

## **Marianna Sadagurski, Ph.D.**

Assistant Professor  
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### **Education and Training:**

- 09/1997-07/2000 B.Sc. Major: Biological Science, Tel Aviv University, Israel
- 09/2000-05/2006 Ph.D. Department of Pathology, Tel Aviv University, Israel
- 02/2002-03/2003 Visiting graduate student, German Research Cancer Center, (DKFZ), Heidelberg, Germany
- 12/2003-03/2005 Graduate student training (TAU-NIH), Derek LeRoith (advisor), Diabetes Branch, NIDDK, NIH
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### **Academic Appointments:**

- 5/2006-8/2012 Postdoctoral research fellow, Morris White lab. Department of Endocrinology, Harvard Medical School, Howard Hughes Medical Institute, Boston, MA
- 8/2011-8/2012 Visiting scientist, Martin Myers lab, MEND Institute, University of Michigan, Ann Arbor, MI
- 8/2012-8/2015 Assistant Research Scientist, Richard Miller lab, Department of Internal Medicine, University of Michigan, Ann Arbor, MI
- 8/2015-11/2016 Assistant Research Professor, Department of Internal Medicine, University of Michigan, Ann Arbor, MI
- 11/2016-present Adjunct Assistant Research Professor, Department of Internal Medicine, University of Michigan, Ann Arbor, MI
- 11/2016-present Assistant Professor, Department of Biological Sciences, IBio, Wayne State University, Detroit, MI
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### **Research Support:**

#### **Ongoing Research support**

Wayne State University startup  
Role: Principal Investigator

11/15/2016-11/1/2019

The purpose of this grant is to set up the PI's laboratory and fund preliminary studies needed to be competitive for extramural research support.

American Diabetes Association  
Junior Faculty Development award 1-18-JDF-063  
Role: Principal Investigator (20% effort)

1/1/2018 – 1/1/2022

In this proposal, we will determine the role of growth hormone receptor in hypothalamic leptin receptor expressing neurons

### **Previous Research Support**

Pilot Grant from the Michigan Diabetes Research Center (MDRC) 1/1/2016 – 1/1/2017  
(P30DK092926)

Role: Principal Investigator (Sadagurski)

Role of growth hormone receptor (GHR) in nutrient-sensing leptin receptor expressing neurons in physiology and neuronal function

The goal of this study is to investigate the role of GH signaling in specific hypothalamic neurons

Pilot Grant from MMOC/MNORC Pilot/Feasibility Program 9/1/2016-8/31/2017  
Growth hormone receptor modulates glucose homeostasis in nutrient-sensing leptin receptor expressing neurons  
Role: Principal Investigator (Sadagurski)

Glenn Foundation for Medical Research 9/1/2015-8/31/2016  
UM Glenn Center for Aging Pilot Grant  
Role: Principal Investigator for Pilot Grant (Sadagurski)

Effect of anti-aging drugs on age-related CNS inflammation

The objective of this study is to evaluate neuroinflammatory changes in mice exposed to anti-aging drugs

Research Career Development Core Award 09/01/2014-08/31/2016  
Claude Pepper Older Americans Center/NIH (P30 AG024824)  
Role: Principal Investigator (Sadagurski)

The goal of this support is to support salary of the PI while conducting the research on the role of hypothalamic inflammation in aging mice models

Claude D. Pepper Older Americans Independence Center/NIH (P30 AG024824)  
Role: Principal Investigator for Pilot Grant (Sadagurski) 12/01/2015-11/30/2016  
UM Geriatrics Center Pilot Grant  
Role of hypothalamic inflammatory response on aging

The objective of this study is to evaluate hypothalamic inflammatory responses in mice exposed to drugs that slow aging

NIH P30 AG013283

02/16/2014-02/10/2015

Nathan Shock Center Aging Rodent Core Support

Role: Principal Investigator (Sadagurski)

Generation of mice lacking GHR in leptin receptor neurons

The major goal of this support is to generate and assess whole body metabolism in mice lacking growth hormone receptor in leptin receptor expressing neurons

Pilot Grant from the Michigan Diabetes Research Center (2P30-DK020572)

Role: Principal Investigator (Sadagurski)

1/1/2014 – 12/31/2014

Hypothalamic inflammation in long-lived mice models

The objective of this study is to test the idea that "crowded litter" or CL mice modulate inflammatory pathways in the hypothalamus

Pilot award from Nathan Shock Center, Biology of Aging (AG-13283) 8/1/2013-7/1/2014

Role: Principal Investigator (Sadagurski)

Hypothalamic regulation in crowded litter mice: early life control of aging and longevity

The objective of this study is to test whether reduced availability of milk during the first 3 weeks of life can "reset" the hypothalamic control of appetite and thus prolong adult health and longevity

Nathan Shock Center of Excellence in Aging/NIH (P30 AG013283)

07/24/2013

Functional Assessment Core Support

Role: Principal Investigator (Sadagurski)

The role of metabolic regulation in the long-lived crowded litter mice

The major goal of this support was to assess parameters of energy balance in the crowded litter (CL) mice

P01-AG031736-01

04/1/2009 – 03/31/2014

Role: Co-investigator (Sadagurski)

Somatotrophic Axis and Healthy Aging: A Search for Mechanisms. Project 3: "IGF-I Effects on Stress Resistance and Lifespan,"

This study analyzes stress responses in skin fibroblasts from mice with organ-specific reductions in GH receptor function.

Ellison Medical foundation

11/01/2008-11/30/2012

White MF, PI, Role: Postdoctoral fellow (Sadagurski)

Irs2 signaling in neuronal degeneration and life span

The objective of this study was to test whether IRS2 promotes neural degeneration, and progression of Huntington disease.

NIH-TAU Graduate Excellence Partnership Fellowship

12/1/2003-03/30/2005

Graduate school fellowship for M. Sadagurski. NIH PI D. LeRoith

The role of IGF1R in skin proliferation and differentiation

The goal of this project was to establish the role of IGF1 receptor in skin cellular processes that effect diabetes wound healing.

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## Honors and Awards

2001	Young investigator award, International Symposium on Insulin Receptor and Insulin Action award, Geneva, Switzerland
2001	Dean's Award, Tel-Aviv University, Israel
2002	Travel Grant award from 38th Annual Meeting of the EASD, Hungary
2003	Minerva Short-Term Student Research Grant, (DKFZ), Germany
2004	Dean's Award, Tel-Aviv University, Israel
2003-2005	NIH-TAU Graduate Excellence Partnership Program, NIDDK, NIH
2010	Young investigator award, American Diabetes Association
2010	Postdoctoral travel award, American Diabetes Association, Orlando, FL
2013	Travel award, 2013 Alliance for Healthy Aging Symposium, Groningen, Netherlands
2018	Junior Faculty Research Award, American Diabetes Association

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## Memberships in Professional Societies and Other Experience

2001-2004	Member, Israel Endocrine society
2002	Member, Israel Diabetes Association
2004	Member, American Society for Cell Biology
2002-2005	Member, European Association for the Study of Diabetes
2008	Member, American Endocrine Society
2008-present	Member, American Diabetes Association
2012-present	Review committee, Undergraduate Research Opportunity Program
2008-present	Reviewed manuscripts for multiple scientific journals (American Journal of Physiology-Endocrinology and Metabolism, Molecular Metabolism, Molecular and Cellular Endocrinology, Journal of Clinical Investigation, Diabetes, Cell Metabolism, Cell Reports
2012-present	Review committee, Undergraduate Research Opportunity Program (UROP) University of Michigan
2016-present	Molecular Genetics Methods Core Advisory Committee (MDRC) University of Michigan
2018	NIH Study Section (Early Career Reviewer (ECR)); Integrative Physiology of Obesity and Diabetes (IPOD) Study Section
2018	Abstract Referee for "The Obesity Society Annual Meeting"

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## Teaching:

2001-2005	Class Instructor in Histopathology (medical students), Tel Aviv University
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2002-2005	Teaching Assistant, Department of Pathology, Tel-Aviv University
2002-2006	BS/MS research, Supervisor, Tel-Aviv University
2013-present	Undergraduate research opportunity program (UROP), Faculty research sponsor, University of Michigan and Wayne State University
2016	Invited lecturer, Chemistry 290-Twenty two ways to think about drugs, University of Michigan
2017	Graduate students' seminar, WSU (2 credits, winter semester)
2017-2018	4012 Comparative Physiology (3 credits, fall semester)
2018	5067 Selective topics on Central regulation of obesity (3 credits, winter semester)

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### Invited Seminars:

2014	Hypothalamic control of aging in long-lived mice models, MichBio, Detroit
2015	School of Public Health, University of Michigan
2015	Molecular and Cellular Endocrinology, City of Hope, Duarte, CA
2016	Department of Biological Sciences, Texas Tech University
2016	Human and Evolutionary Biology, University of Southern California
2016	IBio, Wayne State University (WSU), Detroit, MI
2017	Insight Institute of Neurosurgery and Neuroscience, Flint MI
2017	Department of Pharmacology, Medical School, WSU
2017	Diabetes Research Center, University of Michigan
2017	Eugene Applebaum College of Pharmacy and Health Sciences, WSU
2018	"Lipids at Wayne", WSU

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### Selected Extramural Oral Presentations:

Israel Diabetes Association Annual Meeting. IRS1 and IRS2 have distinct roles in primary skin keratinocytes and skin fibroblasts. **2001, Oral presentation**

Annual Meeting of the Israel Endocrine society. Different roles for IRS2 in primary skin keratinocytes and skin fibroblasts. **2001, Oral presentation**

38th Annual Meeting of the European Association for the Study of Diabetes, Budapest, Hungary. IRS2 have distinct roles in primary skin keratinocytes and skin fibroblasts. **2002, Oral presentation**

Annual Meeting of the Israel Endocrine society. The Role of Insulin Signaling in Diabetes Skin Complications: An Organotypic Skin Co-culture Model. **2003, Oral presentation**

65th Annual Meeting of Society of Investigative Dermatology, St. Louis, MO. Differential roles of insulin and IGF-1 in skin - an organotypic co-culture model. **2004, Oral presentation**

90th Endocrine Society Annual Meeting, San Francisco, CA  
Overexpression of human interleukin 6 prevents diet-induced obesity by suppressing food intake and increasing energy expenditure. 2008, Oral presentation

69th Annual Meeting of the American Diabetes Association, New Orleans, LA.  
Deletion of insulin receptor substrate 2 (Irs2) in leptin receptor (LepRb) expressing neurons causes obesity and diabetes. 2009, Oral presentation

Invited Speaker of Keystone Symposia on Diabetes, Vancouver, Canada  
Inactivation of Foxo1 in leptin receptor (LepRb)-expressing neurons reverses obesity and diabetes, caused by deletion of insulin receptor substrate 2 (Irs2). 2010, Oral presentation

70th scientific sessions of the American Diabetes Association, Orlando, FL.  
Decreased Irs2 signaling ameliorates brain pathologies and extends survival in a mouse model of Huntington disease. 2010, Oral presentation

Invited Speaker of the 42 Annual Meeting of the American Aging Association, Baltimore, MD  
Hypothalamic regulation in crowded litter mice: Early life control of aging and longevity. 2013, Oral presentation

Invited Speaker of the 76th scientific sessions of the American Diabetes Association, New Orleans, LA.  
Growth Hormone Receptor (GHR) Regulates Hepatic Glucose Production in Nutrient-sensing Leptin Receptor Expressing Neurons. 2016, Oral presentation

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## **Bibliography:**

### **Peer-reviewed Publications**

**Sadagurski M**, Weingarten G, Rhodes CJ, White MF and Wertheimer E. Insulin receptor substrate 2 (IRS-2) plays diverse cell-specific roles in the regulation of glucose transport. *J Biol Chem.* 2005 Apr 15; 280(15):14536-44.

**Sadagurski M**, Yakar S, Weingarten G, Holzenberger M, Rhodes CJ, Breitkreutz D, LeRoith D and Wertheimer E. IGF-1 receptor signaling regulates skin development and inhibits skin keratinocytes differentiation. *Mol Cell Biol.* 2006 Apr;26(7):2675-87.

**Sadagurski M**, Nofech-Mozes S, Spravchikov N, Weingarten G, Teruachi Y, White MF, Kadowaki T and Wertheimer E. Insulin receptor substrate 1 (IRS-1) plays a unique role in normal epidermal physiology. *J Cell Physiol.* 2007 Nov;213(2):519-27.

Carew RM, **Sadagurski M**, Goldschmeding R, Martin F, White MF and Brazil DP. (2010) Deletion of Irs2 causes reduced kidney size in mice: role for inhibition of GSK3 $\beta$ . *BMC Developmental Biology* 2010, 10:73.

**Sadagurski M**, Norquay L, Farhang-Fallah J, Copps K, and White MF. Human IL6 enhances leptin action in mice. *Diabetologia*. 2010 Mar;53(3):525-35.

**Sadagurski M**, Cheng Z, Rozzo A, Palazzolo I, Dong X, Krainc D and White MF. IRS2 increases mitochondrial dysfunction and oxidative stress in a mouse model of Huntington disease. *J Clin Invest*. 2011 Oct 3;121(10):4070-81.

**Sadagurski M**, Leshan RL, Patterson C, Rozzo A, Dong X, Skorupski J, Depinho R, Myers MG, and White MF. IRS2 signaling in LepR-b neurons suppresses FoxO1 to control energy balance independently of leptin action. *Cell Metabolism*. 2012 May 2;15(5):703-712.

**Sadagurski M** and White MF. Integrating metabolism and longevity through insulin and IGF1 signaling. *Endocrinol Metab Clin North Am*. 2013 Mar;42(1): 127-148.

**Sadagurski M**, Dong X, Myers MG and White MF. Irs2 and Irs4 synergize in non-LepRb neurons to control energy balance and glucose homeostasis. *Molecular Metabolism*. 2013 Oct 23;3(1):55-63.

**Sadagurski M\***, Landeryou T, Blandino-Rosano M, Cady G, Elghazi L, Meister D, See L, Bartke A, Bernal-Mizrachi E and Miller RA. Long-lived crowded litter (CL) mice exhibit lasting effects on insulin sensitivity and energy homeostasis. (Corresponding author) *Am J Physiol Endocrinol Metab*. 2014 Apr 15.

Tallaksen-Greene S, **Sadagurski M**, Zeng L, Mauch R, Perkins M, Miller RA, Paulson H, and Albin R. Differential Effects of Delayed Aging on Phenotype and Striatal Pathology in a Murine Model of Huntington Disease. *J Neuroscience*. 2014 Nov 19;34(47)

**Sadagurski M\***, Landeryou T, Cady G, Bartke A, Bernal-Mizrachi E and Miller RA. Transient early food restriction leads to hypothalamic changes in the long-lived crowded litter (CL) mice. (Corresponding author) *Physiological Reports* 2015 Apr 3(4)

**Sadagurski M\***, Landeryou T, Cady G, Kopchick JJ, List EO, Berryman DE, Bartke A, and Miller RA (Corresponding author). Growth Hormone Modulates Hypothalamic Inflammation in Long-Lived Pituitary Dwarf Mice. *Aging Cell* 2015 Aug 12

Kuznetsova A, Yu Y, Hollister-Lock J, Opare-Addo L, Rozzo A, **Sadagurski M**, Norquay L, Reed JE, El Khattabi I, Bonner-Weir S, Weir GC, Sharma A, White MF. Tricyclic compounds that increase IRS2 in human Islets and promote beta-cell growth and function in mice. *J Clin Invest*. Insight. 2016 Mar 17

**Sadagurski M\***, Cady G, Miller RA (Corresponding author). Anti-Aging Drugs Reduce Hypothalamic Inflammation in a Sex-Specific Manner. *Aging Cell* 2017. May 20

Cady G, Landeryou T, Kopchick JJ, List EO, Berryman DE, Elias C, Myers MG, Miller RA, **Sadagurski M**. Growth hormone receptor (GHR) in nutrient-sensing neurons regulates hepatic glucose production. *Molecular Metabolism* 2017. Mar 16;6(5):393-405.

Cady G and **Sadagurski M**. Targeting neuroinflammation - a potential for anti-aging interventions. *Aging* 2017, 9, 1951-1952