Thompson, and Williams.

Surveys to Evaluate Core Services The last major survey of the whole MDRC membership was taken for the 2017 renewal which resulted in the expansion of the core to include cellular electrophysiology and ISH. Recently the Imaging Laboratory reached out to 19 principal investigators (12 MDRC and 7 Vision Core members) to generate an interest group for purchasing a Leica SP8 LSM with white light laser and super resolution capabilities. An informative seminar and demonstration is planned for the fall of 2018 with the goal to submit a shared instrument grant in 2019. The MICPC director, laboratory directors, and oversight committee regularly evaluate the Core's effectiveness and ability to meet the needs of MDRC investigators.

Papers Highlighting Scientific Advances Supported by the Core (center members are listed in Bold)

1) Ruebsam A, Dulle JE, Myers AM, Sakrikar D, Green KM, Khan NW, Schey K, **Fort PE**. A specific phosphorylation regulates the protective role of αA-crystallin in diabetes. JCI Insight. 2018 Feb 22;3(4). pii: 97919. doi: 10.1172/jci.insight.97919. [Epub ahead of print] PubMed PMID: 29467334; PubMed Central PMCID: PMC5916248.

A major focus of Dr. Fort's lab is the development of strategies to treat retinal neurodegeneration in diabetic retinopathy. One of Dr. Fort's objectives is to investigate the function and regulation of crystallin proteins in the adaptive responses of retinal cells during chronic disease states such as diabetes. This study focused on testing the hypothesis that α-crystallins play a key role in neuronal survival in the central nervous system, a role regulated by key posttranslational modifications that are affected by chronic neurodegenerative conditions. **Confocal microscopy and image analysis** was used to demonstrates that αA-crystallin is expressed in ganglion and Müller glial cells in diabetic patients and that phosphorylation of αA-crystallin regulates the neuroprotective function. This study unveils mechanisms that could be targeted for the treatment of DR and other neurodegenerative diseases as a means to promote neuronal survival.

2) Kim GH, Shi G, Somlo DR, Haataja L, Song S, Long Q, Nillni EA, **Low MJ**, **Arvan P**, **Myers MG Jr**, **Qi L**. Hypothalamic ER-associated degradation regulates POMC maturation, feeding, and age-associated obesity. J Clin Invest. 2018 Mar1;128(3):1125-1140. doi: 10.1172/JCI96420. Epub 2018 Feb 19. PubMed PMID: 29457782; PubMed Central PMCID: PMC5824855.

Dr. Qi's laboratory explores the physiological role of (a) endoplasmic reticulum (ER) homeostasis and (b) inflammatory responses in the context of metabolic disorders including obesity, type-1/-2 diabetes and inflammatory bowel disease. In this study, **confocal microscopy and image analysis was used** to study the ER protein complex formed between E3 ligase hydroxymethylglutaryl reductase degradation protein 1 (Hrd1) and its cofactor suppressor/enhancer of lin-like 1 (Sel1L) in POMC neurons. They report a role of Sel1L-Hrd1 ER-associated degradation in POMC neurons that is tightly linked to the mechanism underlying the conformational maturation of POMC within the ER. This study not only identifies ERAD as an important mechanism regulating POMC maturation within the ER, but also provides insights into the pathogenesis of monogenic obesity associated with defective prohormone folding.

Use of the Cellular Physiology component of the core has also been initiated including the following example.

3) Oginsky MF, **Goforth PB**, Nobile CW, Lopez-Santiago LF, **Ferrario CR**. Eating 'Junk-Food' Produces Rapid and Long-Lasting Increases in NAc CP-AMPA Receptors: Implications for Enhanced Cue-Induced Motivation and Food Addiction. Neuropsychopharmacology. 2016 Dec;41(13):2977-2986. doi: 10.1038/npp.2016.111. Epub 2016 Jul 7. PubMed PMID: 27383008; PubMed Central PMCID: PMC5101548.

Dr. Ferrario's laboratory examines alterations in hedonic reward pathways that lead to drug addiction and obesity. In this study, Dr. Ferrario demonstrates that a high fat/high sugar diet induces a specific form of plasticity in the nucleus accumbens, a crucial area for regulation of motivated behaviors. Using electrophysiologic analysis of individual NAc neurons, they reveal distinct changes in the subunit composition and function of the AMPA subtype of glutatmate receptors, which mediate excitatory neurotransmission. For these studies, the *MICP core executed electrophysiology experiments, assisted in the setup of electrophysiology in the Ferrario lab, and trained lab personnel in electrophysiology techniques.*

Additionally, use of the *in situ* hybridization component was also initiated with the following example.

4) Cady G, Landeryou T, Garratt M, Kopchick JJ, Qi N, Garcia-Galiano D, **Elias CF**, **Myers MG Jr**, Miller RA, **Sandoval DA**, **Sadagurski M.** Hypothalamic growth hormone receptor (GHR) controls hepatic glucose production in nutrient-sensing leptin receptor (LepRb) expressing neurons. Mol Metab. 2017 Mar 16;6(5):393-405. doi: 10.1016/j.molmet.2017.03.001. eCollection 2017 May. PubMed PMID: 28462074; PubMed Central PMCID: PMC5404104.

The core provided service for *in situ* hybridization to co-localize growth hormone receptor mRNA in LepRb neurons in the hypothalamus.

Number of Users The use table (see **Table B.2**) shows 28 MDRC members and 5 non-members used the Core over the last year. MDRC members account for 87% of the total hours. Confocal microscopy continues

to be the primary service used by core patrons with over 3000 hours, which includes live cell microscopy on the Nikon A1 system. Image analysis was also highly used as more users are taking advantage of access to sophisticated morphometric analysis software packages like Imaris and MetaMorph.

Table B.2: Use of Core Facilities - period December 2016 - July 2018

CORE: Microscopy Imaging and Cellular Physiology Core

Determinations/Services Rendered

A	Microscopy Imaging (confocal and widefield)
B	Image analysis and morphometry including deconvolution
C	Consultation and advice
D	Calcium imaging
E	Electrophysiology analysis (-/+ optogenetics)
F	ISH services

			Services Used					
			Imaging Lab		ALL	Cell Phys		ISH Lab
Core User	**Funded Project**	**Period of Core Use**	A	B	C	D	E	F
Members								
Abcouwer, SF	Private Source	12/16 - 07/18	206	23	11			
Antonetti, DA	NIH-5-R01EY012021-20 NIH-R01EY029349-01	12/16 - 07/18	449	150	30			
Arvan, PR	NIH-5-R01DK048280-25 NIH-5-R01DK040344-30 NIH-R01DK111174-03	12/16 - 07/18	120		6			
Carter-Su, C	NIH-2-R01DK054222-18 NIH-R01DK107730-03	12/16 - 07/18	51		3			
Cone, RD	NIH-R01DK070332-14	12/16 - 07/18			2		1	
Elias, CF	NIH-5R01HD069702-05	12/16 - 07/18					1	
Feldman, EL	NIH-1-R24DK082841-09 NIH-R01DK107956-03	12/16 - 07/18	536	409	47			
Ferrario, CR	5R01DK106188-02	12/16 - 07/18	5				1	
Flak, JN	NIH-K99DK109115-01	12/16 - 07/18						1
Fort, PE	NIH-5-R01EY020895-07	12/16 - 07/18	121	270	20			
Goforth, PB	NIH-sub of P30DK020572 (MDRC P&F)	12/16 - 07/18				1	1	
Harder, JL		12/16 - 07/18	2					
Lentz, SI	1DP3DK104386-01	12/16 - 07/18	120	90				
Liu, M	NIH-5-R01DK088856-05	12/16 - 07/18	153		8			
Low, MJ	NIH-5-R01DK068400-14	12/16 - 07/18	7					
MacDougald, OA	NIH-R01DK062876-14	12/16 - 07/18	196	1	10		1	
Moenter, SM	NIH-5R01HD041469-16	12/16 - 07/18						
Myers, MG	NIH-2-R37-DK056731-20	12/16 - 07/18	64		3		1	
Olson, DP	NIH-R01DK104999-03	12/16 - 07/18				1		
Pennathur, S	NIH-R24-DK082841-09	12/16 - 07/18	10		1			
Qi, L	NIH-R01DK105393-05 NIH-R01GM113188-05	12/16 - 07/18	822	4	41		1	
Rui, L	NIH-5-R01DK114220-02	12/16 - 07/18	2					
Sadagurski, M (Wayne State U)		12/16 - 07/18						5
Satin, LS	NIH- 2-R01DK046409-25	12/16 - 07/18	6					
Shah, YM	NIH-5-R01CA148828-09	12/16 - 07/18	5	1				
Soleimanpour, AS	NIH-R01DK108921-03	12/16 - 07/18	6					
Stuenkel, EL	NIH-R01-NS097498-03	12/16 - 07/18	33	15	2			
Verhey, KJ	NIH-R01GM116204-04	12/16 - 07/18	10		1			
Members TOTAL hrs (A-C) or number of projects (D-F)			**2924**	**963**	**185**	**2**	**7**	**6**

			Services Used					
			Imaging Lab		ALL	Cell Phys		ISH Lab
Core User	**Funded Project**	**Period of Core Use**	A	B	C	D	E	F
Non-members								
Berglund, E (UTSW Dallas)	NIH-5-R01DK109408-03	01/18 - 04/18						2
El-Zaatari, M		12/16 - 07/18	29	10	2			
Fisher, GJ	NIH-R01AG051849-03 1R01AG051849-01A1	12/16 - 07/18	3					
Kao, JY	NIH-R01DK117565-01	12/16 - 07/18	10		1			
Omary, MB	NIH-5-R01-DK047918	12/16 - 07/18	136	297	22			
Non-member TOTAL hrs (A-C) or number of projects (D-F)			**178**	**307**	**25**	**0**	**0**	**2**
Member and Non-member TOTAL hrs (A-C) or number of projects (D-F)			**3102**	**1270**	**210**	**2**	**7**	**8**

B.4 What opportunities for training and professional development has the project provided?

Fifty-six new laboratory personnel were trained on the Core's confocal microscopes, including graduate students, postdoctoral fellows, residents, technicians and undergraduate students. Many of these individuals were also trained to use the core's image analysis software to measure morphological features in their images. About 15% of the new users were trained to do live cell imaging or how to use the Nikon A1 system for large format imaging using the automated XYZ stage and Elements software.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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of the Freedom of Information and Privacy Act

A. COMPONENT COVER PAGE

Project Title: Molecular Genetics Core (MGC)
Component Project Lead Information: OLSON, DAVID P

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

Given the value of model organisms and molecular genetic tools for the study of diabetes and its co-morbidities, the Molecular Genetics Core (MGC) is designed to aid diabetes researchers in the development of novel rodent models and molecular tools to determine the cellular and molecular mechanisms contributing to diabetes. Established in 2015, the MGC is a fee-for-service core that facilitates the application of molecular genetic methods to diabetes-related research. Specifically, the MGC (1) designs and produces genetically-modified rodent models (using CRISPR/Cas9) for use in diabetes-related research; (2) designs and produces AAV vectors for use in diabetes research; (3) produces and provides specialty viral reagents for use in diabetes research; and (4) provides advice and training in the use of these technologies to members of MDRC laboratories. The MG Core also owns and maintains several pieces of shared equipment for the use of MDRC members located at different sites around the UM medical campus.

While CRISPR/Cas9 technology has dramatically increased the speed and decreased the cost at which such models can be generated, the pace at which this new technology continues to evolve prevents many diabetes researchers from taking full advantage of its potential. The MGC fills this gap by using its expertise and personnel to design and construct CRISPR/Cas9 targeting reagents, collaborate with the UM Transgenic Core to test these reagents in embryos and produce founder mice, and identify founders for transfer (along with genotyping protocols) to the MDRC investigator. For the generation of viral reagents, the MGC designs and produces any necessary constructs, which are packaged into viruses by the UM Viral Vector Core. With input from MDRC members and the MGC advisory committee, the MGC also identifies and develops new technologies (viral and genetic) in support of the research programs of MDRC members.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 MG Core.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: B.4 Opportunities MG Core.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

Transgenic models or viral tools generated by the MGC will be described to the scientific community by the principal investigative team on each project. The MGC takes advantage of the annual MDRC symposium to highlight a recent project of interest in an effort to both advertise its services and make members aware of its capacities.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

The major goals of the molecular genetics core have not changed since the initial competing award. The Molecular Genetics Core will continue to support the generation of viral vectors and rodent models for diabetes research. In addition, it also supports the education and training of researchers interested in hands-on learning related to gene editing.

B.2 What was accomplished under these goals?

Research and development in the Molecular Genetics Core

The core has switched its targeting strategy from plasmid-based targeting vectors/constructs to direct injection of commercially available Cas9 protein and synthetic guide RNAs. The use of Cas9 protein and synthetic guides has improved the efficiency of gene targeting. In addition, we are using single stranded DNA templates as exchange cassettes. Use of single stranded DNA has also been shown to increase the efficiency of targeting and many single stranded DNAs can be purchased commercially which streamlines core services. For targeting templates that exceed the size of commercially available synthesis platforms, the Core is working to establish the molecular techniques needed to generate large single stranded DNA on site. The MDRC has supported the development of adeno-associated viruses in the UM Viral Vector core. In conjunction with the MGC, the Viral Vector core is now able to generate AAVs with a broad range of serotypes useful for diabetes researches. In addition, the Vector core produces standard monosynaptic rabies tracing viruses and has recently produced a “self-inactivating” rabies that labels synaptically connected cells without cell injury.

Surveys to evaluate core services

Surveys of MDRC core users are conducted at regular intervals and members’ responses are used to guide changes that improve MGC services for its members. The last survey was done prior to renewal of the grant.

Publications using core services

The following publications exemplify progress made during the current funding period (center members listed in Bold):

1. Bodur C, Kazyken D, Huang K, Ekim Ustunel B, Siroky KA, Tooley AS, Gonzalez IE, Foley DH, Acosta-Jaquez HA, Barnes TM, Steinl GK, Cho KW, **Lumeng CN**, Riddle SM, **Myers MG Jr, Fingar DC**. *The IKK-related kinase TBK1 activates mTORC1 directly in response to growth factors and innate immune agonists.* EMBO J. 2018 Jan 4;37(1):19-38. doi: 10.15252/embj.201696164. Epub 2017 Nov 17. PubMed PMID: 29150432; PubMed Central PMCID: PMC5753041

This study examines the role of the innate immune kinase TBK1 initiates inflammatory responses to infectious pathogens, metabolic processes and cell proliferation and survival. It demonstrates that TBK1 activates mTOR complex 1 (mTORC1) directly through site-specific mTOR phosphorylation (on S2159) in response to certain growth factor receptors and pathogen recognition receptors (i.e., TLR3; TLR4) thereby revealing a stimulus-selective role for TBK1 in mTORC1 regulation. Using genome edited mTOR S2159A knock-in mice generated with the help of the Molecular Genetics core, it was found that mTOR S2159 phosphorylation promotes mTORC1 signaling, IRF3 nuclear translocation, and IFN-β production. These data demonstrate a direct mechanistic link between TBK1 and mTORC1 function as well as physiologic significance of the TBK1-mTORC1 axis in control of innate immune function. These data unveil TBK1 as a direct mTORC1 activator and suggest unanticipated roles for mTORC1 downstream of TBK1 in control of innate immunity, tumorigenesis, and disorders linked to chronic inflammation such as obesity and insulin resistance.

2. Woodworth HL, Beekly BG, Batchelor HM, Bugescu R, Perez-Bonilla P, Schroeder LE, **Leinninger GM**. *Lateral Hypothalamic Neurotensin Neurons Orchestrate Dual Weight Loss Behaviors via Distinct Mechanisms*. Cell Rep. 2017 Dec 12;21(11):3116-3128. doi: 10.1016/j.celrep.2017.11.068. PubMed PMID: 29241540; PubMed Central PMCID: PMC5734099.

The central mechanism by which neurotensin potentiates weight loss is unknown. Dr. Leinninger’s group leveraged chemogenetics to reveal that neurotensin-expressing neurons of the lateral hypothalamic area (LHA) promote weight loss in mice by increasing volitional activity and restraining food intake. These dual weight loss behaviors are mediated by distinct signaling pathways as neurotensin action was shown to be essential for the anorectic effect of the LHA circuit, but not for regulation of locomotor or drinking behavior. Furthermore, although LHA neurotensin neurons cannot reduce intake of freely available obesogenic foods, they effectively restrain motivated feeding in hungry, weight-restricted animals. The authors propose that enhanced action via LHA neurotensin neurons may represent a potential strategy to suppress the increased appetitive drive that occurs after weight loss and prevent weight regain.

3. Rupp AC, Allison MB, Jones JC, Patterson CM, Faber CL, Bozadjieva N, Heisler LK, **Seeley RJ, Olson DP, Myers MG Jr**. *Specific subpopulations of hypothalamic leptin receptor-expressing neurons mediate the effects of early developmental leptin receptor deletion on energy balance.* Mol Metab. 2018 Jun 6. pii: S2212-

8778(18)30432-0. doi: 10.1016/j.molmet.2018.06.001. [Epub ahead of print] PubMed PMID: 29914853. PMCID:PMC6034096

Early developmental ablation of leptin receptor (LepRb) expression from small, circumscribed populations of hypothalamic neurons has only minimally effects on energy balance. In contrast, removal of LepRb from large populations (expressing *vGat* or *Nos1*) across multiple hypothalamic regions results in profound obesity and metabolic dysfunction. This group tested the notion that it is the total number of leptin-responsive hypothalamic neurons rather than specific subsets of defined cell types that determine overall leptin-mediated energy balance. Using new mouse lines deleted for LepRb in growth hormone releasing hormone neurons (confined to the arcuate nucleus) or in serotonin 2C receptor expressing neurons (representing roughly half of all hypothalamic LepRb neurons, distributed across many nuclei), this study compared the phenotypes of these mice to previously-reported models lacking LepRb in defined cell populations. These comparisons revealed that the obesity phenotype that results from early developmental LepRb deficiency depends not simply upon the total number of leptin-responsive hypothalamic LepRb cells, but rather that specific populations of LepRb neurons must play particularly important roles in body energy homeostasis.

Number of Users

Please see attached **Table B.2** regarding “Use of Core Facilities”. The number of users included 18 MDRC members and 7 non-members. The 15 MDRC members represent ~80% of the total projects processed by the Molecular Genetics Core. Of note, non-MDRC members are external clients in diabetes research who do not have on-site access to gene editing technology.

Table B.2: Use of Core Facilities - period December 2016 - July 2018

CORE: Molecular Genetics Core

Determinations/Services Rendered

A	CRISPR editing/knockout (mouse model)
B	CRISPR conditional allele (mouse model)
C	CRISPR knockin allele (mouse model)
D	AAV design and construction
E	Rabies tracing system
F	Consultation
G	Training

Core User	Funded Project	Period of Core Use	A	B	C	D	E	F	G	Actual use and comments
COMPLETED										
Bernal-Mizrachi	DK073716;DK084236	2015-2016	X					X		1 KO
Fingar	DK100722;DK103877	2015-2016	X					X	X	2 edits
Elias	HD69702	2016				X		X		1 AAV
Hu	AG041177	2016	X	X				X		1 KO, 1 flox
Goforth	Private Source DK078056	2016			X			X		1 knockin
Low	DK066604	2016				X	X	X		2 AAV
MacDougald	DK092759;DK62876	2015-2017		X	X			X	X	1 knockin, 1 flox
Moenter	HD041469	2016-2017				X	X	X	X	2 AAV
Myers	DK056731	2015-2017	X	X	X	X	X	X	X	6 edits, 1 flox, 1 knockin, 2 AAV
Olson	DK104999	2016-2017		X		X	X		X	1 flox, 1 AAV
Sandoval	DK107282	2016-2017	X	X				X		1 KO, 1 flox
Seeley	DK093848;DK107652	2016-2017	X	X				X		1 KO, 1 flox
Wu	DK107583	2016-2017	X	X				X		1 flox
* Stein (Vanderbilt)	DK090570	2016-2017						X		1 edit
* Schwartz (UW)	R01 DK101997	2016		X			X	X		1 flox
Burant	DK099034	2016-2018		X			X	X		1 flox
Olson	DK104999	2016-2019			X		X		X	2 knockin
Low	DK066604	2016-2020		X		X	X	X		1 flox, 1 AAV
MacDougald	RO1 DK095705	2017			X	X	X	X	X	2 knockins, 2 AAV
Myers	DK056731	2016-present	X	X				X	X	4 edits, 3 flox

	Core User	Funded Project	Period of Core Use	A	B	C	D	E	F	G	Actual use and comments
	Sadagurski (WSU)	MDRC P&F	2016-present			X			X		1 knockin
*	Zeltser (Columbia)	Private Source	2017-present			X			X		1 knockin
*	Kim (Stanford)	DK104211	2016-present	X		X			X		2 knockins
*	Campbell (Duke)		2016-present			X			X		1 knockin
*	De Kloet (UFla)		2016-present			X			X		2 knockins
	Olson	DK104999	2017-July, 2018			X			X		1 knockin
	Myers	Private Source	2017-July, 2018			X			X		2 knockins
	Liangyou Rui		2017-July, 2018			X			X		4 knockins
	Carter-Su	DK54222	2017-July, 2018	x	x				X		1knockin, 1edit
	Myers	Private Source	2017-July, 2018	x	x				X		1knockin, 1edit
	Myers		2017-July, 2018			X			X		1knockin, 1edit
	Myers/Seeley		2017-July, 2018			X			X		1 knockins
	Myers		2017-July, 2018			X			X		1 knockins
	Flak	DK020572	2017-July, 2018			X			X		1 knockins
	TOTALS (Completed):			**12**	**13**	**17**	**7**	**9**	**33**	**9**	

IN PROCESS

*	Cohen (Rockefeller)		2016-present			x			x		1 knockin
	Myers	Private Source	July, 2018-present			X			X		1 knockin
	Seeley		July, 2018-present			X			X		1knockin - Rat
	Olson		July, 2018-present			X			X		1 knockin
	Myers	DK056731	July, 2018-present				x		X		AAV
	TOTALS (In process):			**4**	**6**	**12**	**3**	**10**	**4**	**3**	

* Non-member

B.4 What opportunities for training and professional development has the project provided?
The MGC continues to offer the opportunity to train members and their trainees in the design, development and production of transgenic tools for diabetes research. Several trainees from MDRC member laboratories have met and worked with the MGC team to design and build targeting vectors for the generation of transgenic mice. The Core director has met with multiple MDRC members and their trainees to discuss in detail the design strategy, pitfalls and alternative options for model design. After production and transfer of transgenic models, the MGC remains available to investigators to troubleshoot issues that arise regarding genotyping and characterization of the genetic modifications generated for each project.

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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A. COMPONENT COVER PAGE

Project Title: Enrichment Program
Component Project Lead Information: CARTER-SU, CHRISTIN

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Enrichment Program of the Michigan Diabetes Research Center (MDRC) promotes scientific interchange and collaboration among investigators from diverse backgrounds and disciplines to accelerate
the pace of research relevant to diabetes, its complications, and related endocrine and metabolic disorders. The program organizes scientific symposia, diabetes grand rounds, research and clinical conferences, visiting professorships, and research clubs for MDRC members, their lab, and others interested in diabetes research. The Enrichment program also organizes training programs for postdoctoral fellows, medical fellows, graduate students, medical students, and undergraduate students. The goal of the MDRC Enrichment Program is to enlarge, enlighten, and energize the Center's most important asset, its research base, and to make the MDRC a catalyst for diabetes research at the University of Michigan, regionally, nationally and internationally.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Enrichment Program.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

File uploaded: B4 Enrichment_Opportunities 2016-2018.pdf

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

The research clubs, seminars and symposia are advertised on the MDRC website and via email to a comprehensive email list of MDRC members and other individuals who might be interested in the topic. Physical announcements are posted throughout the medical school and relevant professional schools and departments. Books containing abstracts of all posters are prepared and distributed to participants at the symposia.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

We plan to continue organizing our 5 research clubs, faculty and trainee targeted seminar series, and annual symposium. Jean Schaffer, MD from Washington University School of Medicine has agreed to be our keynote speaker at our annual symposium in 2019. We are also co-sponsoring a substantial number of diabetes-related seminar speakers with the basic science departments and the MEND division and will continue to co-sponsor the Midwest Islet Club (MIC).

B.2 What was accomplished under these goals?

Significant Accomplishments for the Enrichment Core
MDRC Sponsored Seminars and Symposia

Dr. Christin Carter-Su coordinated the MDRC Annual Diabetes Symposium in March, 2017 and March, 2018 (**Table A.1**). The Symposia presentations were followed by poster sessions. In 2017, 127 people were in attendance and 55 posters were presented. In 2018, 163 people were in attendance and 61 posters were presented.

As part of its enrichment and training program, the MDRC continued to organize and support five Research Clubs. The Cellular Aspects of Diabetes, Obesity & Metabolism Research Club is co-sponsored by the Michigan Nutrition and Obesity Research Center (MNORC) and the Department of Molecular and Integrative Physiology (MIP) (**Table A.2**). Attendance averages ~ 30 faculty, students, fellows and staff. The Integrative Aspects of Diabetes, Obesity & Metabolism Research Club is also co-sponsored by the Michigan Nutrition and Obesity Research Center (MNORC) and the Department of Molecular and Integrative Physiology (MIP) (**Table A.3**). An average of ~ 15 faculty, students, staff, and fellows attend each meeting. The Neuroendocrine Control of Metabolism Research Club is similarly co-sponsored by the Michigan Nutrition and Obesity Research Center (MNORC) and the Department of Molecular and Integrative Physiology (MIP) (**Table A.4**). Average attendance is ~ 30 attendees. The other two research clubs organized and supported by the MDRC are the Islet Research Club (**Table A.5**) and the Complications of Diabetes Research Club (**Table A.6**). The Complications of Diabetes Research Club is co-sponsored by the Department of Ophthalmology. The MDRC also sponsored the Multidisciplinary Training Program in Basic Diabetes Research Summer Seminar Series (**Table A.7**). This series is attended by students participating in the summer Medical Student Research Program (MSRP) in Diabetes and Obesity, which supported 9 students in the summer of 2017 and 9 students in the summer of 2018 (**Table A.8**). The MDRC also continues to co-sponsor speakers within the seminar series of the Department of Molecular and Integrative Physiology (**Table A.9**) and support diabetes-related research and clinical conferences within the Division of Metabolism, Endocrinology, and Diabetes (MEND). **Tables A.10 and A.11** list Diabetes-Related Endocrine Research Conferences and Clinical Conferences, respectively. In 2017 and 2018, the MDRC co-sponsored the First and Second Annual Brehm Summer Diabetes Symposium (**Table A.12**).

The MDRC was a sponsor of the 10th and 11th Annual Mid-West Islet Club meetings. The meetings were held May 24-25, 2017, at the University of Wisconsin, Madison, Wisconsin, and May 14-15, 2018, at Washington University School of Medicine, St. Louis, Missouri.

Table A.1. Enrichment: Activities Enhancing Diabetes Education and Training
2017 and 2018 MDRC Annual Diabetes Symposia and Kroc Lectureship

Saturday, March 18, 2017
Kellogg Eye Center Auditorium, 1000 Wall Street, Ann Arbor, Michigan

Kroc Lecturer: Mitchell A. Lazar, MD, PhD
Willard and Rhoda Ware Professor in Diabetes and Metabolic Diseases
Director, Institute for Diabetes, Obesity and Metabolism
Chief, Division of Endocrinology, Diabetes and Metabolism
University of Pennsylvania
Genes, environment, and the transcriptional regulation of metabolism

Ken Inoki, MD, PhD
Associate Professor, Molecular & Integrative Physiology and Internal Medicine
Research Associate Professor and Biological Sciences Scholars Program Scholar, Life Sciences Institute
University of Michigan
Role of mTOR signaling in the development of diabetic nephropathy

Gina M. Leinninger, PhD
Assistant Professor, Physiology
Michigan State University
Neurotensin neurons promote weight loss behaviors

Elizabeth K. Speliotes, MD, PhD, MPH
Associate Professor, Internal Medicine and Computational Medicine & Bioinformatics
University of Michigan
Human genetics studies identify new causes of obesity and non-alcoholic fatty liver disease

Saturday, March 10, 2018
Kellogg Eye Center Auditorium, 1000 Wall Street, Ann Arbor, Michigan

Kroc Lecturer: Ruth Loos, PhD
Professor, Preventive Medicine
Director, Genetics of Obesity and Related Metabolic Traits Program
Charles Bronfman Institute of Personalized Medicine
Icahn School of Medicine at Mt. Sinai
The genetics of obesity – What have we learned from 10 years of Genome-wide Association Studies?

Xuequn Chen, PhD
Associate Professor, Physiology
Wayne State University
Regulation of beta cell endoplasmic reticulum homeostasis and COPII-dependent endoplasmic reticulum export in health and diabetes

Katherine A. Gallagher, MD
John R. Pfeifer Collegiate Professor of Vascular Surgery
Associate Professor, Surgery
University of Michigan
Epigenetics influence chronic inflammation in diabetic wounds

David Olson, MD, PhD
Associate Professor, Pediatrics and Communicable Diseases
University of Michigan
Hypothalamic control of energy balance and metabolism

Randy J. Seeley, PhD
Henry King Ransom Professor of Surgery
Professor, Surgery and Internal Medicine
Professor, Nutritional Sciences, School of Public Health
Director, Michigan Nutrition Obesity Research Center
University of Michigan
Identifying the molecular mechanisms that mediate the effects of bariatric surgery on obesity and diabetes

Table A.2. Enrichment: Activities Enhancing Diabetes Education and Training
Cellular Aspects of Diabetes, Obesity and Metabolism Research Club, December 2016 – July 2018

DATE	LABORATORY	SPEAKER	TITLE
December 13, 2016	Ling Qi, PhD	Yewei Ji, PhD Zhangsen Zhou, PhD	Toll-like receptors 2 and 4 signaling controls diet-induced proliferation of pancreatic β cells Sel1L in brown adipocytes regulates mitochondrial function and thermogenesis
February 14, 2017	Diane Fingar, PhD	Diane Fingar, PhD	AMPK activates mTORC2 to promote cell survival during acute metabolic stress
March 14, 2017	Liangyou Rui, PhD	Lin Jiang, PhD Yan Liu, PhD	Adipose snail1 regulates adipose tissue-liver crosstalk Hepatic slug couples metabolic signals to epigenetic reprogramming of liver metabolic pathways
April 11, 2017	Jun Hee Lee, PhD	Allison Ho Chun-Seok Cho, PhD	Sestrin2 is critical for hepatic glucose homeostasis Lipotoxicity induces hepatic protein inclusions through TBK1-mediated p62/SQSTM1 phosphorylation
May 9, 2017	Dave Bridges, PhD	Dave Bridges, PhD Innocence Harvey	Role of muscle mTORC1 in energy expenditure The effects of elevated glucocorticoids on metabolic outcomes in obesity
September 5, 2017	Tae-Hwa Chun, MD, PhD	Eric Buras, MD, PhD	Fibro-adipogenic remodeling of the obese diaphragm
October 3, 2017	Jun Wu, PhD	Margo Emont	Cinnamaldehyde induces fat cell-autonomous thermogenesis and metabolic reprogramming
November 7, 2017	Jiandie Lin, PhD	Liang Guo, PhD	Hepatic neuregulin 4 signaling defines an endocrine checkpoint for steatosis-to-NASH progression
December 5, 2017	Yatrik Shah, PhD	Sadeesh Kumar Ramakrishnan, PhD	Role of hypoxia signaling in hepatic metabolic homeostasis
February 6, 2018	Jun Hee Lee, PhD	Chun-Seok Cho, PhD Allison Ho	Lipotoxicity induces hepatic protein inclusions through TBK1-mediated p62/SQSTM1 phosphorylation Defining the Sestrin2-AKT signaling pathway, a novel mechanism in the insulin signaling network
March 6, 2018	Ormond MacDougald, PhD	Ziru Li, PhD Hiroyuki Mori, MD, PhD	Does granulocyte-colony stimulating factor mediate vertical sleeve gastrectomy-induced loss of bone and marrow adipose? Temperature regulation of lipid metabolism in adipocytes
April 3, 2018	Lei Yin, PhD	Xin (Tony) Tong, MD, PhD Deqiang Zhang, PhD	A hepatic CRY for degradation in FOXO1-driven gluconeogenesis The protective role of circadian protein BMAL1 in alcohol liver disease

May 1, 2018	Martin Myers, MD, PhD	Tammy Barnes, PhD	Leptin receptor signaling and the control of mammalian physiology

Table A.3. Enrichment: Activities Enhancing Diabetes Education and Training
Integrative Aspects of Diabetes, Obesity and Metabolism Research Club, December 2016 – July 2018

DATE	LABORATORY	SPEAKER	TITLE
January 17, 2017	David Olson, MD, PhD	Hongjuan Pei, PhD Ian Gonzalez, PhD	Mc3R-expressing neurons in the lateral hypothalamus regulate energy balance Central control of metabolism by neurons expressing calcitonin receptors
February 21, 2017	Monica Dus, PhD	Monica Dus, PhD	Persistent reprogramming of behavior by diet
March 21, 2017	Malcolm Low, MD, PhD	Graham Jones	The impact of POMC, hyperleptinemia, and body weight set-point in motivated behavior
April 18, 2017	Kanakadurga Singer, MD	Kanakadurga Singer, MD	Sex differences in myeloid inflammatory responses to diet-induced obesity
May 16, 2017	Elif Oral, MD	Nevin Ajluni, MD Rasimcan Meral	Leptin for the treatment of NASH in lipodystrophy; what have we learned? Amlexanox for the treatment of diabetes in humans: early translational studies
June 20, 2017	Ling Qi, PhD	Neha Shrestha, PhD Zhangsen Zhou, PhD	Novel role of ER associated degradation in pancreatic beta cells Sel1L regulates mitochondrial function and thermogenesis in brown adipocytes
September 21, 2017	James Granneman, PhD (Wayne State University)	James Granneman, PhD (Wayne State University)	Deconstructing adipogenic niches in vivo
October 19, 2017	Peter Mancuso, PhD	Peter Mancuso, PhD	The impact of obesity on pulmonary host defense against Klebsiella pneumonia
November 16, 2017	Gregory Cartee, PhD	Mark Pataky Haiyan Wang Amy Zheng	Fiber type-selective effects of a high fat diet and acute exercise on muscle glucose uptake Fiber type-selective effects of acute exercise on key signaling proteins in skeletal muscle Genetic approaches to assess the role of AS160/TBC1D4 in glucose uptake by rat skeletal muscle
December 21, 2017	Liangyou Rui, PhD	Lin Jiang, PhD Yan Liu, PhD	Regulation of energy balance and body weight by neuronal slug Epigenetic regulation of liver lipid metabolism by hepatic snail1
January 18, 2018	Charles Burant, MD, PhD	Charles Evans, PhD Jennifer LaBarre, MPH, RD	Using 'omics science to identify molecular signals that contribute to the health benefits of exercise Sex specific metabolites predicting weight trajectory in adolescents

February 15, 2018	Beata Lecka-Czernik, PhD (University of Toledo)	Beata Lecka-Czernik, PhD (University of Toledo)	Diabetic bone disease: Clinical evidence and basic research implications
March 15, 2018	Darleen Sandoval, PhD	Chelsea Hutch, PhD Ki-Suk Kim, PhD	The impact of biological sex The role of preproglucagon peptides
April 19, 2018	Vasantha Padmanabhan, MS, PhD	Vasantha Padmanabhan, MS, PhD	Developmental programming of insulin resistance in female sheep: Is androgen the culprit?
May 17, 2018	Laura McCabe, PhD (Michigan State University)	Naiomy Rios-Arce, Jonathan Schepper, & Ho Jun Kang (Michigan State University)	Mechanisms and therapeutic targets of diabetic and glucocorticoid induced osteoporosis

Table A.4. Enrichment: Activities Enhancing Diabetes Education and Training
Neuroendocrine Control of Metabolism Research Club, August 2017 – July 2018

DATE	LABORATORY	SPEAKER	TITLE
September 6, 2017	Darleen Sandoval, PhD	Chelsea Hutch, PhD	Using preclinical models to determine mechanisms underlying successful metabolic therapies
September 28, 2017	Sebastien Bouret, PhD (University of Southern California)	Sebastien Bouret, PhD (University of Southern California)	Neurodevelopmental origins of obesity and diabetes
October 4, 2017	David Olson, MD, PhD	Ian Gonzalez	CalcR neurons of the paraventricular nucleus of the hypothalamus and the regulation of energy homeostasis
November 1, 2017	Marianna Sadagurski, PhD (Wayne State University)	Marianna Sadagurski, PhD (Wayne State University)	Role of metabolic reprogramming in hypothalamic inflammation and aging
December 6, 2017	Liangyou Rui, PhD	Liangyou Rui, PhD	Regulation of energy intake and expenditure by distinct Sh2b1 circuits
January 10, 2018	Martin Myers, MD, PhD	Alan Rupp, PhD	Identifying novel LepRb hypothalamic subpopulations regulating energy balance
February 7, 2018	Alex Johnson, PhD (Michigan State University)	Alex Johnson, PhD (Michigan State University)	Neuropeptide modulation of learned appetitive behavior
March 7, 2018	Carrie Ferrario, PhD	Carrie Ferrario, PhD	Neural and behavioral differences in obesity-prone and obesity-resistant rats
April 4, 2018	Randy Seeley, PhD	Henriette Frikke-Schmidt, PhD	GDF15. A biomarker of death or a new therapy for obesity?
May 2, 2018	Stephen Liberles, PhD (Harvard University)	Stephen Liberles, PhD (Harvard University)	Internal and external sensory systems
June 6, 2018	Malcolm Low, MD, PhD	Hui Yu, PhD	The role of POMC neurons in regulating circulating adipokines
July 11, 2018	Carol Elias, PhD	Alexandra Cara	Role of androgen receptor in central regulation of metabolism and reproduction

Table A.5. Enrichment: Activities Enhancing Diabetes Education and Training
Islet Research Club, August 2017 – July 2018

DATE	LABORATORY	SPEAKER	TITLE
September 5, 2017	Brigid Gregg, MD	Brigid Gregg, MD	Prenatal and neonatal islet programming
October 3, 2017	Santiago Schnell, DPhil (Oxon), FRSC	Santiago Schnell, Dphil (Oxon), FRSC	Mathematical modeling of the unfolded protein response
November 7, 2017	Ling Qi, PhD	Ling Qi, PhD	ERAD deficiency in pancreatic beta cells
December 5, 2017	Corentin Cras-Meneur, PhD	Corentin Cras-Meneur, PhD	Live imaging of insulin secretion: GLP-1 and islets in development and in the adult
January 9, 2018	Les Satin, PhD	Xiaoqing Tang, PhD	The role of microRNAs in pancreatic beta cells
February 6, 2018	Scott Soleimanpour, MD	Vaibhav Sidarala, PhD Gemma Pearson, PhD	Mitochondrial quality control in response to toxic beta cell stressors
March 6, 2018	Ming Liu, MD, PhD	Xin Li, PhD	Role of TRAP alpha in insulin biosynthesis
April 3, 2018	Jeffery Tessem, PhD (Brigham Young University)	Jeffery Tessem, PhD (Brigham Young University)	The Role of Nr4a family members in beta cell proliferation and function
May 1, 2018	Darleen Sandoval, PhD	Darleen Sandoval, PhD	The role of preproglucagon peptides in islet mass and function
June 5, 2018	Xuequn Chen, PhD (Wayne State University)	Xuequn Chen, PhD (Wayne State University)	Recent insights from islet proteomic and lipidomic studies
July 3, 2018 Journal Club	Scott Soleimanpour, MD Mehboob Hussain, MD Peter Arvan, MD, PhD	Scott Soleimanpour, MD Mehboob Hussain, MD Peter Arvan, MD, PhD	Mitochondria-ER communication in beta cells Alpha cell Fam20C and Ero1alpha in the secretory pathway

Table A.6. Enrichment: Activities Enhancing Diabetes Education and Training
Complications of Diabetes Research Club, December 2016 – July 2018

DATE	SPEAKER/LAB	TITLE
January 12, 2017	Thomas Gardner, MD, MS	Senescence-associated secretory phenotype contributes to pathological angiogenesis in retinopathy
March 9, 2017	Steven Abcouwer, PhD	Effect of mTORC1 deficiency on retinal development
April 13, 2017	Eva Feldman, MD, PhD	Saturated fatty acids alter mitochondrial trafficking in sensory neurons
May 18, 2017	David A. Antonetti	Rap activation in prevention and restoration of the blood retinal barrier
October 12, 2017	Jeffrey Hodgin, MD, PhD	Identification of cross-species shared transcriptional networks of diabetic nephropathy in human and mouse glomeruli
November 16, 2017	Patrice Fort, PhD, MS	Intrinsic protective mechanisms and their roles in diabetic retinopathy
January 11, 2017	Steven Abcouwer, PhD	Role of mTORC1 in retinal development
February 8, 2018	Eva Feldman, MD, PhD	Metabolic reprogramming: the crux of diabetic neuropathy?
April 12, 2018	David A. Antonetti, PhD	Identification of mfsd7c as a possible novel regulator of blood-retinal barrier formation/restoration
June 14, 2018	Jeffrey Hodgin, MD, PhD	Mutations in SGPL1 (SPL) as a cause of steroid-resistant nephrotic syndrome and focal segmental glomerulosclerosis

Table A.7. Enrichment: Activities Enhancing Diabetes Education and Training Multidisciplinary Training Program in Basic Diabetes Research Summer Seminar Series, December 2016 – July 2018

DATE	SPEAKER	TITLE
July 14, 2017	William Rainey, PhD Jerome W. Conn Collegiate Professor Professor, Molecular & Integrative Physiology and Internal Medicine, Medical School	Grant writing strategies for the changing times
August 18, 2017	S. Joseph Austin, JD, LLM Assistant Director, IRBMED University of Michigan	IRBMED – Introduction to human subjects research
June 6, 2018	Kanakadurga Singer, MD Assistant Professor, Pediatrics and Communicable Diseases, Medical School University of Michigan	Metabolic disease and obesity-induced inflammation
June 13, 2018	Randy Seeley, PhD Henry King Ransom Professor of Surgery Professor, Surgery and Internal Medicine Professor, Nutritional Sciences, School of Public Health Director, Michigan Nutrition Obesity Research Center University of Michigan	Molecular underpinnings for the effects of bariatric surgery to improve glucose regulation
June 20, 2018	Darleen Sandoval, PhD Associate Professor, Surgery and Internal Medicine, Medical School Associate Professor, Nutritional Sciences, School of Public Health University of Michigan	Using genetics and pharmacology to understand GLP-1 physiology
June 27, 2018	Eva Feldman, MD Russell N. DeJong Professor of Neurology Professor, Neurology Director, Medical School Administration Dean's Office, Medical School University of Michigan	Diabetic neuropathy: From bench to bedside

Table A.8 Enrichment: Activities Enhancing Diabetes Education and Training
Participants in the Medical Student Research Program in Diabetes and Obesity, December 2017 - July 2018

Student	Medical School	Start Date	End Date	Preceptor	Department of Preceptor	Research Description
Ajagbe, Oluwabukola, O	Lincoln Memorial Univ, DeBusk College of Osteopathic Medicine	5/29/2017	7/28/2017	Sandoval, Darleen, PhD	Department of Surgery	Project: 80% of patients who receive bariatric surgery are women. However, the majority of preclinical work aimed at determining mechanisms for the success of surgery is performed in males. Our work has uncovered important sex differences in hepatic lipid metabolism after bariatric surgery. The aim of this project is to determine if hepatic estrogen receptor signaling is necessary for this sex difference. The student will gain experience in utilizing the latest genetic techniques and in vivo methodologies to study hepatic lipid metabolism in rodents after bariatric surgery.
Coombs, Lauren M	University of Toledo College of Medicine	5/30/2017	8/3/2017	Ferrario, Carrie, PhD	Pharmacology	Studies examining the effects of insulin on neural function and behavior. Experiments will involve preparation and dissection of brain tissue, treatment of tissue with insulin and other compounds, and western blotting. This study may also involve surgical procedures for the infusion of compounds into the brain, depending on the progress of the project.
Katiyar, Urvashi	Wayne State University Medical School	5/15/2017	8/4/2017	Rosland, Ann-Marie, MD, MS	Assistant Professor of Internal Medicine and Research Investigator, VA Ann Arbor Center for Clinical Management Research	Engaging Patients and Family Supporters in Primary Care to Improve Diabetes Management. This study will test a strategy to strengthen the capacity of supporters to help patients with high-risk diabetes engage in patient centered care and successfully enact care plans. The central hypothesis is that by providing health care engagement tools to both caregivers and patients we will increase patient activation and improve management of diabetes complication risks. Status: Recruitment is ongoing. Students could gain experience with intervention study recruitment, surveys and other evaluation techniques, and quantitative data analysis and reporting. Students will be included in an active research group with both interventional and observational diabetes health services research studies.
Lewis, Sean P (Complications)	University of Toledo College of Medicine and Life Sciences	5/22/2017	7/28/2017	Fort, Patrice, PhD	Ophthalmology and Visual Sciences and Molecular and Integrative Physiology	Diabetic retinopathy is the main ocular complication associated with diabetes, and is the main cause of blindness in the working age population. Our laboratory focuses specifically on the neurodegeneration of the retina which leads to blindness in diabetic patients. Our main project focuses on the mechanisms by which diabetes affect retinal cell survival by disrupting intrinsic protective mechanisms. The student would directly assist in the characterization of those mechanisms and their disruption.
Patterson, Kaitlyn	University of Michigan Medical School	6/26/2017	8/18/2017	Saslow, Laura, PhD	Health Behavior and Biological Sciences, School of Nursing	My intern will be conducting a systematic investigation of nutrition education content in the context of diabetes, metabolic syndrome, and obesity in the medical school as well as the other health professional schools at the University of Michigan. The objective is to determine consistency of content and delivery as well as the material's strength of evidence. The intern will be responsible for compiling educational resources, analyzing content and citations, and preparing results for publication.
Reingold, Laura J	Boston University School of Medicine	5/18/2017	7/14/2017	Qi, Ling, PhD	Molecular and Integrative Physiology	The Qi laboratory is interested in the crosstalk between endoplasmic reticulum (ER) and mitochondria in metabolism, as well as the crosstalk among three ER quality-control systems including Sel1L-Hrd1 ER-associated degradation (ERAD), unfolded protein response (UPR) and autophagy in adipocytes. We have generated adipocyte-specific ERAD- and autophagy-double deficient mice. The fellow will be involved in the characterization of their metabolic phenotypes and possible underlying mechanisms.
Su, Lydia (Complications)	Wayne State University School of Medicine	5/8/2017	7/28/2017	Gardner, Thomas, MD, MS	Ophthalmology and Visual Sciences	Studies of how proliferative diabetic retinopathy and its treatment affects vision. The purpose is to understand the pathophysiology of vision loss in persons with diabetes with the long term goal of finding means to improve their vision. Lydia will be responsible for the patient testing, data collection and analysis.

Student	Medical School	Start Date	End Date	Preceptor	Department of Preceptor	Research Description
Tisack, Aaron M	Wayne State University School of Medicine	5/8/2017	7/21/2017	Richardson, Caroline, MD	Family Medicine	This summer we will be developing and pilot testing a Diabetes Prevention Program intervention using a low carbohydrate rather than the traditional low fat diet. If successful, this new curriculum will be used a future large scale comparative effectiveness trial. Our hypothesis is that the low carbohydrate version of the DPP will be more effective than the traditional low fat DPP.
Vaidya, Palavi P (Complications)	University of Toledo College of Medicine	5/15/2017	7/28/2017	Wrobel, James, DPM, MS	Internal Medicine - Metabolism, Endocrinology and Diabetes	We have been developing image processing models that extract surface area, wound base color and surrounding skin to predict healing and infection in diabetes-related foot ulcers. For the summer project, research experience will include creating a anonymized database of relevant clinical measures that predict foot ulcer healing and to digitize (or outline) the ulcer margins on the images to provide ground truth for the image processing techniques. You will be working with wound care clinicians and engineers.

Table A.9. Enrichment: Activities Enhancing Diabetes Education and Training
Seminars co-sponsored with the Department of Molecular & Integrative Physiology, December 2016 – July 2018

YEAR	SPEAKER	TITLE
Nov. 1, 2017	Sue Ritter, PhD Regents Professor of Integrative Physiology and Neuroscience College of Veterinary Medicine Washington State University	Why I can't say 'no' to hindbrain catecholamine neurons
Nov. 8, 2017	Xiaoyong Yang, PhD Associate Professor of Comparative Medicine and Cellular & Molecular Physiology Yale School of Medicine	Nutrient sensing and metabolic communication
Nov. 15, 2017	Chih-Hao Lee, PhD Professor of Genetics & Complex Diseases Harvard T.H. Chan School of Public Health	Bmal1 in macrophage mitochondrial bioenergetics and inflammatory response: beyond circadian regulation
May 9, 2018	Matthew Rodeheffer, PhD Associate Professor of Biological & Biomedical Sciences & Comparative Medicine Yale University	Understanding how we get fat: Dietary regulation of adipocyte stem cells

Table A.10. Enrichment: Activities Enhancing Diabetes Education and Training
MDRC Sponsored Diabetes-Related Endocrine Research Conferences, December 2016 – July 2018

YEAR	SPEAKER	TITLE
Dec. 2, 2016	Anne Reifel Miller, PhD Research Fellow, Diabetes Research Eli Lilly and Company Lilly Corporate Center Indianapolis, IN	Targeting the gastrointestinal tract for the treatment of type 2 diabetes and obesity
Dec. 9, 2016	Elizabeth R. Seaquist, MD Pennock Family Chair in Diabetes Research Professor of Medicine Director, Division of Endocrinology and Diabetes Department of Medicine University of Minnesota	Impaired awareness of hypoglycemia in diabetes: Effects of recurrent hypoglycemia on the brain
Jan. 13, 2017	Matthew Delano, MD, PhD Assistant Professor of Surgery University of Michigan	Diabetes and sepsis: Risk, resolution, recurrence and ruination
Jan. 27, 2017	Kent Berridge, PhD Professor of Psychology and Neuroscience University of Michigan	Eating and brain reward circuitry: food liking vs. wanting
Feb. 3, 2017	Maria Papaleontiou, MD Assistant Professor of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	New insights on complications following thyroid cancer surgery
Feb. 10, 2017	Scott Soleimanpour, MD Assistant Professor of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Deciphering the role of the mitochondrial life in beta cell growth and function
Feb. 24, 2017	Roger Cone, PhD Mary Sue Coleman Director, Life Sciences Institute Professor, Department of Molecular and Integrative Physiology	Melanocortins: from pharmacology to pharmacotherapy
Mar. 3, 2017	Ernestina Schipani, MD, PhD Professor Department of Orthopaedic Surgery Department of Medicine/Division of Endocrinology Department of Cell and Developmental Biology Center for Organogenesis University of Michigan	In vivo impairment of mitochondrial respiration is an indispensable requirement for survival of hypoxic cells
Mar. 10, 2017	Carole Sztalrud-Woodle, PhD Associate Professor of Medicine Division of Endocrinology University of Maryland School of Medicine	Human genetic variants: Metabolic disease insights
Mar. 24, 2017	Jannik Hilsted, MD, DMSci Chief Medical Office	Five Danish Steno Diabetes Centers- the opportunity for continued international collaboration

	Head of Steno Unified Denmark Diabetes Centers and Novo Nordisk Foundation CEO Righospitalet Copenhagen University Hospitals	
Apr. 14, 2017	Anna Mathew, MD Assistant Professor, Internal Medicine-Nephrology University of Michigan	Myeloperoxidase, chronic kidney disease and atherosclerosis
May 5, 2017	Mark S. Cohen, MD, FACS Associate Professor of Surgery and Pharmacology Associate Chair in Surgery for Innovation and Entrepreneurship Director, Medical School Pathway of Excellence in Innovation and Entrepreneurship Director of Endocrine Surgery Research Principal Investigator, Translational Oncology Program, UMCCC	Translating novel HSP90 inhibitors as an innovative therapeutic strategy for endocrine malignancies
Jun. 16, 2017	Thomas Mandrup-Poulsen, MD, DMSc Professor Department of Biomedical Sciences University of Copenhagen	Iron handling in inflammatory and metabolic pancreatic beta-cell failure
Jun. 23, 2017	Joseph T. Bass, MD, PhD Charles F. Kettering Professor of Medicine Chief, Division of Endocrinology, Metabolism, and Molecular Medicine Department of Medicine and Neurobiology Northwestern University	Metabolic regulation by molecular clocks
Jun. 30, 2017	Durga Singer, MA, MD Assistant Professor Edith Briskin/SKS Foundation Taubman Emerging Scholar Division of Pediatric Endocrinology Department of Pediatrics and Communicable Diseases	Investigating obesity induced inflammation; translational studies from mouse models to childhood obesity
Sep. 15, 2017	Tae-Hwa Chun, MD Associate Professor Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Three-dimensional biology unraveling metabolic and endocrine disease processes
Sep. 29, 2017	Marzieh Salehi, MD, MS Director, Clinical Research in the Diabetes and Obesity Research Institute Cedars-Sinai Medical Center	Replumbing the gut to treat diabetes
Oct. 6, 2017	Arun Anantharam, PhD Assistant Professor Department of Pharmacology University of Michigan	The role of secretory granule heterogeneity in regulated exocytosis
Oct. 20, 2017	William H. Herman, MD, MPH Professor Division of Metabolism, Endocrinology and Dia Department of Internal Medicine	What is new in cardiovascular disease prevention for type 2 diabetes?

	University of Michigan	
Oct. 27, 2017	Christin Carter-Su, PhD Anita H Payne Distinguished University Professor of Physiology Henry Sewall Collegiate Professor of Physiology Professor, Molecular & Integrative Physiology Associate Director, Michigan Diabetes Research Center University of Michigan	Effect of isoform-specific C-termini on the function and subcellular location of SH2B1, a tyrosine kinase binding protein that regulates energy balance
Nov. 3, 2017	Jereon A.L. Jeneson, PhD Research Assistant Professor of Radiology Neuroimaging Center University Medical Center Gronigen, The Netherlands	Acute mild ketosis as therapy in human metabolicmyopathy: Observations in VLCAD deficiency
Dec. 8, 2018	Alessandro Doria, MD, PhD Associate Professor Department of Epidemiology Joslin Diabetes Center Harvard Medical School	Leveraging genetics to personalize cardiovascular prevention in diabetes
Dec. 15, 2018	Robert Ward O'Rourke, MD Professor Department of General Surgery University of Michigan	Adipose tissue fibrosis and its relationship to metabolism
Jan. 26, 2018	Kevin R Ward, MD, FACEP, FAAEM Executive Director Fast Forward Medical Innovation Professor Emergency Medicine and Biomedical Engineering University of Michigan	Innovation, critical care, and big data…the perfect storm
Feb. 2, 2018	Geun Hyang Kim, PhD Department of Molecular and Integrative Physiology University of Michigan	A Novel role of Se11L-Hrd1 ERAD in POMC neurons
Feb. 23, 2018	Grace Su, MD Professor Department of Internal Medicine Division of Gastroenterology University of Michigan	Analytic morphomics: linking phenotypes to clinical outcome
Mar. 2, 2018	Jacqueline Jonklaas, MD, PhD, MPH Professor of Medicine Georgetown University	T4/T3 combination therapy: where are we now?
Mar. 9, 2018	Kenneth Cusi, MD, FACP, FACE Professor of Medicine Chief, Division of Endocrinology, Diabetes and Metabolism The University of Florida	Nonalcoholic fatty liver disease (NAFLD): The overlooked complication of type 2 diabetes
Apr. 6, 2018	Stefan S. Fajans Lecture in Diabetes Bruce A Beutler, MD Regental Professor and Director Center for the Genetics of Host Defense UT Southwestern Medical Center Dallas, Texas	New metabolic phenotypes caused by random germline mutagenesis in the mouse

Apr. 13, 2018	Steven Grinspoon, MD Professor of Medicine, Harvard Medical School MGH Endowed Chair in Neuroendocrinology and Metabolism Director, MGH Program in Nutritional Metabolism in Nutritional Metabolism and Nutrition Obesity Research Center at Harvard Boston, Massachusetts	Novel strategies augmenting pulsatile GH to target visceral and ectopic adipose tissue
Apr. 20, 2018	Michael R Rickels, MD, MS Associate Professor of Medicine Division of Endocrinology, Diabetes and Metabolism University of Pennsylvania Perelman School Of Medicine Philadelphia, Pennsylvania	Islet transplantation for type 1 diabetes
Apr. 27, 2018	Brigid Gregg, MD Assistant Professor Department of Pediatrics Pediatric Endocrinology University of Michigan	Lactational programming of offspring metabolic health: A window of opportunity
May 11, 2018	Darren K McGuire, MD, MHSc Professor of Internal Medicine University of Texas Southwestern Medical Center Dallas, Texas Deputy Editor, Circulation	Selected lessons learned from diabetes and cv outcome trials: A cardiologist's perspective

Table A.11. Enrichment: Activities Enhancing Diabetes Education and Training
MDRC Sponsored Diabetes-Related Endocrine Clinical Conferences, December 2016 – July 2018

YEAR	SPEAKER	TITLE
Dec. 2, 2016	Jennifer Iyengar, MD Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Emerging technologies in diabetes mellitus
Dec. 16, 2016	Elif Oral, MD Associate Professor of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Cases from the molecular metabolism and diabetes program: Beginning of a new series
Jan. 20, 2017	Sari Priesand, DPM Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Multiple cases exhibiting limb salvage
Jan. 27, 2017	Ravi Iyengar, MD Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Nesidioblastosis: A clinical dilemma
Feb. 10, 2017	Hussain Alquraini, MD Kara Mizokami-Stout, MD Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Genetic obesity syndromes
Feb. 17, 2017	Michael S. Conte, MD E.J. Wylie Chair Professor and Chief, Division of Vascular and Endovascular Surgery Co-Director, Heart and Vascular Center University of California, San Francisco	The threatened limb: Evolving concepts in amputation prevention
Apr. 21, 2017	Hertzel C. Gerstein, MD, MSc, FRCPC Professor, Department of Medicine Director, Division of Endocrinology & Metabolism Deputy Director, Population Health Research Institute McMaster University & Hamilton Health Sciences	What have we learned from the large CV RCTS in diabetes?
May 19, 2017	Corey Lager, MD Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Review of lipid guidelines and how PCSK-9 inhibitors may or may not rock the boat
Jun. 2, 2017	Rachel Reinert, MD Department of Internal Medicine Division of Metabolism, Endocrinology, and Diabetes University of Michigan	Complementary and alternative therapies for endocrine disorders
Sep. 29, 2017	Israel Hodish, MD, PhD Associate Professor Department of Internal Medicine	Insulin therapy, weight and prognosis

	Division of Metabolism, Endocrinology and Diabetes University of Michigan	
Oct. 13, 2017	Corey Lager, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	Male infertility for the endocrinologist
Oct. 20, 2017	William H. Herman, MD Professor Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	What is new in cardiovascular disease prevention for type 2 diabetes?
Dec. 1, 2017	Andrew T. Kraftson, MD Clinical Assistant Professor Metabolism, Endocrinology and Diabetes University of Michigan	Faculty development: The millennial learner (and other topics)
De. 8, 2017	Alessandro Doria, MD, PhD Associate Professor Department of Epidemiology Joslin Diabetes Center Harvard Medical School	Leveraging genetics to personalize cardiovascular prevention in diabetes
Dec. 15, 2017	Gabriel Corfas, PhD Professor Department of Otolaryngology Head and Neck Surgery Director, Kresge Hearing Research Institute The Lynn and Ruth Townsend Professor of Communication Disorders Associate Chair for Research, Department of Otolaryngology Head and Neck Surgery University of Michigan	Sensing translation: from neuron-glia interactions to therapies for peripheral neuropathies
Jan. 12, 2018	Raad Haddad, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	Catch 22
Jan. 26, 2018	Rachel Reinert, MD, PhD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	Glucagon and metabolic disease
Feb. 16, 2018	Robert Daniel Brook, MD Professor Department of Internal Medicine Hypertension Michigan Medicine Cardiovascular Medicine University of Michigan	Update on lipid management
Mar. 2, 2018	Rodrigo Valerrabano, MD, MSe Assistant Professor University of Miami Miller School of Medicine	Bone health in diabetes
Mar. 9, 2018	Alison Affinati, MD Department of Internal Medicine	Endocrinopathy and immune checkpoint inhibitor therapy

	Division of Metabolism, Endocrinology and Diabetes University of Michigan *And* Joshua Evron, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	
Mar. 23, 2018	Heather Klingeman, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	Adult human growth hormone deficiency: To treat or not to treat
Apr. 6, 2018	Stefan S. Fajans Lecture in Diabetes Bruce A Beutler, MD Regental Professor and Director Center for the Genetics of Host Defense UT Southwestern Medical Center Dallas, Texas	New metabolic phenotypes caused by random germline mutagenesis in the mouse
Apr. 13, 2018	Raad Haddad, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	Brown adipose tissue
May 4, 2018	Shafaq Khairi, MD Department of Internal Medicine Division of Metabolism, Endocrinology and Diabetes University of Michigan	What to expect when you are expecting with your pregnant plump pituitary
Jun. 15, 2018	James Dupree, MD, MPH Assistant Professor Urology University of Michigan	Practical management of erectile dysfunction: Perspective from a urologist

Table A.12. Enrichment: Activities Enhancing Diabetes Education and Training
Brehm Summer Diabetes Symposia 2017-2018

Tuesday, August 8, 2017
Cure Room, 5050 Brehm Tower, 1000 Wall Street, Ann Arbor, MI

Targeting brainstem → VMN circuits to understand hypoglycemia pathogenesis
Jonathan Flak, PhD – Myers Lab

Regulation of systematic water homeostasis by ER-associated degradation
Guojun Shi, PhD – Qi Lab

Hif2α as a molecular target underlying the metabolic effects of bariatric surgery
Simon Evers, PhD – Seeley Lab

Proinsulin folding and misfolding in diabetes
Leena Haataja, PhD – Arvan Lab

Bone mass and marrow adipose loss after vertical sleeve gastrectomy surgery in mice
Ziru Li, PhD – MacDougald Lab

Transmitting information-rich signals of ER stress
Wylie Stroberg, PhD – Schnell Lab

Diabetes-associated regulatory signatures of islet gene expression across human, mouse, and rat
Arushi Varshney, PhD – Parker Lab

Using biological mass spectrometry to study diabetic and chronic kidney disease complications
Sub Pennathur, MD

Using machine learning to develop a predictive model for familial partial lipodystrophy
Rasimcan Meral, MD – Oral Lab

Investigating the anorectic mechanisms of Glp-1 agonists
Jessica Adams, PhD – Olson Lab

Closing in on the mechanisms of pulsatile insulin secretion: Updates from the Satin Lab
Leslie Satin, PhD

MIDY: Learning from monogenic diabetes
Xin Li – Liu Lab

Lactational programming of offspring body composition and glucose homeostasis
Brigid Gregg, MD

Transplantation of stem cells derived immature beta cells
Tadas Kasputis, PhD – Shea Lab

Evidence that high oxidative capacity is associated with slowed metabolic aging in humans
Chanisa Thonusin – Burant Lab

Tuesday, August 7, 2018
Kellogg Eye Center Auditorium, 1000 Wall Street, Ann Arbor, MI

CD4+ adipose tissue T cells assume a senescent phenotype in obese mice and humans
Cara Porsche – Lumeng Lab

Hepatic Sel1L-Hrd1 ER-associated degradation (ERAD) manages FGF21 levels and systemic metabolism via CREBH
Asmita Bhattacharya – Qi Lab

A stress-induced microRNA degradation pathway in non-alcoholic fatty liver disease
Kezhong Zhang, PhD – Zhang Lab (Wayne State University)

Efficacy of recombinant human leptin (Metreleptin) in nonalcoholic steatohepatitis (NASH) associated with partial lipodystrophy
Baris Akinci, MD – Oral Lab

GLP-1 controls pancreatic endocrine development
Corentin Cras-Meneur, PhD – Islet Core/Seeley Lab

An iron-mitophagy axis balances beta cell responses to cytokine toxicity
Vaibhav Sidarala, PhD – Soleimanpour Lab

Proinsulin misfolding in pancreatic beta-cells
Anoop Arunagiri, PhD – Arvan Lab

Translocon-associated protein Alpha (TRAPα) determines effective preproinsulin translocation and insulin production
Xin Li – Liu Lab

Deletion of the phosphofructokinase-M gene in mouse beta cells reduces glucose tolerance but does not result in the loss of beta cell glycolytic oscillations
Vishal S. Parekh, PhD – Satin Lab

Activation of area postrema Gfral neurons reduces food intake
Paul Sabatini, PhD – Myers Lab

Illuminating fatty acid metabolism
Emilio Mottillo, PhD – Granneman Lab (Wayne State University)

Closing the loop of diabetes: Extending continuous subcutaneous insulin infusion (CSII) in vivo: CSII biocompatibility and effective insulin delivery
Ulrike Klueh, PhD – Klueh Lab (Wayne State University)

Obesity in type-2 diabetic mice: A role for aldehyde dehydrogenase 2
Suresh Palaniyandi, PhD – Palaniyandi Lab (Wayne State University)

Retinal mTORC expression and protein synthesis
Tom Gardner, MD – Gardner Lab

Monounsaturated fatty acids prevent saturated fatty acid-induced impairment of mitochondrial trafficking in dorsal root ganglion sensory neurons
Amy Rumora, PhD – Feldman Lab

Maternal metabolomic profiles associated with fetal growth and birth weight
Jennifer LaBarre, MPH – Burant Lab

The tight junction protein occludin regulates neovascularization
Xuwen Liu, MD, PhD – Antonetti Lab

B.4 What opportunities for training and professional development has the project provided?

All of the enrichment activities (research clubs, seminar series, symposia with poster sessions) are activities designed to provide training and professional development related to research relevant to diabetes, its complications and/or related metabolic disease. The targeted audience is the faculty, staff and trainees at the University of Michigan and regional institutions (University of Toledo, Wayne State University and Michigan State University). The MDRC organizes and supports five research clubs (Cellular Aspects of Diabetes, Obesity, and Metabolism Research Club, Integrative Aspects of Diabetes, Obesity, and Metabolism Research Club, Neuroendocrine Control of Metabolism Research Club, Islet Research Club, and Complications of Diabetes Research Club). We continue to co-sponsor the Midwest Islet Club (MIC).

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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Withheld pursuant to exemption

Budget ; Redacted by agreement

of the Freedom of Information and Privacy Act

A. COMPONENT COVER PAGE

Project Title: Pilot and Feasibility Program
Component Project Lead Information: CARTER-SU, CHRISTIN

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The purpose of the Michigan Diabetes Research Center (MDRC) Pilot and Feasibility (P/F) Grants Program is to stimulate new research in the areas of diabetes, its complications, and related endocrine and metabolic disorders. This research may be in areas of basic biomedical science or clinical research. This program provides a minimum of $250,000 per year for P/F grant awards; additional funding may be provided for highly-rated applications using funds provided by the University of Michigan. The MDRC P/F program will fund two types of awards: (1) standard one-year $50,000 P/F awards with a single PI, and (2) two-year, $100,000 Diabetes Interdisciplinary Studies Program (DISP) awards that seek to support and promote new collaborations between two or more University of Michigan (UM) faculty members from distinct disciplines, to focus their combined research strengths on cutting-edge areas in diabetes research. Each year, the MDRC solicits applications for P/F and DISP grants from full-time instructional or research faculty at UM. Those eligible include: 1) new investigators without past or current NIH research support who are beginning careers in diabetes research, 2) established investigators who have not previously worked in diabetes research but wish to focus their expertise on diabetes, and 3) established diabetes investigators who propose innovative research in diabetes that represents a clear departure from their ongoing research. Highest priority is given to new investigators. Applications are actively solicited from across the university and are peer-reviewed by two or more extramural reviewers with expertise in the area of the application. Grant applications with the highest merit, as judged by this review process and the intramural Grants Program Advisory Council, receive awards. The balance of standard P/F and DISP awards may vary from year to year, depending upon the relative strength of applications for each award type. The ultimate goal of the program is to enable awardees to generate sufficient preliminary data to support a successful application for major research funding from the NIH or another national granting agency. The P/F Grants Program attracts investigators from diverse schools, departments, and institutes into diabetes research and fosters new, innovative, interdisciplinary, and collaborative diabetes research at UM.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Pilot and Feasibility.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

No major changes are planned for the Pilot and Feasibility Grant Program. The Pilot and Feasibility Grant Program will continue to award funds to enable awardees to generate sufficient bodies of preliminary data to successfully apply for major research funding from the NIH or other national granting agencies and to accelerate the pace of discovery to prevent, treat and ultimately cure diabetes and its complications.

B.2 What was accomplished under these goals?

In August 2017 the following applications were received for consideration:

- Eight (8) Pilot and Feasibility (**Table A**)
- Four (4) Diabetes Interdisciplinary Study Program (DISP) (**Table A.1**)

These applications were reviewed by thirty-five (35) external reviewers. The applications and reviewer comments were considered at the November 6, 2017 meeting of the Grants Advisory Council.

- Two (2) Pilot and Feasibility applications were funded (**Table B**)
- Two (2) Diabetes Interdisciplinary Study Program (DISP) applications were funded (**Table B.1**)

Pilot project outcomes and Metabolomics (OMICS) Pilot outcomes are listed in **Tables C and C.1**.

Progress to date for Pilot and Feasibility and Diabetes Interdisciplinary Study Program (DISP) awards funded for the period December 2016 – November 2017 are listed in **Table D**.

Details about human research subjects and vertebrate animals for Pilot and Feasibility and Diabetes Interdisciplinary Study Program (DISP) awards are listed in **Table E**.

Table A. Pilot and Feasibility Grants Program
Pilot and Feasibility Grants Program Applications Reviewed for the Funding Period December 2017 – November 2018

Investigator	Type of Investigator	Department/School	Type of Application	Title
Farsad Afshinnia, MD, MS	New Investigator	Internal Medicine - Nephrology	Basic Biomedical Research	Improving cardiovascular risk prediction in diabetic kidney disease
David Bridges, PhD	Established Investigator – not an extension or outgrowth	Nutritional Sciences, School of Public Health	Basic Biomedical Research	The role of adipose tissue in obesity-associated glucocorticoid responses
Proprietary Info				
Amy Chang, PhD	Established Investigator Transferring	Molecular, Cellular & Developmental Biology, College of Literature, Science & the Arts	Basic Biomedical Research	Endoplasmic reticulum stress, cell death and diabetes
Corentin Cras-Meneur, PhD	New Investigator	Internal Medicine – Metabolism, Endocrinology & Diabetes	Basic Biomedical Research	In vivo model for the study of β-cell programming in gestational diabetes
Amiya Ghosh, MSc, PhD	New Investigator	Internal Medicine – Geriatric & Palliative Medicine	Basic Biomedical Research	Epigenetic regulation of senescence by plasma factors in aging adipose tissue
Darleen Sandoval, PhD	Established Investigator – not an extension or outgrowth	Surgery and Nutritional Sciences, School of Public Health	Basic Biomedical Research	The source and function of GLP-1 in severe inflammation
Bin Xu, PhD	New Investigator	Internal Medicine – Metabolism, Endocrinology & Diabetes	Basic Biomedical Research	Novel role of Nkx transcription factors in regulation of adipogenesis
Total: 8				

Table A.1. Pilot and Feasibility Grants Program
Diabetes Interdisciplinary Studies Program (DISP) Grant Applications Reviewed for the Funding Period December 2017 – November 2019

Investigator	Type of Investigator	Department/School	Type of Application	Title
Michael T. Freehill, MD William Herman, MD, MPH	New Investigator Established Investigator – not an extension or outgrowth	Orthopaedic Surgery Internal Medicine – Metabolism, Endocrinology & Diabetes and Epidemiology	Clinical, Type T1 Translational Research	Acute effects on blood glucose levels after large joint intra-articular corticosteroid injection
Venkateshwar Keshamouni, PhD Kanakadurga Singer, MD	Established Investigator Transferring Established Investigator – not an extension or outgrowth	Internal Medicine – Pulmonary & Critical Care Pediatrics	Basic Biomedical Research	Paradoxical role of obesity in lung cancer
Robert O'Rourke, MD Lonnie Shea, PhD	Established Investigator – not an extension or outgrowth Established Investigator Transferring	Surgery Biomedical Engineering	Clinical, Type T1 Translational Research	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes
Amy E. Rothberg, MD Andrew D. Schrepf, PhD	Established Investigator – not an extension or outgrowth New Investigator	Internal Medicine – Metabolism, Endocrinology & Diabetes Anesthesiology	Clinical, Type T1 Translational Research	The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes
Total: 4				

Table B. Pilot and Feasibility Grants Program
Pilot and Feasibility Awards Funded for the Period December 2017 – November 2018

Investigator	Title	Type of Investigator	Type of Science	Type of Research	Brief Description
David Bridges, PhD	The role of adipose tissue in obesity-associated glucocorticoid responses	Established Investigator – not an extension or outgrowth	Basic Biomedical Research	Diabetes, Endocrinology, Obesity	Glucocorticoids result in adverse metabolic effects including diabetes, NAFLD and weight gain. We have generated preliminary data suggesting that while these risks are present in lean individuals, the consequences are dramatically worse in obese individuals. This proposal aims to identify the molecular and physiological mechanisms that cause these effects by testing effects of obesity on chromatin availability and the role of adipocytes in these effects. Our goal is to identify why and in what tissues obesity causes increased metabolic risk to glucocorticoids.

Proprietary Info

					Proprietary Info

Table B.1. Pilot and Feasibility Grants Program
Diabetes Interdisciplinary Study Program (DISP) Awards Funded for the Period December 2017 – November 2019

Investigator	Title	Type of Investigator	Type of Science	Type of Research	Brief Description
Robert O'Rourke, MD Lonnie Shea, PhD	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	Established Investigator – not an extension or outgrowth Established Investigator Transferring	Clinical, Type T1 Translational	Diabetes, Obesity	Adipose tissue metabolic dysfunction contributes to the pathogenesis of obesity-related type 2 diabetes. The association between adipose tissue metabolic dysfunction and diabetes is depot-specific, as visceral adipose tissue exerts disproportionate detrimental effects on systemic metabolism, while subcutaneous adipose tissue exerts protective metabolic effects. Both adipocytes and their surrounding extracellular matrix (ECM) contribute to these disease- and depot-specific differences in adipose tissue metabolism and their effects on systemic metabolic state. These observations suggest that disease- and depot-specific differences in adipose tissue ECM and adipocytes might be exploited to manipulate systemic metabolism by *in vivo* delivery of metabolically beneficial adipose tissue as therapy for diabetes. Nonetheless, challenges exist with respect to technology for design and delivery of such therapeutic adipose tissue. This proposal will determine if artificial bioscaffold-based adipose tissue, engineered with ECM and seeded with preadipocytes, can be used to manipulate cellular and systemic metabolism. Aim 1 will test whether artificial bioscaffolds, conditioned with adipose tissue ECM and seeded with adipocytes from diabetic and non-diabetic humans, can be used to regulate the metabolic phenotype of engineered adipose tissue *in vitro*. Aim 2 use a murine model of visceral transplant of scaffold-based adipose tissues to determine if visceral transplant of artificial bioscaffold-based adipose tissue can be used to ameliorate systemic insulin resistance in murine obesity. These experiments represent a first step in the development of artificial 'designer' bioscaffold-based adipose tissues as a therapeutic vehicle for diabetes.
Amy E. Rothberg, MD	The impact of calorie restriction and	Established Investigator – not an	Clinical, Type T1 Translational	Diabetes	Individuals with and at risk for diabetes suffer from diffuse pain, fatigue, cognitive difficulties, and depressive symptoms at a higher rate than individuals in the general

Andrew D. Schrepf, PhD	weight loss on inflammation and centralized pain in individuals at risk for diabetes	extension or outgrowth New Investigator			population. This cluster of symptoms has been described as 'centralized pain' in other populations in recognition of the important role the central nervous system plays in their generation and maintenance. Despite the widely acknowledged association of diabetes, pre-diabetes, and obesity with inflammation, surprisingly little is known about how inflammation may promote centralized pain in these populations. We present preliminary data from a burgeoning collaboration between Amy Rothberg (Co-PI) and Andrew Schrepf (Co-PI) demonstrating that calorie restriction (CR) and weight loss (WL) reduced centralized pain symptoms, possibly through anti-inflammatory mechanisms. In this proposal we will use the successful CR intervention run by Dr. Rothberg and measures of inflammation and centralized pain used by Dr. Schrepf to probe how the effects of both CR and WL impact inflammation and measures of these symptoms in obese individuals with and at risk for diabetes. Inflammatory measures will include both inflammatory output from isolated immune cells and inflammatory gene expression, and centralized pain will be measured with both self-reported outcomes and through psychophysical pain testing. We will employ alternating periods of ad libitum eating ("normal diet") and CR in an ABAB design (n=50). This project will form the basis of joint applications between Dr. Rothberg and Dr. Schrepf for external funding of more definitive studies of these effects in individuals with and at risk for diabetes.

N= New Investigator
NTD= Established Investigator, New to Diabetes research
E = Established Investigator, with new, innovative research idea
A = # of Abstracts
P = # of Publications

Table C: Pilot & Feasibility and DISP Pilot Project Outcomes (renewal applications only)

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
1	Patrick J. Hu, MD, PhD, (Internal Medicine)	12/01/2006-11/30/2007 $45,000	A novel endocrine pathway regulating insulin-like signaling in C. elegans	Dr. Hu hypothesized that C. elegans XXX cells secrete a factor that potentiates insulin-like signaling in the rest of the animal. He anticipates that his studies will provide insight into conserved mechanisms of insulin signaling, perhaps leading to the development of new treatments for diabetes that modulate the activity of secreted factors that regulate insulin signaling in target tissues.	N	0	3	NIH R56DK078183 Private Source	Funded Funded Funded	07/15/2008-06/30/2010 07/01/2010-06/30/2014 01/01/2011-12/31/2012	Yes
2	Jiandie Lin, PhD, (LSI and Cell & Developmental Biology)	12/01/2006-11/30/2007 $45,000	Genome-wide analysis of transcription factors in the regulation of mitochondrial biogenesis by PGC-1α	Recent studies have demonstrated that mitochondrial oxidative phosphorylation (OXPHOS) activity is significantly decreased in skeletal muscle from patients with type 2 diabetes. In this proposal, we will utilize functional genomic tools that we have recently developed to identify key transcription factors and cofactors in the PGC-1 pathway. We anticipate capturing a global molecular signature that mediates the effects of PGC-1 on energy metabolism. These pilot studies will provide novel insight into the qenetic control of mitochondrial oxidative metabolism in normal and diabetic states.	N	0	3	NIH/NIDDK R01DK095151	Funded Funded	07/01/2008-06/30/2013 04/20/2012-03/31/2016	Yes
3	Julie C. Lumeng, MD, (Pediatrics)	12/01/2006-11/30/2007 $45,000	Factors impacting maternal beliefs and feeding practices in mothers of low-income African American preschoolers	This proposal seeks to explore potential relationships between observed maternal feeding behaviors, self-reported maternal feeding behaviors, observed child eating behaviors, mother-reported child eating behaviors, genetically-mediated taste preferences, mother's perceived and ideal body image of the child, mother and child dietary intake, current and historical food insecurity, arid maternal belief systems about feeding and child overweight.	N	0	4	NIH R01HD061356	Funded	04/01/2011-03/31/2016	Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
4	Heike Munzberg, PhD, (Internal Medicine)	12/01/2006-11/30/2007 $45,000	Leptin signaling in the DMH and its role in feeding circuits	This proposal evaluates the neuroanatomy of leptin responsive neurons in the DMH and investigates their efferent target sites as well as inputs from other hypothalamic sites. These data about the DMH leptin signaling system will be important for understanding LRb related neuronal circuits that regulate feeding behavior.	N	9	5	NIH/NIDDK R01DK092587	Funded	07/01/2012-04/30/2017	Yes
5	Subramaniam Pennathur, MD, (Internal Medicine – Nephrology)	12/01/2006-11/30/2007 $45,000	Molecular mechanisms of pancratic □-cell failure in vivo	The overall goals of this proposal are to explore the biochemical pathways through which a diabetogenic diet accelerates b-cell failure in vivo. The PI hypothesizes that constituents of a diabetogenic diet induce oxidative stress in the pancreatic beta-cells which results in eventual beta-cell failure and onset of hyperglycemia in the susceptible host.	E	0	4	NIH R24DK082841	Funded	09/30/2008-03/31/2015	Yes
6	Martin G. Myers, MD, PhD, (Internal Medicine) and Robert C. Thompson, PhD (Psychiatry)	12/01/2006-11/30/2007 $80,000	Genomic analysis of novel leptin-regulated neural metabolic pathways	These PI will analyze novel leptin-regulated neural pathways in the lateral hypothalamic area (LHA) and ventral premammilary nucleus (PMv) of the hypothalamus in order to gain insight into their roles in metabolism. The Aims are to utilize: 1) genomic methods to interrogate leptin-regulated gene expression in the LHA and PMv; and 2) quantitative and anatomical methods to probe the expression of specific genes in the LHA and PMv.	E/E	0	4	Private Source NIH R01DK078056	Funded Funded	01/01/2007-12/01/2009 01/01/2008-12/30/2012	Yes and Yes
7	Maria Dolors Sans Gili, PhD, (Molecular & Integrative Physiology)	12/01/2007-11/30/2008 $50,000	Insulin, diabetes and the regulation of pancreatic digestive enzymes	Dr. Sans Gili's hypothesized that insulin deficiency inhibits the synthesis of pancreatic digestive enzymes in response to nutrients. Her aims were to: 1)analyze whether streptozotocin-induced insulin deficiency inhibits translation of pancreatic digestive enzyme mRNAs after feeding; 2)analyze whether insulin effects are independent of cholecystokinin (CCK) and there is a synergistic action of insulin and branched-chain amino acids; and 3) evaluate the importance of insulin for digestive enzyme synthesis using novel mouse models.	N	4	0	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
8	Ming Liu, MD, PhD, (Internal Medicine – MEND)	12/01/2007-11/30/2008 $49,976	Dominant negative effects of misfolded proinsulin in pancreatic beta cells	The mechanisms of ß-cell dysfunction caused by misfolded proinsulin remain unknown. Dr. Liu plans to use Akita mice and hProCpepGFP/Akita compound heterozygotes to examine dominant negative effects of misfolded proinsulin on wild type proinsulin with the goal of elucidating the molecular mechanisms of how misfolded proinsulin specifically affects wild type proinsulin folding and trafficking in pancreatic beta cells.	N	0	5	MI Initiative Program on Rare Disease	Funded	04/01/2011-03/31/2012	Yes
								NIH/NIDDK R01DK088856	Funded	08/01/2011-04/30/2016	
								Private Source	Funded	06/01/2011-05/31/2014	
								MI Initiative Program on Rare Disease	Funded	05/01/2008-open	
9	Ayyalusamy Ramamoorthy, PhD, (Chemistry and Biophysics)	12/01/2007-11/30/2008 $50,000	Solid-state NMR studies on human islet amyloid polypeptide and its role in beta-cell membrane disruption	Dr. Ramamoorthy proposed to use solid-state NMR spectroscopy and other biophysical techniques to provide insight into the catalytic role of membranes on the formation of misfolded and toxic forms of hIAPP, and the process of membrane-disruption by hIAPP. This information will be essential to understand what makes some individuals susceptible to Type II diabetes and why Type II diabetes strikes late in life.	E	0	4	NIH/NIDDK R21DK078885	Funded	01/01/2009-03/31/2011	Yes
10	Allison Rosen, MD, MPH, ScD, (Internal Medicine – General Medicine)	12/01/2007-11/30/2008 $50,000	Trends in the cost of diabetes care in the United States: 1996-2004	The proposed research was designed to document longitudinal trends in diabetes spending and determine the extent to which changes in diabetes prevalence and changes in per-person diabetes costs are driving U.S. health care cost growth. These data will serve as preliminary analyses for an R-01 that will synthesize cost and health information to explore trends in the value of diabetes spending.	N	5	1	None	N/A	N/A	Yes
11	Annette Chang, MD, (Internal Medicine) and Michael Kilbourne, (Radiology)	12/01/2007-11/30/2008 $100,000	Evaluation of human pancreatic beta-cell mass with [11C]	In a multidisciplinary collaboration, the PIs proposed to investigate the potential of [11C]dihydrotetrabenazine (DTBZ), a radioligand for the vesicular monoamine transporter type-2 (VMAT2), as a positron emission tomography (PET) imaging tool to estimate human pancreatic β-cell mass.	N/NTD	0	0	None	N/A	N/A	Yes and Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
12	Peter J. Dempsey, PhD, (Pediatrics and Communicable Diseases)	12/01/2008-11/30/2009 $50,000	Role of Erb4 receptor signaling in the central regulation of energy metabolism	The mechanism(s) underlying the integration of afferent inputs within hypothalamic neurons and downstream brain circuitry to regulate energy balance have not been clearly delineated. Dr. Dempsey proposed to use his Pdx-Creearly;ErbB4flox/flox (Pdx-ErbB4KO) mice to investigate the role of ErbB4 receptor signaling axis on the central regulation of energy metabolism.	N	1	1	None	N/A	N/A	Yes
13	Bhumsoo Kim, PhD, (Neurology)	12/01/2008-11/30/2009 $50,000	Animal models of increased Alzheimer's disease progression with diabetic background	Increasing evidence links the incidence of diabetes to the development of Alzheimer's Disease (AD). AD patients have a higher than normal tendency to develop type II diabetes or impaired fasting glucose. In parallel, diabetic patients have a greater than 50% risk of developing AD. Dr. Kim plans to test his central hypothesis that diabetes accelerates the progression of AD by developing an animal model of AD with type II diabetes and analyzing its behavior, neuropathological and biochemical characteristics.	N	4	2	None	N/A	N/A	Yes
14	Carey Lumeng, MD, PhD, (Pediatrics0	12/01/2008-11/30/2009 $50,000	Depot-specific differences in adipose tissue macrophages – Michigan macrophages in adipose tissue	Obesity-induced inflammation contributes to insulin resistance. Adipose tissue macrophages (ATMs) contribute to this inflammation as they are recruited to adipose tissue with obesity. Dr. Lumeng's goal was to translate to the setting of human obesity his laboratory findings in mice showing that there are subtypes of ATMs with different inflammatory properties that are altered with obesity in a fat depot specific manner.	N	0	0	NIH/NIDDK R01DK090262	Funded	01/11/2011-12/31/2015	Yes
15	Sandeep Pandit, PhD, (Internal Medicine – Cardiology)	12/01/2008-11/30/2009 $50,000	Arrhythmogenesis in type-1 diabetes	The objective of this feasibility grant proposal was to study the electrophysiological substrate in a clinically relevant type-1 diabetes model of the rabbit heart. The general hypothesis is that diabetic hearts will display an enhanced dispersion of repolarization and thus greater incidence of sustained ventricular tachyarrhythmias and fibrillation in response to sympathetic/hypokalemic stress. Moreover, blockade of the A-II receptor will be a potent antiarrhythmic strategy in diabetic hearts.	N	2	1	None	N/A	N/A	Yes

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16	Rodica Pop-Busui, MD, PhD, (Internal Medicine – MEND)	12/01/2008-11/30/2009 $50,000	Stress induced hyperglycemia: a predictor of long-term glucose abnormalities in patients undergoing cardiovascular surgery.	Large cohort studies have demonstrated that impaired glucose tolerance (IGT) and/or impaired fasting glucose (IFG) are associated with an increased risk of cardiovascular disease, type 2 diabetes and diabetic microvascular complications years before the threshold for diabetes is reached. The study's specific aim was to prospectively evaluate the risk of developing persistent abnormalities of glucose metabolism in patients with SIH after CVS.	E	1	1	None	N/A	N/A	Yes
17	Elif Oral, MD, (Internal Medicine – MEND) John D. Birkmeyer, MD, (General Surgery)	12/01/2008-11/30/2009 $100,000	Effect of dietary macrocomposition on non-alcoholic fatty liver disease in bariatric surgery candidates	Drs. Oral and Birkmeyer's objectives were to: 1. Compare differences in weight loss by 3-month hypocaloric low fat vs. low carbohydrate diets in individuals who are candidates for laparoscopic Roux-en-Y gastric bypass surgery. 2. Determine the efficacy of a low carbohydrate vs. a low fat diet to reduce hepatic steatosis.	N/NTD	0	0	NIH/NIDDK R01DK088114	Funded	02/05/2011-12/31/2015	Yes and Yes
18	Munmun Chattopadhyay, PhD, (Neurology)	12/01/2009-11/30/2010 $50,000 Funded by ARRA	Role of neuroinflammation in painful neuropathy in type 2 diabetes	The PI proposes to test the hypothesis that pain in Type 2 diabetes is due at least in part to activation of an inflammatory cascade and increases in voltage gated sodium channels in DRG with the ultimate aim of developing a therapy that will effectively treat the patients with painful diabetic neuropathy (PDN).	N	4	1	Private Source	Funded	07/01/2012-06/30/2015	Yes
19	Alla Karnovsky, PhD., (Center for Computational Medicine & Bioinformatics)	12/01/2009-11/30/2010 $50,000	Development and application of bioinformatics tools for metabolomics and diabetes	The PI will: 1) develop the bioinformatics tool Metscape to enable the analysis and visualization of metabolomics, lipomics and transcription profiling data in the context of molecular networks, and 2) perform comprehensive analysis of the longitudinal gene expression, metabolomic and lipidomic data from islets, liver and skeletal muscle of the female ZFF rats exposed to high unsaturated fat and high saturated fat diets.	N	4	1	Contributed to NIH/NIDDK U24DK097153 (PI: Burant) NIH/NCI R03CA211817	Funded Funded	09/04/2012-08/31/2017 09/14/2016-08/31/2017	Yes
20	Joyce Lee, MD, MPH, (Pediatrics)	12/01/2009-11/30/2010 $50,000	The Pediatric Diabetes Consortium (PDC): Improving care in children with type 1 diabetes through collaborative research	The specific aim of this proposal is to develop and utilize a common data repository to assess treatment approaches for children and youth with new onset type 1 diabetes (T1DM) at the University of Michigan, through its inclusion as an additional clinical center to the Pediatric Diabetes Consortium.	N	6	1	Private Source	Funded	01/01/2012-12/01/2013	Yes

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21	Sung Kyun Park, ScD, MPH, (Environmental Health Sciences)	12/01/2009-11/30/2010 $50,000	Bisphenol-A, epigenetics and type-2 diabetes	The overall goal of this proposal is to examine the relationship between bisphenol-A (BPA) and T2DM and how epigenetic changes play a role in such an association in a population-based case control study. Dr. Park will use existing health data and repository specimens that have been biobanked from the Normative Aging Study (NAS) and also state-of-the-art biomarker and epigenetic techniques to examine the impact of BPA on T2DM, providing evidence of a potential molecular mechanism.	N	1	1	None	N/A	N/A	Yes
22	Scott Pletcher, PhD, (Molecular & Integrative Physiology and Geriatrics)	12/01/2009-11/30/2010 $50,000	Identification of novel mechnisms of metabolic homeostasis in drosophila	Dr. Pletcher uses the powerful genetics of D. melanogaster to study the mechanisms underlying the impact of diet on organism aging and lifespan. He has identified new candidate genes that modulate metabolic homeostasis in flies. He proposes to study a subset of these new candidate genes to dissect the underlying genetic mechanisms that link diet with obesity, energy balance and overall health.	N	0	2	NIH/NIA R01AG023166	Funded	01/30/2010-08/31/2015	Yes
23	Bin Xu, PhD, (Internal Medicine)	12/01/2009-11/30/2010 $50,000	Novel function of the RNA activator SRA in adipogenesis	Dr. Xu will generate a steroid receptor RNA activator (SRA) adipose tissue specific knockout mouse and further characterize the mechanism of SRA in adipogenesis.	N	3	3	None	N/A	N/A	Yes
24	Eva L. Feldman, MD, PhD, (Neurology) Matthias Kretzler, MD, (Internal Medicine) Hosagrahar V. Jagadish, PhD., (Electrical Engineering and Science)	12/01/2009-11/30/2010 $50,000 Funded by ARRA	Biomarkers of diabetic microvascular complications: a bioinformatics approach to human samples	This interdisciplinary team plans to use a comparative approach to discover regulatory networks involved in the initiation and progression of DN and DPN in presence of dyslipidemia Differentially expressed genes (DEG) in patients with and without elevated triglycerides at early stages of DN and DPN will be identified and studied.	E/E/E	0	4	Private Source NIH/NIDDK R24DK082841	Funded Funded	03/01/2011-02/28/2014 04/01/2010-03/31/2015	Yes, Yes and Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
25	Catherine Kim, MD, MPH, (Internal Medicine and OB/GYN0 Caroline Richardson, MD, (Family Medicine)	12/01/2009-11/30/2010 $50,000 Funded by ARRA	Pedometers in gestational diabetes	These PIs will test the effectiveness of a 12-week web-based pedometer intervention in women with histories of GDM to improve glucose tolerance. They will use a randomized controlled trial design and randomize women with histories of GDM to the web-based intervention (n=30) vs. usual care (n=30) and compare glucose area under the curve by intervention arm, with secondary outcomes of weight change and physical activity.	N/E	6	3	NIH/NIDDK R01DK083297	Funded	07/01/2010-05/31/2013	Yes and Yes
26	Meng Hee Tan, MD, (Internal Medicine – MEND) David Hanauer, MD, MS, (Pediatrics & Communicable Diseases)	12/01/2009-11/30/2010 $100,000 Funded by ARRA	Creating a diabetes research registry to enhance recruitment of patients in clinical trials and studies at University of Michigan	These PI will develop a Diabetes Research Registry (DRR) for the Division of Metabolism, Endocrinology and Diabetes (MEND)'s ~3500 diabetes patients at University of Michigan Health System (UMHS). The DRR will have two components: the existing UMHS Quality Management Program (QMP) Diabetes Registry (with fields used for quality improvement purposes) and the new research module (with fields relevant to clinical research).	E/E	3	0	NIH/NIDDK P30DK020572	Funded	02/10/2013-11/30/2017	Yes and Yes
27	Roseanne Armitage, PhD, (Psychiatry)	12/01/2010-11/30/2011 $40,000	Measurement of sleep physiology in obese and type 2 diabetic patients	The purpose of the proposed study is to conduct a pilot study of slow-wave activity (SWA) homeostasis in adolescents at risk for type 2 diabetes. The goal of this project is to evaluate whether impaired SWA homeostasis is directly associated with insulin resistance and if it accounts for more variance than BMI alone.	NTD	1	1	None	N/A	N/A	Yes
28	Markus Bitzer, MD, (Internal Medicine)	12/01/2010-11/30/2011 $50,000	The role of microRNA-21 in diabetic nephropathy	Dr. Bitzer hypothesizes that miR-21 has a protective role in diabeteic nephropathy (DN). He proposes to determine whether miR-21 deficiency retards DN in a robust murine model using miR-21 KO DBA/2J mice made diabetic using streptozotocin.	N	1	1	NIH/NIDDK R01DK100449	Funded	09/15/2014-07/31/2019	Yes

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29	Christopher Krebs, PhD, (Internal Medicine)	12/01/2010-11/30/2011 $50,000	Distinguishing the mouse Rsl genes as genetic modifiers of hepatic insulin sensitivity	Dr. Krebs hypothesizes that Rsl's genetic repression modulates normal dietary responses and, with greater stress, influences disease susceptibility. Aim 1 will establish a causal link between Rsl and susceptibility to metabolic disease, by monitoring hormone and lipid profiles of fasted or high-fat fed wild type and mutant mice, and by histopathology. Aim 2 will determine whether Rsl affects the insulin responsiveness of Pck1 and Scd1, genes critical to energy balance in the liver.	N	0	0	None	N/A	N/A	Yes
30	David Lombard, MD, PhD, (Pathology)	12/01/2010-11/30/2011 $50,000	Novel mechanisms of pyruvate dehydrogenase complex regulation	Dr. Lombard proposes to elucidate the impact of increased pyruvate dehydrogenase complex (PDC) acetylation and activity in the response to high fat diet (HFD). These studies will provide a detailed picture of the role of PDC acetylation in vivo and may lay the groundwork for the eventual use of sirtuin-directed therapies to increase PDC activity in T2D.	N	4	2	NIH/NIGMS R01GM101171	Funded	04/01/2012-03/31/2017	Yes
31	Lei Yin, PhD, (Molecular & Integrative Physiology)	12/01/2010-11/30/2011 $50,000	Circadian regulation of AMPK signaling and glucose metabolism by the transcription repressor E4BP4	To elucidate key molecular components that link the circadian timing system to energy metabolism, Dr. Yin will 1) determine the role of E4BP4-FGF21 regulator axis on the circadian oscillation of AMPK signaling and AMPK-regulated glucose metabolism in the cultured hepatocytes; and 2) investigate the in vivo role of E4BP4 in regulating liver FGF21 expression, AMPK signaling and glucose metabolism.	N	0	3	None	N/A	N/A	Yes
32	Steven Lentz, PhD., (Internal Medicine) Roni M. Shtein, MD, Ophthalmology)	12/01/2010-11/30/2011 $100,000	In vivo corneal confocal microscopy for non-invasive assessment of diabetic peripheral neuropathy	The goal of this collaboration is to develop a non-invasive protocol for the evaluation of DPN. The use of in vivo confocal microscopy to study corneal nerve fibers will provide a repeated, non-invasive diagnostic tool for monitoring the onset and progression of DPN in diabetic patients. Extending this technology to a mouse model of diabetes will allow for sophisticated longitudinal studies to improve our understanding of the progression of disease and examine the effectiveness of novel therapeutic options for DPN.	E/E	4	1	NIH/NEI R01EY012021 19 NIH/NIDDK 1DP3DK104386	Funded Funded	01/01/2015-12/31/2019 09/30/2014-08/31/2017	Yes and Yes

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33	Amy Rothberg, MD, (Internal Medicine) Jon-Kar Zubieta, MD, PhD, (Psychiatry and Radiology)	12/01/2010-11/30/2011 $100,000	Neurohormonal and behavioral correlates of obesity	The present proposal will examine the function of the μ-opioid receptor system in lean and obese individuals following an overnight fast and the change in μ-opioid receptor occupancy following the consumption of a standardized meal using PET imaging with [11C]carfentenil. This information will provide novel information regarding the role of opioid pathways in the context of obesity and its potential role in weight regain.	N/E	2	0	Private Source	Funded	01/01/2014-12/01/2016	Yes and Yes
34	Tae-Hwa Chun, MD, PhD, (Internal Medicine – MEND)	12/01/2011-11/30/2012 $25,000	Peri-adipocyte fibrosis and adipocyte dysfunction in diabetes	To determine the role of peri-adipocyte collagen turnover in regulating adipocyte function and metabolism, the PI will 1) Characterize the role of adipocyte MMP14 in preventing peri-adipocyte fibrosis and adipocyte dysfunction; 2) Define type I collagen-dependent and –independent regulation of adipocyte function; and 3) Define the epigenetic histone modification regulated by MMP14.	N	4	5	NIH/NIDDK R01DK095137	Funded	09/01/2012-06/30/2017	Yes
35	Jeffrey B. Hodgin, MD, PhD, (Pathology)	12/01/2011-11/30/2012 $50,000	Deep sequencing of the podocyte transcriptome in diabetic and hypertensive mice	This proposal will define cell lineage specific transcriptional networks in isolated podocytes that contribute to glomerular filtration failure in a diabetic and hypertensive mouse model. The PI will: 1) employ a mouse model that combines diabetes and hypertension; 2) profile gene expression in the podocyte instead of the entire glomerulus or whole kidney; and 3) use high-throughput transcriptome sequencing (RNA-seq) to study podocyte transcript sequence and abundance at a much higher resolution and scale than previous studies.	N	0	0	Private Source	Funded	07/01/2013-06/30/2015	Yes
36	David P. Olson, MD, PhD, (Pediatrics – Endocrinology)	12/01/2011-11/30/2012 $50,000	Translational profiling of neurons involved in feeding	This proposal is focused on analyzing PVH neuron-specific transcriptional changes that occur in response to satiety signals to characterize the molecular mechanisms by which feeding is regulated. Cre/loxP technology will be used to express a green fluorescent protein(eGFP)- tagged ribosomal subunit only in defined subsets of PVH neurons.	N	2	1	NIH/NIDDK R01DK104999	Funded	04/01/2016-03/31/2021	Yes

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37	Deneen Wellik, PhD., (Internal Medicine – Molecular Medicine & Genetics)	12/01/2011-11/30/2012 $50,000	The role of Hox6 genes in the pancreatic niche	The objective in this application is to explore the adult phenotype of the surviving Hox6 compound mutants and to generate a Hoxb6 conditional allele that will allow us to specifically assess the adult contribution of Hox6 genes in the pancreatic niche.	E	7	2	Private Source	Funded	07/01/2013-06/30/2016	Yes
38	James Wrobel, DPM, (Internal Medicine – MEND)	12/01/2011-11/30/2012 $41,578	Multi-material, layer, and density approach to shear and pressure reduction in the treatment and prevention of diabetes-related foot ulcer	Dr. Wrobel will begin to test a multi-material, region, and density insoles in the prevention of diabetes-related foot (DFU). He will bench test a novel shear reducing insole and compare it to current standard insoles and shoes. He will study twenty-seven diabetes patients with pre-ulcerative foot callus to examine for changes in spatial temporal gait including gait initiation, risk of falling, static and dynamic balance in both footwear conditions. He will also study plantar temperature response to walking and consecutive plantar stress in both footwear conditions.	E	3	2	Private Source	Funded	09/01/2017-08/31/2018	Yes
39	Steven K. Lundy, PhD., (Internal Medicine – Rheumatology) Massimo T. Pietropaolo, MD, (Internal Medicine – MEND)	12/01/2011-11/30/2012 $100,000	Targeting killer and regulatory B lymphocyte function in IDDM	This multidisciplinary team hypothesizes that a population of antigen presenting cells that should actively suppress autoreactive T cell development and survival is functionally deficient in T1D. The Aims are 1) compare MPS-B cell phenotypic and functional properties in NOD and control mice; and 2) utilize a novel method of expanding MPS-B cells to facilitate an adoptive transfer study in NOD-scid mice.	E/E	2	0	None	N/A	N/A	Yes and Yes
40	Joshua D. Stein, MD, (Ophthalmology and Visual Sciences) David W. Hutton, PhD, (Health Management and Policy)	12/01/2011-11/30/2012 $93,715	Assessing the cost-effectiveness of different interventions for clinically significant diabetes macular edema	This interdisciplinary team wishes to: 1) capture utilization patterns of some newer interventions for the management of clinically significant macular edema (CSME) among enrollees in a large national U.S. managed care network over the past decade: 2) capture rates of ocular and systemic side effects associated with these interventions and the need for subsequent repeat or alternative interventions for CSME; 3) perform a cost-effectiveness analysis to determine whether these newer interventions are more cost effective and to identify which intervention confers the greatest value.	N/N	5	4	NIH/JAEB Center for Health Research 15-PAF05628	Funded	04/01/2015-09/30/2015	Yes and Yes

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41	Atta Ahmad, PhD (Life Sciences Institute)	02/10/2013-11/30/2013 $50,000	Examining the role of chaperones in insulin quality control and its relation to type II diabetes	Dr. Ahmad proposes to: 1) characterize the interaction between IAPP and both cytosolic and ER-resident Hsp70s; and 2) determine structures of IAPP peptides bound to the SBD of Hsp70. These studies will reveal how Hsp70 binds to monomeric and oligomeric IAPP and the results will provide a strong basis for pursuing further studies on the role of PQC in type II DM.	N	0	0	None	N/A	N/A	Yes
42	Anuska V. Andjelkovic-Zochowska, MD, PhD, (Pathology)	02/10/2013-11/30/2013 $50,000	Blood brain barrier dysfunction in diabetes: the role of miRNA126 in regulation of blood brain barrier integrity	This proposal addresses the mechanisms underlying the effects of hyperglycemia on brain endothelial cell-cell interactions and consequently blood brain barrier (BBB) permeability by evaluating: 1) morphological and functional alterations in the brain endothelial barrier under hyperglycemic conditions; and 2) the molecular mechanisms by which miRNA126 regulates connexin43 and BBB integrity during diabetes.	N	0	0	Pending Support	Pending	04/01/2017-03/31/2022	Yes
43	Jun Li, PhD, (Human Genetics)	02/10/2013-11/30/2013 $50,000	Genetic analysis of a rat model of aerobic capacity and diabetes risk	Dr. Li proposes to analyze two lines of rat that differ significantly in intrinsic (untrained) running capacity and a wide range of diabetes-related phenotypes. This pilot project will study genomic evolution of the two lines as they undergo selection from the same base population.	N	0	1	NIH/NIDDK R01DK099034	Funded	06/01/2014-05/31/2017	Yes
44	Diane M. Robins, PhD, (Human Genetics)	02/10/2013-11/30/2013 $50,000	KRAB-ZFPs as genetic modifiers of sex-dependent metabolic disease	Dr. Robins's central hypothesis is that Rsl counters hormonal and nutritional cues in a gene-, sex- and tissue-specific manner to modulate genes that affect metabolism, impacting risk of metabolic disease. The proposed integrative approach in the uniquely accessible Rsl model will elucidate epigenetic control of sex-dependent metabolic function and how loss of this control predisposes sex- biased metabolic disease.	N	1	2	Private Source	Funded	02/15/2016-02/14/2017	Yes
45	Xin Tong, MD, PhD, (Molecular & Integrative Physiology)	02/10/2013-11/30/2013 $50,000	Regulation of lipid metabolism by DDB1-CUL4A E3 ligase in liver steatosis	This proposal will investigate how DDB1-CUL4A E3 ligase regulates hepatic lipogenesis during HFD-induced liver steatosis. The proposed study will provide insights into novel therapeutic avenues for targeting ChREBP to treat fatty liver diseases in diabetic patients.	N	0	5	None	N/A	N/A	Yes

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46	Paula Goforth, PhD, (Pharmacology)	01/01/2014-12/31/2014 $50,000	Chronic regulation of lateral hypothalamic circuits by leptin	Dr. Goforth will examine the molecular mechanisms mediating chronic leptin regulation of Orexin (OX) neurons by electrophysiological analysis of OX function in NT LepRb KO animals and in diet-induced obesity (DIO), also characterized by chronic leptin perturbations.	N	0	1	None	N/A	N/A	Yes
47	Marianna Sadagurski, PhD, (Internal Medicine)	01/01/2014-12/31/2014 $49,935	Hypothalamic inflammation and energy homeostasis in long-lived mice models and its impact on whole body metabolism and metabolic signaling pathways	Aim 1 will use the crowded litter (CL) model to probe the effects of early life nutritional signals on hypothalamic function through inflammatory pathways. Aim 2 will exploit three drugs that extend mouse lifespan: the insulin sensitizer metformin, the anti-inflammatory agent nordihydroguaiaretic acid (NDGA), and acarbose, used in diabetes therapy to blunt post-prandial glucose excursions. We will test the hypothesis that each of these agents modulates the same hypothalamic functions changed in CL mice. Aim 3 will use the CL and drug models to see if they can prevent, or reverse, the effects of HFD in mice by changes in hypothalamic status.	N	3	5	U. Michigan Private Source	Funded	09/01/2015-08/31/2016	Yes
								Research Career Development Core Award NIH/NIA P30AG024824	Funded	09/01/2014-08/31/2016	
								UM Geriatrics Center Pilot Grant NIH/NIA P30AG024824	Funded	12/01/2015-11/30/2016	
48	Steven R. Buchman, MD, (Plastic Surgery) Karl J. Jepson, PhD, (Orthopaedic Surgery) Ernestina Schipani, MD, PhD, (Orthopaedic Surgery and Internal Medicine - MEND)	01/01/2014-12/31/2014 $100,000	Remediating diabetes-impaired bone fracture with Deferoxamine	The PIs have developed the use of Deferoxamine (DFO) therapy, an iron chelating agent, to restore the regenerative capacity of irradiated bone for the purpose of Distraction Osteogenesis. By up-regulating the hypoxia-inducible 1 alpha factor pathway (HIF-1α), DFO has been shown to be both vasculogenic and to assist in osteoblast proliferation.They will test the hypothesisthat DFO will restore vascularity and thereby re-establish the ability for diabetic bone to undergo normal fracture healing.	NTD/E /NTD	0	0	None	N/A	N/A	Yes, Yes and Yes

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49	Blake Roessler, MD, (Internal Medicine - Rheumatology) Crystal Holmes, DPM, (Internal Medicine - Metabolism, Endocrinology & Diabetes) Bin Nan, PhD, (School of Public Health - Biostatistics)	01/01/2014-12/31/2014 $49,074	Point-of-care bone composition measurements for early-stage detection of osteomyelitis in the diabetic foot	This proposal represents the next steps toward translating the Raman technology for point-of-care bone composition measurements in diabetic foot ulcers. A clinical study will enable us to address technological and infrastructure hurdles in translating the Raman technology. We plan a prospective longitudinal study of bone composition in diabetic foot ulcers using portable Raman instrumentation.	NTD/N /NTD	0	0	None	N/A	N/A	Yes, Yes and Yes
50	Craig Harris, PhD, (School of Public Health – Toxicology)	01/01/2015-12/31/2015 $39,265	Fetal programming of oxidative stress and insulin resistance	This proposal investigates the potential for fetal exposure to bisphenol A (BPA) and high fat diets (HFD) to alter redox status and signaling in adolescence and adulthood following fetal epigenetic reprogramming of redox-regulated lipid metabolism and antioxidant genes. The proposed research will examine developmental pathways linked through the redox signaling and oxidation observed in many chronic diseases to altered insulin resistance and metabolism.	NTD	5	0	None	N/A	N/A	Yes
51	Elizabeth Speliotes, MD, PhD, MPH, (Internal Medicine - Gastroenterology)	01/01/2015-12/31/2015 $50,000	Metabolic studies on Lyplal1 mutant mice	We hypothesize that LYPLAL1 acts to break down triglycerides and thus loss of its function would lead to hepatic steatosis but not to serum lipid or glucose abnormalities. To test this hypothesis, we created human cell line models of NAFLD where we show that knocking down LYPLAL1 results in triglyceride accumulation. We used cas9/CRISPR to disrupt Lyplal1 in mice and here aim to characterize liver and serum lipid/glycemic changes in these animals.	N	0	0	NIH/NIDDK R01DK106621 NIH/NIDDK R01DK107904	Funded Funded	09/05/2015-05/31/2020 09/01/2016-08/31/2021	Yes

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52	Jun Wu, PhD, (Neurology)	01/01/2015-12/31/2015 $50,000	Molecular regulation of beige fat through CHRNA2	Proposed studies will uncover molecular mechanisms how this ion-channel is functionally regulated in beige adipocytes and how signaling through CHRNA2 impacts systemic metabolic homeostasis. This information will suggest new approaches for the prevention and treatment of obesity and associated medical conditions, including diabetes.	N	0	4	NIH/NIDDK R01DK107583 Private Source	Funded Funded	01/11/2016-12/31/2020 01/01/2016-12/31/2017	Yes
53	Brian Callaghan, MD, (Neurology) Justin Dimick, MD, MPH, (Surgery)	01/01/2015-12/31/2015 $60,000	The association between the metabolic syndrome and neurologic outcomes in a bariatric surgery population	Patients with diabetes are at a high risk for the metabolic syndrome. Specific aims are: 1) To complete a cross sectional study utilizing rigorous definitions of neurologic complications to identify prevalent cases in bariatric surgery subjects. 2) To determine which modifiable risk factors of the metabolic syndrome are associated with an increased prevalence of neurologic complications.	N/E	2	0	NIH/NIDDK R01DK115687	Funded	07/01/2018-06/30/2023	Yes and Yes
54	Jun Hee Lee, PhD, (Molecular & Integrative Physiology) Uhn-Soo Cho, PhD, (Biological Chemistry)	01/01/2015-12/31/2015 $100,000	Biochemical basis for Sestrin2 in metabolism	Chronic activation of mTOR complex 1 (mTORC1) and prolonged ER stress during obesity induces desensitization of insulin signaling, which contributes to progression of type 2 diabetes. The PIs will determine the tertiary structure of human Sestrin2 (hSesn2) through X-ray crystallography. Based on this information, they will determine the biochemical role of hSesn2. The identified key residues will be mutated to generate mutant hSesn2 proteins, which will be examined for mTOR- and metabolism- controlling activities in cultured cells and in live mice.	N/N	0	1	NIH/NIA R21AG050903 NIH/NIDDK R01DK111465	Funded Funded	09/01/2015-05/31/2017 09/19/2016-08/31/2021	Yes and Yes
55	Kevin B. Atkins, PhD, (Internal Medicine – Nephrology)	01/01/2016-11/30/2016 $50,000	The role of GLUT4 on the development of vasculopathy in diabetes	Dr. Atkins proposes to test the hypothesis that expression of GLUT4 in vascular smooth muscle exerts effects that regulate vascular endothelial function and that changes in GLUT4 expression might be associated with the onset of endothelial dysfunction and the subsequent development of related vascular pathologies such as atherosclerosis.	N	1	0	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
56	Renny T. Franceschi, PhD, (Periodontics & Oral Medicine)	01/01/2016-11/30/2016 $50,000	Discoidin receptor 2 and adiponectin in energy and mineral homeostasis	Dr. Franceschi hypothesizes that Ddr2 regulates energy metabolism by controlling osteoblast/adipocyte ratio and by acting as an alternate Ddr2 receptor to control non-canonical aspects of adiponectin action. The Aims are: 1) Define the function of Ddr2 in energy metabolism and bone homeostasis in vivo. ate bone and fat-specific knockouts for initial phenotyping; and 2) Determine if Ddr2 can function as an alternate adiponectin receptor in bone and adipose tissue.	NTD	1	4	Michigan Integrative Musculoskeletal Health Center Pilot & Feasibility Grant P30 AR069620	Funded	07/01/2018-06/30/2019	Yes
57	Brigid Gregg, MD, (Pediatrics)	01/01/2016-11/30/2016 $50,000	Understanding the role of metformin during lactation in programming of offspring weight and glucose homeostasis	The objective of this proposal is to determine the effect of metformin during lactation on β-cell programming and type 2 diabetes (T2D) risk. Dr. Gregg hypothesizes that metformin programs offspring glucose homeostasis to decrease T2D risk through alterations in milk composition, which may then alter the intestinal microbiome.	N	5	0	None	N/A	N/A	Yes
58	Wei Perng, PhD, MPH (Nutritional Sciences, School of Public Health)	01/01/2016-11/30/2016 $18,754	A prospective study of metabolomics patterns and glycemia in U.S. and Mexican children	Using metabolomics data quantified on untargeted platforms in two pediatric populations undergoing the pubertal transition, Dr. Perng will: 1) ascertain whether the BCAA metabolite pattern precedes worsening glycemia, as indicated by fasting glucose, fasting insulin, and the homeostatic model assessment of insulin resistance (HOMA-IR) during ~4.5 years of follow-up; 2) assay specific metabolites on targeted platforms at baseline and follow-up and determine which are most predictive of worsening glycemia.	N	0	0	None	N/A	N/A	Yes
59	Marianna Sadagurski, PhD, (Internal Medicine)	01/01/2016-11/30/2016 $50,000	Role of growth hormone receptor (GHR) in nutrient-sensing leptin receptor expressing neurons (LEPR-B) in physiology and neuronal function	The PI hypothesizes that LepR-b neurons may represent the crucial locus for GH signaling to control metabolism. To test this,the PI will use a novel mouse lacking GH receptor in leptin receptor (LeprRb)-containing neurons to assess the role of the GH receptor in these cells to regulate energy balance, glucose homeostasis, gene expression and GH hypothalamic neuronal circuitry.	N	0	1	Private Source	Funded	01/01/2018-01/01/2022	Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
60	Tae-Hwa Chun, MD, PhD, (Internal Medicine) Shuichi Takayama, PhD, (Biomedical Engineering)	01/01/2016-11/30/2016 $100,000	Developing human adipose tissue on-a-chip (Fat Chip)	This interdisciplinary team aims to develop human adipose depot in a microfluidic device. Human white adipose tissue (WAT) mimetic will be developed from human mesenchymal stem cells and adipose tissue-derived stem cells as 3-D spheroid (adiposphere) using macromolecular crowding. The functionality of human WAT on-a-chip will be assessed with insulin-induced glucose lowering effect and lipolysis induced by the pulsatile delivery of growth hormone.	NTD /NTD	5	4	None	N/A	N/A	Yes and Yes
61	Carol F. Elias, PhD, (Molecular and Integrative Physiology)	01/01/2017-11/30/2017 $50,000	Cellular and molecular basis of diabetes-induced placental dysfunction	Dr. Elias will use unique mouse models of obesity and/or diabetes to assess changes in placental differentiation and embryo development. Her overall objective is to dissociate the molecular players and mechanisms by which obesity and diabetes may independently cause placental dysfunction. She hypothesizes that obesity and diabetes perturb distinct subsets of placental genes.	NTD	1	1	None	N/A	N/A	Yes
62	Jonathan Flak, PhD, (Internal Medicine)	01/01/2017-11/30/2017 $50,000	Uncovering the neurocircuitry that drive counterregulation downstream from the VMN	Dr. Flak has defined a novel subset of neurons within the ventromedial hypothalamus (VMN) that, when silenced, lowers baseline blood glucose, decreases the CRR to both insulin-induced hypoglycemia and glucoprivation, and eliminates hypoglycemia associated autonomic failure (HAAF)-like responses. He will further evaluate the role of these cells in the CRR to understand the mechanisms, both in terms of VMNcckbr neurons and pacap systems recruited to drive the CRR.	N	1	0	None	N/A	N/A	Yes
63	Jennifer Harder, MD, (Internal Medicine-Nephrology) Cristina Cebrian-Ligero, PhD, (Internal Medicine-Gastroenterology) Edgar Otto, PhD, (Internal Medicine-Nephrology)	01/01/2017-11/30/2017 $100,000	Modeling diabetic kidney disease using kidney organoids generated from human iPSC	This interdisciplinary team proposes to combine their unique expertise to establish a human induced pluripotent stem cell (iPSC)-based 3D kidney organoid culture system to be used to identify factors relevant to DKD progression. By comparing data from extremes of DKD phenotype, they hope to be able to identify alterations in tubular epithelial cell morphogenesis associated with progression in DKD.	N/N/N	1	0	None	N/A	N/A	Yes, Yes and Yes

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
64	Jiandie Lin, PhD, (Cell & Developmental Biology/Life Sciences Institute) Katsuo Kurabayashi, PhD, (Mechanical Engineering and Electrical Engineering) Jun Li, PhD, (Human Genetics)	01/01/2017-11/30/2017 $100,000	Elucidating the landscape of liver cell heterogeneity in normal and insulin resistant states by single cell RNA sequencing	This proposal has assembled an interdisciplinary team of investigators to elucidate the cell heterogeneity of mouse liver in health and disease states using single cell RNA sequencing. They will test the hypothesis that the quantitative and qualitative changes in liver cell heterogeneity may contribute to the development of obesity-associated insulin resistance.	E/NTD /NTD	0	0	None	N/A	N/A	Yes, Yes and Yes
65	David Bridges, PhD, (Nutritional Sciences)	01/01/2018-11/30/2018 $45,000	The role of adipose tissue in obesity-associated glucocorticoid responses	Glucocorticoids result in adverse metabolic effects including diabetes, NAFLD and weight gain. Dr. Bridges has generated preliminary data suggesting that while these risks are present in lean individuals, the consequences are dramatically worse in obese individuals. This proposal aims to identify the molecular and physiological mechanisms that cause these effects by testing effects of obesity on chromatin availability and the role of adipocytes in these effects. The goal is to identify why and in what tissues obesity causes increased metabolic risk to glucocorticoids.	E	0	0	None	N/A	N/A	Yes
66	Proprietary Info										

P&F #	PI (Dept.)	Dates & Amount of P&F Award	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
67	Robert O'Rourke, MD, (Surgery) Lonnie Shea, PhD, (Biomedical Engineering)	01/01/2018-11/30/2019 $80,000	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	This proposal will determine if artificial bioscaffold-based adipose tissue, engineered with ECM and seeded with preadipocytes, can be used to manipulate cellular and systemic metabolism. Aim 1 will test whether artificial bioscaffolds, conditioned with adipose tissue ECM and seeded with adipocytes from diabetic and non-diabetic humans, can be used to regulate the metabolic phenotype of engineered adipose tissue in vitro. Aim 2 use a murine model of visceral transplant of scaffold-based adipose tissues to determine if visceral transplant of artificial bioscaffold-based adipose tissue can be used to ameliorate systemic insulin resistance in murine obesity. These experiments represent a first step in the development of artificial 'designer' bioscaffold-based adipose tissues as a therapeutic vehicle for diabetes.	E/NTD	0	0	None	N/A	N/A	Yes and Yes
68	Amy E. Rothberg, MD, (Internal Medicine) Andrew D. Schrepf, PhD, (Anesthesiology)	01/01/2018-11/30/2019 $80,000	The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes	In this proposal the investigators will use the successful CR intervention run by Dr. Rothberg and measures of inflammation and centralized pain used by Dr. Schrepf to probe how the effects of both CR and WL impact inflammation and measures of these symptoms in obese individuals with and at risk for diabetes. Inflammatory measures will include both inflammatory output from isolated immune cells and inflammatory gene expression, and centralized pain will be measured with both self reported outcomes and through psychophysical pain testing. We will employ alternating periods of ad libitum eating ("normal diet") and CR in an ABAB design (n=50). This project will form the basis of joint applications between Dr. Rothberg and Dr. Schrepf for external funding of more definitive studies of these effects in individuals with and at risk for diabetes.	E/N	0	0	None	N/A	N/A	Yes and Yes

N= New Investigator
NTD= Established Investigator, New to Diabetes research
E = Established Investigator, with new, innovative research idea
A = # of Abstracts
P = # of Publications

Table C.1: OMICS Pilot Project Outcomes (renewal applications only)

P&F #	PI (Dept.)	Dates/Amount of P&F Award (direct costs)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
1	Ernesto Bernal-Mizrachi, MD (Internal Medicine - MEND)	2013-2014 $5,000	The role of the mechanistic target of rapamycin complex 1 (mTORC1) on β-cell mass, growth and proliferation	Dr. Bernal-Mizrachi proposed to perform metabolomic analysis of islets following genetic or pharmacologic manipulation of the beta cell mTORC1 pathway in vivo.	Omics	0	0	None	N/A	N/A	Yes
2	Gregory Cartee, PhD (Movement Science, Muscle Biology Laboratory)	2013-2014 $5,000	Comparing the mechanisms that lead to increased insulin-stimulated glucose uptake in skeletal muscle after a single bout of exercise	Dr. Cartee proposed to perform metabolomic analysis of rat skeletal muscle before, during or after a bout of exercise, to determine the alteration in metabolism that may contribute to overall improvement in glucose homeostasis with exercise.	Omics	0	2	NIH/NIDDK R01DK071771	Funded	05/05/2018-04/30/2021	Yes
3	Ormond MacDougald, PhD (Molecular & Integrative Physiology)	2013-2014 $5,000	Differential metabolism of regulated and constitutive marrow adipose tissues	Dr. MacDougald proposed to perform comparative RNA-seq to determine the transcriptomic differences that may underlie the divergent regulation and metabolic impact of two types of maarrow adipose tissue.	Omics	0	1	NIH/NIDDK R24DK092759	Funded	09/01/2015-08/31/2020	Yes
4	Diane M. Robins, PhD Christopher J. Krebs, PhD (Human Genetics)	2013-2014 $5,000	Genetic modulation of sex-dependent obesity by KRAB-zfp repressors	Drs. Robins and Krebs proposed to investigate the potential transcriptional basis for sex-dependent obesity in KRAB-zip knockout mice byRNA-seq transcriptional profiling of adipose tissue to identify potentially causative alterations in gene expression.	Omics	0	1	Private Source	Funded	02/15/2016-02/14/2017	Yes
5	Martin Myers, MD, PhD (Internal Medicine – MEND)	2014-2015 $10,000	Regulation of gene expression using mRNA recovered from ARC LepRb neurons by TRAP, for comparison to non-LepRb (non-TRAP) samples	The Myers lab is examining the regulation of gene expression using mRNA recovered from ARC LepRb neurons by TRAP, for comparison to non-LepRb (non-TRAP) samples. Dr. Myers requested funds to test a new method of deep sequencing that will enable the lab to assess much smaller samples (e.g. the ARC). He will be examining the transcriptome of metabolically crucial ARC LepRb neurons to try to understand what may go awry in these cells during obesity.	Omics	0	2	NIH/NIDDK R01DK056731	Funded	07/01/2018-06/30/2022	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (direct costs)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
6	Julie Lumeng, PhD (Environmental Health Sciences, Nutritional Sciences)	2014-2015 $10,000	Examining microbiome and metabolome mechanisms contributing to the development of obesity in early childhood	Dr. Lumeng proposes to use this P/F money to perform untargeted metabolomics analysis in the Metabolomics Core of a subset of her cohort representing the extreme quartiles of the distributions of psychosocial stress and among obese vs. non-overweight children. These results will be used as preliminary data for an RO1 grant application that will perform targeted metabolomic analysis with the full cohort to fully test her hypothesis that there are novel metabolomic biomarkers associated with both psychosocial stress exposure and obesity in young children.	Omics	0	0	None	N/A	N/A	Yes
7	Monica Dus, PhD (Molecular, Cellular & Developmental Biology)	2014-2015 $10,000	Biomarkers of metabolic syndrome in drosphilla	Dr. Dus is interested in the fine molecular mechanisms through which the environment/diet contributes first to obesity, and then to pre- and diabetes remain elusive. Her goal is to understand how an obesogenic diet impinges on the metabolome and epigenome to alter the central regulation of energy homeostasis. Our hypothesis is that a shift in the levels of metabolites because of diet, results in alterations in the proper functioning of neural circuits involved in energy homeostasis, which, in turn, leads to obesity and pre-diabetes.	Omics	0	0	None	N/A	N/A	Yes
8	Patrick Hu, PhD (Internal Medicine)	2014-2015 $10,000	Identification of DAF-16/FoxO target genes regulated by the conserved histone methyltransferase SET-4	Dr. Hu will use the DNA Sequencing and Bioinformatics Cores to define the subset of DAF-16/FoxO target genes regulated by DPY-21 and SET-4. Pair-wise comparisons of whole transcriptome profiles of five C. elegans strains and three triple mutants will be made to identify those genes.	Omics	0	1	None	N/A	N/A	Yes
9	Jiandie Lin, PhD (Life Sciences Institute, Cell & Develpmental Biology)	2014-2015 $8,514	Transcriptomic profiling of Nrg4 targets in the liver using RNA sequencing and Microarray profiling of liver and white adipose tissue gene expression in mice lacking Tsk	Dr. Lin proposed to use RNA-seq and microarray profiling of adipose and liver tissue from mice lacking Tsk, an important cofactor for Nrg4, to understand the potential mechanisms by which Tsk and Nrg4 control metabolism.	Omics	0	0	NIH/NIDDK R01DK102456 NIH/NIA R21AG055379	Funded Funded	07/15/15-05/31/20 04/01/17-03/31/19	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (direct costs)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
10	Lei Yin, PhD (Molecular & Integrative Physiology)	2014-2015 $10,000	Identification of molecular targets of hepatic E4BP4 in regulation of glucose metabolism through "OMICS" approaches	Dr. Yin proposed to take advantage of state-of-the-art technology at various OMICS cores to identify novel interacting proteins and post-translational modifications of the b-ZIP transcription repressor E4-binding protein 4 (E4BP4) as well as E4BP4 binding sites and target genes. Her lab studies the role of E4BP4 in the liver during the pathogenesis of obesity-induced insulin resistance. She will use the Proteomics Core to identify post-translational modifications of E4BP4 and E4BP4 binding partners, and the DNA sequencing Core to perform RNA-seq and ChIP-seq analysis to identify gene targets of E4BP4 using their liver-specific E4bp4 knockout mice.	Omics	0	0	None	N/A	N/A	Yes
11	Tae-Hwa Chun, MD (Internal Medicine)	2014-2015 $1,792	The role of CD47 in regulating muscle metabolism in obesity	Dr. Chun proposed to perform metbolomic profiling of skeletal muscles to study the roles of CD36 and CD47 downstream of thrombospondin 1, an ECM peptide released from visceral fat tissues during obesity and which may impact glucose homeostasis	Omics	1	0	None	N/A	N/A	Yes
12	Carey Lumeng, MD, PhD (Pediatrics & Communicable Diseases)	2014-2015 $10,000	Transcriptional profiling of human adipose tissue in relation to diabetes and weight loss	Dr. Lumeng hypothesizes that features of adipose tissue in the obese state will predict bariatric surgery outcomes in regards to percent weight loss and DM remission. He proposes to use the DNA Sequencing and Bioinformatics Cores to deep sequence both subcutaneous and visceral adipose tissue from diabetic and non-diabetic bariatric surgery patients.	Omics	0	0	NIH/NIDDK R01DK115190 Pending Support	Funded	07/18/17-06/30/21	Yes
13	David Olson, MD, PhD (Pediatrics & Communicable Diseases)	03/15/2016-03/15/2017 $10,000	Determining the molecular mechanisms through which the ventral medial nucleus of the hypothalamus regulates glucose homeostasis	Dr. Olson proposed to identify potential markers for and functionally important mediators of action in Mc3R-expressing VMN neurons, using RNA-seq of TRAP-purified mRNA from these cells. Dr. Olson hypothesizes that these neurons control skeletal muscle glucose uptake.	Omics	0	0				Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (direct costs)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
14	Liangyou Rui, PhD (Molecular & Integrative Physiology)	03/28/2016-03/27/2017 $10,000	Role of TRAF3, Snail1, and Slug in obesity and diabetes progression	Dr. Rui's studies suggest that TRAF3- or other TRAF family member-mediated ubiquitination of insulin signaling molecules couples inflammation to insulin resistance and type 2 diabetes progression. He will use the Proteomics Core to identify novel TRAF3 substrates and to identify K48-linked and K63-linked ubiquitination sites in these insulin signaling molecules. His lab observed that adipocyte-specific deletion of the transcription factor Snail1 promotes lipid trafficking from adipose tissue to the liver, leading to nonalcoholic fatty liver disease. They also observed that Slug is highly expressed in brown and beige adipocytes leading them to hypothesize that Slug regulates body weight and glucose metabolism at least in part by regulating brown and beige adipose thermogenesis and energy expenditure. Using his adipocyte-specific as well as brown/beige adipocyte-specific Snail1 and Slug knockout mice, he will use the DNA sequencing Core to perform RNA-seq to identify their targets in adipose and other metabolic tissues, and will use ChiP-seq to profile their genomic actions.	Omics	0	0	None	N/A	N/A	Yes
15	Kanakadurga Singer, MD (Pediatrics & Communicable Diseases)	04/12/2016-04/11/2017 $10,000	Probing sex differences in diet induced macrophages through transcriptional profiling	Given the potential important of adipose tissue macrophage-mediated inflammation, and the diffrences in inflammation between obese males and females, Dr. Singer proposed profiling differences in cellular metabolism and gene expression in male and female adipose tissue macrophages in the lean and high fat diet state.	Omics	0	0	None	N/A	N/A	Yes

Table D. Pilot and Feasibility Grants Program
Progress to Date for Pilot and Feasibility and Diabetes Interdisciplinary Study Program (DISP) Awards
Funded for the Period December 2016 – November 2017

Investigator(s)	Research Title	Brief Description	Progress —Brief Description	Presentations/ Manuscripts	New Funding
Carol F. Elias, PhD, Associate Professor, Molecular and Integrative Physiology	Cellular and molecular basis of diabetes-induced placental dysfunction	We will use unique mouse models of obesity and/or diabetes to assess changes in placental differentiation and embryo development. Our overall objective is to dissociate the molecular players and mechanisms by which obesity and diabetes may independently cause placental dysfunction. We hypothesize that obesity and diabetes perturb distinct subsets of placental genes.	The project is finalized and the findings have been published (Mahany et al., 2018). The abstract is below: Obese women are at high risk of pregnancy complications, including preeclampsia, miscarriage, preterm birth, stillbirth and neonatal death. In the present study, we aimed to determine the effects of obesity on pregnancy outcome and placental gene expression in preclinical mouse models of genetic and nutritional obesity. The leptin receptor null reactivatable (LepRloxTB), the LepR deficient (Leprdb/+) and high fat diet (HFD) fed mice were assessed for fertility, pregnancy outcome, placental morphology and placental transcriptome using standard qPCR and qPCR arrays. The restoration of fertility of LepRloxTB was performed by stereotaxic delivery of AAV-Cre into the hypothalamic ventral premammillary nucleus. Fertile LepRloxTB females were morbidly obese, whereas the wild type mice fed HFD showed only a mild increase in body weight. About 80% of the LepRloxTB females had embryo resorptions (about 40% of the embryos). In HFD mice, the number of resorptions was not different from controls fed a regular diet. Placentas of resorbed embryos from obese mice displayed necrosis and inflammatory infiltrate in the labyrinth, and changes	**Presentations:** **1)** Erica B Mahany, Nicole H Bellefontaine, Xingfa Han, **Carol F Elias**. “Hyperglycemia is associated with infertility and placental dysfunction in obese mice.” Endo 2017. April 1, 2017. Orlando, FL. **Manuscripts:** **1)** Mahany EB, Han X, Borges BC, da Silveira Cruz-Machado S, Allen SJ, Garcia-Galiano D, Hoenerhoff MJ, Bellefontaine NH, **Elias CF**. Obesity and high-fat diet induce distinct changes in placental gene expression and pregnancy outcome. Endocrinology. 2018 Apr 1;159(4):1718-1733. PubMed PMID: 29438518	None

			in the expression of genes associated with angiogenesis and inflammation (e.g., Vegfa, Hif1a, Nfkbia, Tlr3, Tlr4). In contrast, placentas from embryos of females on HFD showed changes in a different set of genes, mostly associated with cellular growth and response to stress (e.g., Plg, Ang, Igf1, Igfbp1, Fgf2, Tgfb2, Serpinf1). Sexual dimorphism in gene expression was only apparent in placentas from obese LepRloxTB mice. Our findings indicate that an obese environment and HFD have distinct effects on pregnancy outcome and the placental transcriptome.		
Jonathan Flak, PhD, Research Investigator, Internal Medicine	Uncovering the neurocircuitry that drive counterregulation downstream from the VMN	We have defined a novel subset of neurons within the ventromedial hypothalamus (VMN) that, when silenced, lowers baseline blood glucose, decreased the CRR to both insulin-induced hypoglycemia and glucoprivation, and eliminates hypoglycemia associated autonomic failure (HAAF)-like responses. We will further evaluate the role of these cells in the CRR to understand the mechanisms, both in terms of VMNcckbr neurons and pacap systems recruited to drive the CRR.	I am studying the downstream connections from the VMN in hypoglycemic counterregulation. I am trying to reveal which specific connections and factors released from these connections are important for hypoglycemic counterregulation.	**Presentations:** Presenting at Society for Neuroscience Meeting in November 2018 **Manuscripts:** None	None

Jennifer Harder, MD, Clinical Assistant Professor, Internal Medicine-Nephrology, Cristina Cebrian Ligero, PhD, Clinical Lecturer, Internal Medicine-Gastroenterology and Edgar Otto, PhD, Research Assistant Professor, Internal Medicine-Nephrology	Modeling diabetic kidney disease using kidney organoids generated from human iPSC	We propose to combine the unique expertise of three researchers to establish a human induced pluripotent stem cell (iPSC)-based 3D kidney organoid culture system to be used to identify factors relevant to DKD progression. By comparing data from extremes of DKD phenotype, we will be able to identify alterations in tubular epithelial cell morphogenesis associated with progression in DKD.	We generated kidney organoids from the Pima-DKD derived iPSCs as planned. While we were generating organoids, we established an alternative and improved transcriptomic analysis pipeline, single cell RNA-sequencing by Drop-seq. So in lieu of bulk RNA-seq as planned in our proposal, we opted to proceed with single cell RNA-seq of our organoids. We determined that we still have reprogramming viral (Sendai virus) contamination of our first rounds of organoids, so are currently in the process of clearing the lines & planning to regenerate organoids & repeat our analysis pipeline.	**Presentations:** **1) Harder JL, Otto EA**, Menon R, **Cebrian Ligero C**, Zou J, Freedman BS, Nelson RJ, Kretzler M. "Defining cellular ontologies in inducible pluripotent stem cell (iPSC)-derived kidney organoids by mapping into human nephrogenesis via scRNAseq." 2017 American Society of Nephrology Annual Meeting – Kidney Week. November 3, 2017. New Orleans, LA. **Manuscripts:** In Progress	None
Jiandie Lin, PhD, Associate Professor, Cell & Developmental Biology/Life Sciences Institute, Katsuo Kurabayashi, PhD, Professor, Mechanical Engineering and Electrical Engineering and Jun Li, PhD, Associate Professor, Human Genetics	Elucidating the landscape of liver cell heterogeneity in normal and insulin resistant states by single cell RNA sequencing	In this proposal, we have assembled an interdisciplinary team of investigators to elucidate the cell heterogeneity of mouse liver in health and disease states using single cell RNA sequencing. We will test the hypothesis that the quantitative and qualitative changes in liver cell heterogeneity may contribute to the development of obesity-associated insulin resistance.	We have completed single cell sequencing studies on the non-parachymal cell populations isolated from healthy and fatty livers. We are currently analyzing data and preparing a manuscript for submission in the next two months.	**Presentations:** None **Manuscripts:** In Progress	None

Table E. Pilot and Feasibility Grants Program
Human Subject and Animal Use Approvals, 2017-2018

Human Subject Use Approvals, 2017-2018

Principal Investigator	Project Title	Human Subject Information	Human Subjects No.	Approval Period
2017-18				
Ulrike Klueh, PhD, Wayne State University	Development of blood biomarkers for clinical management of diabetic foot ulcers	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	Protocol #: 1801001124/ IRB013118MP2E	05/03/18-05/02/21
Robert O'Rourke, MD Lonnie Shea, PhD	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	HUM00074075/ IRB00001996	12/07/17-12/06/18
Amy E. Rothberg, MD Andrew D. Schrepf, PhD	The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	HUM00030088/ IRB00000244	05/10/18-05/09/19

Animal Use Approvals, 2017-2018

Principal Investigator	Project Title	IACUC No./Animal Model	Approval Period
2017-18			
Dave Bridges, PhD	The role of adipose tissue in obesity-associated glucocorticoid responses	PRO00007103/mice	07/08/16-07/08/19
Proprietary Info			
Robert O'Rourke, MD Lonnie Shea, PhD	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	PRO00006911/mice	03/01/16-03/01/19
Suresh Palaniyandi, PhD, Wayne State University	Role for ALDH2 in endothelial cell energy metabolism in diabetic cardiomyopathy: An iPSC approach	1587/mice	10/19/17-10/18/20

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

Yes

Is the research exempt from Federal regulations?

No

Does this project involve a clinical trial?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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Withheld pursuant to exemption

Budget ; Redacted by agreement

of the Freedom of Information and Privacy Act

A. COMPONENT COVER PAGE

Project Title: Expanded Pilot and Feasibility Program
Component Project Lead Information: CARTER-SU, CHRISTIN

B. COMPONENT ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The specific aim of the Michigan Diabetes Research Center (MDRC) expanded Regional Pilot/Feasibility Study (P/F) Grants Program is to stimulate new research and collaboration in the areas of diabetes, its complications and related endocrine and metabolic disorders in the region. This research may be in areas of basic biomedical science or clinical research. This program will fund at least 2 P/F grants submitted by investigators from our three regional partners per year. A minimum of $100,000 per year will be provided by the MDRC and a minimum of an additional $20,000 per year will be provided through cost-sharing agreements with the University of Toledo, Michigan State University, and Wayne State University. Each year, the MDRC will solicit applications for grants from full-time instructional or research faculty at these three institutions. Those eligible include: 1) new investigators without current or past NIH research support who are beginning careers in diabetes research, 2) established investigators new to diabetes research who wish to focus their expertise on diabetes, and 3) established investigators who propose innovative research in diabetes that represents a clear departure from their ongoing research. Applications are peer-reviewed by at least two extramural investigators with expertise in the area of the application. Those with merit, as judged by this review process and the Grants Program Advisory Council, which includes representatives from the three regional partner universities, will receive P/F awards. The ultimate goal of the grant program is to enhance communication and collaboration among regional diabetes researchers, accelerate the pace of research, and enable awardees to generate sufficient preliminary data for successful applications for major research funding from the NIH or other national granting agencies.

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

File uploaded: B.2 Pilot and Feasibility Expanded.pdf

B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

Not Applicable

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

NOTHING TO REPORT

B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

NOTHING TO REPORT

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

No major changes are planned for the Expanded (Regional) Pilot and Feasibility Grant Program. The Expanded (Regional) Pilot and Feasibility Grant Program will continue to award funds to enable awardees to generate sufficient bodies of preliminary data to successfully apply for major research funding from the NIH or other national granting agencies and to accelerate the pace of discovery to prevent, treat and ultimately cure diabetes and its complications.

B.2 What was accomplished under these goals?

In August 2017 eight (8) applications were received for consideration for the Expanded (Regional) Pilot and Feasibility Study (**Table A**).

These applications were reviewed by twenty-one (21) external reviewers. The applications and reviewer comments were considered at the November 6, 2017 meeting of the Grants Advisory Council.

Two (2) Expanded (Regional) Pilot and Feasibility Study applications were funded (**Table B**).

Pilot project outcomes are listed in **Table C**.

Progress to date for Expanded (Regional) Pilot and Feasibility awards funded for the period December 2016 – November 2017 are listed in **Table D**.

Details about human research subjects and vertebrate animals for Expanded (Regional) Pilot and Feasibility awards are listed in **Table E**.

Table A. Expanded (Regional) Pilot and Feasibility Grants Program
Expanded (Regional) Pilot and Feasibility Grants Program Applications Reviewed for the Funding Period December 2017 – November 2018

Investigator	Type of Investigator	Department/School	Type of Application	Title
Elizabeth Berger, PhD	Established Investigator Transferring	Anatomy & Cell Biology, Wayne State University	Basic Biomedical Research	Neutrophils: A novel approach to the pathogenesis of diabetic retinopathy
Shahnawaz Imam, DVM, PhD	New Investigator	Medicine – Endocrinology, Diabetes & Metabolism, University of Toledo	Basic Biomedical Research	Antibody mediated insulin resistance, and concentrated insulin
Ulrike Klueh, PhD	Established Investigator – not an extension or outgrowth	Biomedical Engineering, Wayne State University	Clinical, Type T1 Translational Research	Development of blood biomarkers for clinical management of diabetic foot ulcers
Menq-Jer Lee, PhD	Established Investigator Transferring	Pathology, Wayne State University	Basic Biomedical Research	Sphingosine kinase 2 in nutritionally-stimulated adipose tissue expansion
Leonard Lipovich, PhD	Established Investigator Transferring	Neurology, Wayne State University	Basic Biomedical Research	LOC157273 long noncoding RNA controls the glycogen pathway in human hepatocytes
Marcia McInerney, PhD	Established Investigator – not an extension or outgrowth	Medicinal & Biological Chemistry, University of Toledo	Clinical, Type T1 Translational Research	The role of insulin receptor on T cells in type 1 diabetes and prediabetes
Suresh Palaniyandi, PhD	New Investigator	Internal Medicine – Hypertension & Vascular Research, Henry Ford Health System and Wayne State University	Basic Biomedical Research	Role for ALDH2 in endothelial cell energy metabolism in diabetic cardiomyopathy: An iPSC approach
Erik Shapiro, PhD	Established Investigator Transferring	Radiology, Michigan State University	Basic Biomedical Research	Multi-omics and non-invasive imaging to measure alterations in gene and protein expression in liver in large animal models of diabetes
Total: 8				

Table B. Expanded (Regional) Pilot and Feasibility Grants Program
Regional (Expanded) Pilot and Feasibility Awards for the Funding Period December 2017 – November 2018

investigator	Title	Type of Investigator	Type of Science	Type of Research	Brief Description
Ulrike Klueh, PhD	Development of blood biomarkers for clinical management of diabetic foot ulcers	Established Investigator – not an extension or outgrowth	Clinical, Type T1 Translational Research	Diabetes, Endocrinology, Obesity	Blood biomarkers serve an important role in the clinical management of a wide variety of disorders, including diabetes mellitus [DM]. While blood biomarkers such as blood glucose and HbA1C are useful for blood sugar regulation, there are no widely accepted blood biomarkers or blood biomarker profiles that are useful in identifying persons at-risk for developing diabetic foot ulcers (DFU) or monitoring their response to treatment. Currently, 25% of patients with diabetes will develop DFU, and account for approximately 60% of all non-traumatic lower-limb amputations in the United States (ADA). Recurring hospitalizations and outpatient treatment options for DFU are estimated to cost the United States upwards of $15 billion annually. As such, there is a clear need for the development of specific blood biomarkers able to predict and track disease progression, treatment and outcomes in DFU patients. The goal of the present application is to identify and validate blood biomarkers that are based on a specific subclass of extracellular vesicles (EV), known as exosomes. Specifically, we will focus on characterizing and correlating DFU derived exosome proteins (surface markers and contents) as well as RNA, with clinical metrics in these patients. To achieve these goals, we have developed the following Specific Aims: **Aim 1.** Characterization and correlation of RNAs present in exosomes derived from the blood (plasma) of patients with diabetic foot ulcers **Aim 2.** Characterization and correlation of proteins present in exosomes derived from the blood (plasma) of patients with diabetic foot ulcers
Suresh Palaniyandi, PhD	Role for ALDH2 in endothelial cell energy metabolism in diabetic	New Investigator	Basic Biomedical Research	Diabetes	Coronary endothelial cells are the first cardiac cells to encounter glucose and fatty acids from circulation in normal and diabetes mellitus (DM) conditions. Therefore, we suppose endothelial cells should play a critical role in the energy metabolism of the diabetic myocardium.

	cardiomyopathy : An iPSC approach				Decrease in the activity of aldehyde dehydrogenase (ALDH) 2, a cardiac mitochondrial enzyme, was associated with diabetic cardiac damage. East Asians (~500 million) have an E487K single-point mutation in the ALDH2 gene, denoted as ALDH2*2, which has intrinsically low ALDH2 activity and is linked with diabetic cardiomyopathy. DM reduces myocardial ALDH2 activity in general people too. Therefore, we hypothesize that reduced myocardial ALDH2 activity in type-2 diabetes contributes to impaired fatty acid and glucose utilization in coronary endothelial cells and thereby contributes to microvascular damage and heart failure. Our specific aims: **Aim 1** Low ALDH2 activity contributes to aberrations in glucose and fatty acid metabolism in the endothelial cells obtained from both ALDH2*2 diabetic mouse hearts and induced pluripotent stem cells (iPSC)s of ALDH2*2 carriers. **Aim 2** Augmenting ALDH2 activity via an ALDH2 activator, Alda-1 or overexpression via adeno associate virus (AAV)2 under endothelial cell specific Tie-2 promoter rescues fatty acid and glucose metabolism in those endothelial cells. **Aim 3** Augmenting ALDH2 activity decreases microvascular dysfunction and thus improves cardiac contractile function in ALDH2*2 mutant diabetic mice. Ultimately, our goal is to identify specific metabolic biomarkers (by metabolomics) and metabolic pathways (by gene array) that are regulated by ALDH2 and are involved in crucial metabolic changes in diabetic cardiomyopathy.

N= New Investigator
NTD= Established Investigator, New to Diabetes research
E = Established Investigator, with new, innovative research idea
A = # of Abstracts
P = # of Publications

Table C: Expanded (Regional) Pilot Project Outcomes (renewal applications only)

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
1	Menq-Jer Lee, PhD, (Pathology) Wayne State University	12/01/2011-11/30/2012 $50,000	Role of lipolysis activated autocrine sphingosine-1-phosphate signaling in adipocyte function	The role of sphingosine-1-phosphate (S1P) signaling in adipose inflammation remains to be elucidated. Dr. Lee proposed to test the hypothesis that β3-adrenergic receptors activate a novel autocrine S1P1/S1P3 signaling pathway that plays an important role in lipolysis-induced adipocyte inflammation.	N	0	2	None	N/A	N/A	Yes
2	Xuequn Chen, PhD, (Physiology) Wayne State University	02/10/2013-11/30/2013 $50,000	Quantitative proteomic analysis of altered ER homeostasis in pancreatic beta cells	The overall goal of this proposal is to understand the molecular mechanisms by which diabetes-causing conditions perturb ER homeostasis. Two approaches will be used to perturb ER homeostasis in MIN6 cells: 1) introduce proinsulin mutants, and 2) block ER exit of proinsulin. Using a state-of-the-art quantitative proteomics approach, Dr. Chen proposed to obtain a systematic characterization of ER protein changes regulating separate steps at ER entry, folding, export and degradation.	N	0	2	NIH/NIDDK R56DK102039 NIH/NIDDK R01DK110314	Funded Funded	09/15/2015-08/31/2016 09/01/2016-08/31/2021	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
3	Gina M. Leinninger, PhD, (Physiology) Michigan State University	02/10/2013-11/30/2013 $50,000	Role of lateral hypothalamic neurotensin signaling in energy balance and obesity	This proposal will examine how energy status modulates the activation and transcription of LHA Nts neurons, identifying molecular markers for subsets of LHA Nts neurons. Additionally, we will ablate LHA Nts neurons, or the midbrain neurons to which they project, to reveal the importance of this pathway in regulation of motivated behavior and energy balance. Collectively these studies will illuminate the roles of LHA Nts neurons in normal energy balance and how interruption of this signaling system contributes to obesity.	N	4	4	NIH/NIDDK R01DK103808	Funded	09/15/2014-07/31/2019	Yes
4	Jennifer W. Hill, PhD, (Physiology & Pharmacology) University of Toledo	01/01/2014-12/31/2014 $50,000	Inflammatory processes driving insulin resistance in polycystic ovary syndrome	The central hypothesis of this proposal, based on preliminary data from the applicant's laboratory, is that inflammatory cells, such as lymphocytes or monocytes, contribute to the development of PCOS-related insulin resistance. This hypothesis will be tested using a prenatally androgenized mouse model of PCOS that replicates the infertility and insulin resistance seen in the human disorder.	N	2	3	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
5	Dawn P. Misra, PhD, MHS, (Family Medicine & Public Health Sciences) Wayne State University	01/01/2014-12/31/2014 $50,000	Epigenetic mediators of the obese intrauterine environment	Capitalizing on data and biological samples from a well characterized longitudinal cohort study of obesity in pregnancy, Dr. Misra proposed to measure genome-wide methylation in DNA isolated from umbilical cord blood and assess maternal inflammation in a cohort of 100 large for gestational age (LGA; N=36) and appropriate for gestational age births (AGA; N=64). Specifically she aimed to identify methylated sites associated with an increased risk of LGA births.	NTD	0	0	None	N/A	N/A	Yes
6	Ren Zhang, PhD, (Center for Molecular Medicine and Genetics) Wayne State University	01/01/2015-12/31/2015 $50,000	Examination of therapeutic potentials of lipasin monoclonal antibodies and the ChREBP-mediated transcriptional regulation	Dr. Zhang will examine ChREBP-mediated regulation of lipasin expression and test the triglyceride-lowering effects of monoclonal lipasin neutralizing antibodies. Knowledge of 1) the molecular mechanism of its transcriptional regulation in response to nutritional stimulation and diabetes; and 2) therapeutic potentials of its neutralizing antibodies, is critical in understanding this newly discovered hormone and in developing therapeutic approaches to treating metabolic disease.	N	0	2	NIH/NHLBI R01HL134787	Funded	06/01/2017-03/31/2022	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
7	Jian Wang, PhD, (Pathology) Wayne State University	01/01/2015-12/31/2015 $50,000	Regulation of glycine metabolism in diabetes	Dr. Wang proposed that defects in Foxa2- dependent regulation of GLDC in insulin resistant states lead to reduced glycine, reduced glutathione, and reduced protection against diabetes-related oxidative stress. The goals of this pilot project were to characterize the role of Foxa2 in the transcriptional regulation of hepatic GLDC in cells and in a mouse model of diet-induced insulin resistance.	N	0	0	None	N/A	N/A	Yes
8	Kyle J. Burghardt, PharmD, (College of Pharmacy & Health Sciences) Wayne State University	01/01/2016-11/30/2016 $37,400	Insulin resistance induced by antipsychotic medication in the absence of weight gain: Impact of skeletal muscle epigenetic and protein mechanisms	The objective of this proposal is to identify skeletal muscle molecular changes underlying obesity-independent, AAP-induced insulin resistance in a clinical population. This work is expected to establish the role of the skeletal muscle in the epigenetic changes that underlie insulin resistance development for patients on AAPs.	N	0	0	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
9	Jennifer W. Hill, PhD, (Physiology & Pharmacology) University of Toledo	01/01/2016-11/30/2016 $12,600	Intergenerational obesity resulting from lactational impairment	Based on novel preliminary data, Dr. Hill hypothesized that glutamatergic neurons of the PVN that sense melanocortins influence pre- and postnatal hyperphagia and modify the activity of oxytocin neurons involved in lactation. To test her hypothesis, she planned to combine the use of novel mouse models and genetically encoded calcium indicators to determine whether loss of melanocortin sensing in the PVN increases weight gain during pregnancy and lactation and/or interferes with glutamatergic interneuron control of oxytocin release during lactation.	N	0	0	None	N/A	N/A	Yes
10	Alexander Johnson, PhD, (Psychology) Michigan State University	01/01/2016-11/30/2016 $50,000	Modulation of predictive regulation via chemogenetic and optogenetic control of melanin concentrating hormone	The studies in this proposal will examine lateral hypothalamic (LH) Melanin Concentrating Hormone (MCH) neurons and their role in modulating susceptibility to, and damage from, diet-induced obesity. The approach will be to use chemogenetic and optogenetic techniques, measures of ingestive behavior (e.g., licking microstructure, taste reactivity), and consummatory behaviors that are mediated by mechanisms of associative learning.	N	0	0	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
11	Robert Wessells, PhD, (Physiology) Wayne State University	01/01/2017-11/30/2017 $50,000	Cardiac lipolysis in drosophila is controlled by the ABHD5 homolog bremse (CG1882)	To understand the therapeutic potential of ABHD5 as a target for protection of cardiac function, it is essential to gain a better understanding of the genetic interactions of ABHD5 in heart specifically and how those may differ from its role in other tissues. To do this, Dr. Wessells has characterized a homologous gene in Drosophila and named it bremse. He proposed to take advantage of the rapid genetics and established assays for real-time cardiac physiology in the fly model to understand ATGL-dependent and -independent roles of ABHD5 in the heart.	N	0	0	None	N/A	N/A	Yes
12	Xiangmin Zhang, MD, PhD, (Pharmaceutical Sciences) Wayne State University	01/01/2017-11/30/2017 $50,000	Recombinant attenuated bacteria as drug to initiate insulin synthesis in vivo	In this project, Salmonella will be engineered to initiate insulin synthesis in vivo. Treatment efficacy of different recombinant Salmonella strains will be evaluated in diabetic rats by measuring blood glucose, plasma insulin, glucose tolerance, as well as glycogen and fat distribution in liver. Dr. Zhang anticipates developing an attenuated Salmonella that can efficiently initiate insulin synthesis in vivo.	N	0	0	None	N/A	N/A	Yes

P&F #	PI (Dept.)	Dates/Amount of P&F Award (DC)	Pilot Projet Title	Brief Project Description	P&F Type	A	P	Applications/ Grants	Pending/ Funded	Project Period	Still in Diabetes Research?
13	Ulrike Klueh, PhD, (Biomedical Engineering) Wayne State University	01/01/2018-11/30/2018 $70,000	Development of blood biomarkers for clinical management of diabetic foot ulcers	Dr. Klueh's goal of this application is to identify and validate blood biomarkers that are based on a specific subclass of extracellular vesicles (EV), known as exosomes. Specifically, she will focus on characterizing and correlating DFU derived exosome proteins (surface markers and contents) as well as RNA, with clinical metrics in these patients.	E	0	0	None	N/A	N/A	Yes
14	Suresh Palaniyandi, PhD, (Internal Medicine - Hypertension & Vascular Research) Wayne State University	01/01/2018-11/30/2018 $70,000	Role for ALDH2 in endothelial cell energy metabolism in diabetic cardiomyopathy: An iPSC approach	Dr. Palaniyandi hypothesizes that reduced myocardial ALDH2 activity in type-2 diabetes contributes to impaired fatty acid and glucose utilization in coronary endothelial cells and thereby contributes to microvascular damage and heart failure. His goal is to identify specific metabolic biomarkers (by metabolomics) and metabolic pathways (by gene array) that are regulated by ALDH2 and are involved in crucial metabolic changes in diabetic cardiomyopathy.	N	0	0	None	N/A	N/A	Yes

Table D. Expanded (Regional) Pilot and Feasibility Grants Program
Progress to Date for Expanded (Regional) Pilot and Feasibility Awards Funded for the Period December 2016 – November 2017

Investigator(s)	Research Title	Brief Description	Progress —Brief Description	Presentations/ Manuscripts	New Funding
Robert Wessells, PhD, Assistant Professor, Physiology, Wayne State University	Cardiac lipolysis in drosophila is controlled by the ABHD5 homolog bremse (CG1882)	In order to understand the therapeutic potential of ABHD5 as a target for protection of cardiac function, it is essential to gain a better understanding of the genetic interactions of ABHD5 in heart specifically and how those may differ from its role in other tissues. To do this, we have characterized a homologous gene in Drosophila and named it bremse. Here, we propose to take advantage of the rapid genetics and established assays for real-time cardiac physiology in the fly model to understand ATGL-dependent and ATGL-independent roles of ABHD5 in the heart.	Unfortunately, this work has encountered several delays, so there are not yet any resulting grants or papers, although I still expect there will be some in the future. I will nevertheless continue this work using discretionary funding sources and will acknowledge that the work was begun with MDRC funding as soon as it is published and/or funded.	**Presentations:** None **Manuscripts:** None	None
Xiangmin Zhang, MD, PhD, Assistant Professor (Research), Pharmaceutical Sciences, Wayne State University	Recombinant attenuated bacteria as drug to initiate insulin synthesis in vivo	In this project, Salmonella will be engineered to initiate insulin synthesis in vivo. Treatment efficacy of different recombinant Salmonella strains will be evaluated in diabetic rats by measuring blood glucose, plasma insulin, glucose tolerance, as well as glycogen and fat distribution in liver. We	It turned out the Salmonella delivery system is not as efficient in vivo as in vitro, and can only mildly lower blood glucose in STZ-induced diabetic rats. I decided to make more significant improvements to the system before submitting the proposal to NIH. With this award, we constructed a number of Salmonella strains with various mutations and many plasmids for insulin production. We also learned a lot from the animal experiments. I am	**Presentations:** None **Manuscripts:** In Progress	None

		anticipate to develop an attenuated Salmonella which can efficiently initiate insulin synthesis in vivo.	sure these pilot work will help my diabetic research project in the future. We have one manuscript under preparation and an invention disclosure for this award. Zhengping Yi and Xiangmin Zhang, "Isolating adherent cell clones by tracing circular petroleum jelly walls", 2017.		

Table E. Pilot and Feasibility Grants Program
Human Subject and Animal Use Approvals, 2017-2018

Human Subject Use Approvals, 2017-2018

Principal Investigator	Project Title	Human Subject Information	Human Subjects No.	Approval Period
2017-18				
Ulrike Klueh, PhD, Wayne State University	Development of blood biomarkers for clinical management of diabetic foot ulcers	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	Protocol #: 1801001124/ IRB013118MP2E	05/03/18-05/02/21
Robert O'Rourke, MD Lonnie Shea, PhD	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	HUM00074075/ IRB00001996	12/07/17-12/06/18
Amy E. Rothberg, MD Andrew D. Schrepf, PhD	The impact of calorie restriction and weight loss on inflammation and centralized pain in individuals at risk for diabetes	Human Subjects Involved: Yes Research Exempt: No Clinical Trial: No Phase III Clinical Trial: No hESC Research: No	HUM00030088/ IRB00000244	05/10/18-05/09/19

Animal Use Approvals, 2017-2018

Principal Investigator	Project Title	IACUC No./Animal Model	Approval Period
2017-18			
Dave Bridges, PhD	The role of adipose tissue in obesity-associated glucocorticoid responses	PRO00007103/mice	07/08/16-07/08/19
Proprietary Info			
Robert O'Rourke, MD Lonnie Shea, PhD	Engineered adipose tissue-bioscaffolds as a therapeutic tool for type 2 diabetes	PRO00006911/mice	03/01/16-03/01/19
Suresh Palaniyandi, PhD, Wayne State University	Role for ALDH2 in endothelial cell energy metabolism in diabetic cardiomyopathy: An iPSC approach	1587/mice	10/19/17-10/18/20

C. COMPONENT PRODUCTS

C.1 PUBLICATIONS

Not Applicable

C.2 WEBSITE(S) OR OTHER INTERNET SITE(S)

Not Applicable

C.3 TECHNOLOGIES OR TECHNIQUES

NOTHING TO REPORT

C.4 INVENTIONS, PATENT APPLICATIONS, AND/OR LICENSES

Not Applicable

C.5 OTHER PRODUCTS AND RESOURCE SHARING

Nothing to report

D. COMPONENT PARTICIPANTS

Not Applicable

E. COMPONENT IMPACT

E.1 WHAT IS THE IMPACT ON THE DEVELOPMENT OF HUMAN RESOURCES?

Not Applicable

E.2 WHAT IS THE IMPACT ON PHYSICAL, INSTITUTIONAL, OR INFORMATION RESOURCES THAT FORM INFRASTRUCTURE?

Not Applicable

E.3 WHAT IS THE IMPACT ON TECHNOLOGY TRANSFER?

NOTHING TO REPORT

E.4 WHAT DOLLAR AMOUNT OF THE AWARD'S BUDGET IS BEING SPENT IN FOREIGN COUNTRY(IES)?
Not Applicable

F. COMPONENT CHANGES

F.1 CHANGES IN APPROACH AND REASONS FOR CHANGE

Not Applicable

F.2 ACTUAL OR ANTICIPATED CHALLENGES OR DELAYS AND ACTIONS OR PLANS TO RESOLVE THEM

NOTHING TO REPORT

F.3 SIGNIFICANT CHANGES TO HUMAN SUBJECTS, VERTEBRATE ANIMALS, BIOHAZARDS, AND/OR SELECT AGENTS

F.3.a Human Subjects

No Change

F.3.b Vertebrate Animals

No Change

F.3.c Biohazards

No Change

F.3.d Select Agents

No Change

G. COMPONENT SPECIAL REPORTING REQUIREMENTS

G.1 SPECIAL NOTICE OF AWARD TERMS AND FUNDING OPPORTUNITIES ANNOUNCEMENT REPORTING REQUIREMENTS

Not Applicable

G.2 RESPONSIBLE CONDUCT OF RESEARCH

Not Applicable

G.3 MENTOR'S REPORT OR SPONSOR COMMENTS

Not Applicable

G.4 HUMAN SUBJECTS

G.4.a Does the project involve human subjects?

No

G.4.b Inclusion Enrollment Data

Not Applicable

G.4.c ClinicalTrials.gov

Not Applicable

G.5 HUMAN SUBJECTS EDUCATION REQUIREMENT

Not Applicable

G.6 HUMAN EMBRYONIC STEM CELLS (HESCS)

Does this project involve human embryonic stem cells (only hESC lines listed as approved in the NIH Registry may be used in NIH funded research)?

No

G.7 VERTEBRATE ANIMALS

Not Applicable

G.8 PROJECT/PERFORMANCE SITES

Not Applicable

G.9 FOREIGN COMPONENT

Not Applicable

G.10 ESTIMATED UNOBLIGATED BALANCE

Not Applicable

G.11 PROGRAM INCOME

Not Applicable

G.12 F&A COSTS

Not Applicable

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Withheld pursuant to exemption

Budget ; Redacted by agreement

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