BIOGRAPHICAL SKETCH

Steering Committee, Senior Trainer

NAME: Davis, Dawn Belt

eRA COMMONS USER NAME: ddavis3

POSITION TITLE: Associate Professor, Division of Endocrinology, University of Wisconsin-Madison;

Section Chief, Endocrinology, William S. Middleton Memorial VA Hospital

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	MM/YYYY	FIELD OF STUDY
University of Wisconsin–Madison, Madison, WI	B.S.	05/95	Biochemistry
University of Chicago, Chicago, IL	Ph.D.	08/01	Pathology
University of Chicago, Chicago, IL	M.D.	06/03	
University of Washington, Seattle, WA		2003–2005	Internal Medicine
University of Wisconsin–Madison, Chicago, IL		2005–2009	Endocrinology

A. Personal Statement

I head a multi-faceted research program centered on diabetes and metabolism. My laboratory studies the adaptive responses of the pancreatic beta cell to stressors such as obesity. I also have expertise in clinical diabetes and obesity research. I am well versed in diverse fields of biological research including mouse and human genetics, molecular biology, cellular biology, physiology, and bioinformatics, which we can combine to answer complex biological questions. In addition, my clinical experience provides me with both the inspiration and the knowledge of to translate my work at the bench into improvements in patient care. Using models of obesity and diabetes, I have been able to identify regulatory pathways that drive beta cell proliferation and prevent apoptosis. My laboratory is interested in genetic, epigenetic, and fetal environmental impacts on pancreatic beta cell mass. **I have over 15 years of research mentoring experience and experience in graduate and post-graduate research training and programming.**

B. Positions and Honors

Positions and Employment

2009–2016 Assistant Professor – Department of Medicine, Division of Endocrinology, Diabetes, and Metabolism, University of Wisconsin, Madison, WI

2011–pres. Staff Physician – William S. Middleton Veterans Hospital – Madison, WI: Department of Medicine, Division of Endocrinology, Diabetes, and Metabolism

2013–pres. Madison VA Geriatric Research, Education and Clinical Center – Researcher/Member

2014–pres. Section Chief, Endocrinology – William S. Middleton Veterans Hospital – Madison, WI

2016-pres. Associate Professor, Director of Research – Department of Medicine, Division of Endocrinology, Diabetes, and Metabolism, University of Wisconsin, Madison, WI

Other Experience and Professional Memberships

Peer Review

2010 Research Grants Council – Hong Kong – ad hoc reviewer

2012–present *PLOS One, J Clin Endocrin & Metab, JOVE, AJP-Endocrin and Metab, Endocrinology, Diabetes, Diabetologia, Mol Endo, Islets, Nature:Scientific Reports, Mol Metab* – ad hoc reviewer

2012–2018 Midwest Islet Club – poster session judge, oral session judge

2013, 2016 Ad Hoc Reviewer – Diabetes UK RD Lawrence Fellowships

2014, 15, 18,19 American Diabetes Association Scientific Sessions abstract reviewer

2017-2019 Endocrine Society ENDO abstract reviewer

2010-2019 NIDDK Study Sections: NIDDK-B (K awards), UC4 Human Islet Research Network-Consortium on Targeting and Regeneration, Diabetes Research Centers (P30), CADO (R01/R21), F31/32 Training Grant Awards, Special Emphasis Panel R01- “Early-Stage Preclinical Validation of Therapeutic Leads”, UC4 HIRN Competitive Collaborative Projects for Human Islet Biology, Molecular and Cellular Endocrinology (R01/R15/R21), Special Emphasis Panel R01 (Co-Chair) – Reviewer Conflicts

Editorial Boards

2007–pres. *Endocrine Today*

2015-pres. *Journal of Investigative Medicine, JIM- High Impact Case Reports, AJP:Regulatory, Integrative, and Comparative Physiology*

Society Positions

2013-2014 Councilor – American Federation for Medical Research (AFMR) – Midwest Region
2013-present Board Member – Pearl Stetler Foundation Research Fund
2014-2016 Secretary/Treasurer- Midwest and National Council Member -AFMR
2016-2017 Chair-Elect - Midwest and National Council Member – AFMR
2017- 2018 Chair- Midwest and National Council Member - AFMR
2016-pres Program Planning Committee – Midwest Islet Club – Host of 2017 meeting at UW-Madison
2017-pres FASEB Clinical and Translational Research Subcommittee
2018-2021 The Endocrine Society Annual Meeting Steering Committee, Diabetes Lead for ENDO 2020
2018-2019 Vice President - Central Society for Clinical and Translational Research
2018-pres American Diabetes Association – Islet Biology Interest Group Leadership Team

Invited Presentations

2008, 2009 American Diabetes Association 68th Annual Scientific Sessions – oral abstract presentation
2010 Central Society for Clinical Research Annual Meeting – moderated oral poster presentation
2010 Midwest Islet Club Annual Conference – oral abstract presentation
2010 Endocrine Society Annual Meeting (ENDO) – session chair
2010 University of Michigan Islet Research Group Seminar
2010 University of Wisconsin Department of Surgery Research Conference
2011 Midwest Islet Club Annual Conference – oral abstract presentation
2011 American Diabetes Association 71st Annual Scientific Sessions – late breaking poster session
2011 University of Wisconsin Department of Nutrition Seminar Series
2011 University of Wisconsin Institute on Aging Seminar Series
2013 American Diabetes Association 73rd Annual Scientific Sessions – invited symposium speaker
2014 American Diabetes Association 74th Annual Scientific Sessions – session chair, guided poster
2015 Northwestern University – Endocrinology Seminar Series - invited speaker
2015 Vanderbilt University – Diabetes Research and Training Center Seminar – invited speaker
2016 Indiana University – Diabetes Research Center Seminar – invited speaker
2016 Chicago Sugar Club/Central Society of Clinical and Translational Research – invited speaker
2017,18 Medical College of Wisconsin – Depts of Biochem and Endo Seminar Series – invited speaker
2018 Endocrine Society Annual Meeting (ENDO) – invited symposium speaker
2018 University of Iowa – Diabetes Center Seminar series – invited speaker
2019 University of Kansas – Diabetes Seminar Series – invited speaker
2019 American Diabetes Association 79th Annual Scientific Sessions – invited symposium speaker

Honors

1995-2003 Medical Scientist Training Program Award (T32)
1998–1999 American Diabetes Association Medical Scholars Research Fellowship
1999-2000 NIH Cardiovascular Pathophysiology Training Grant (T32)
2000–2001 American Association for University Women American Dissertation Fellowship
2005 Huseby Award–Providence Hospital, Seattle, WA – Resident Award
2008 Wolfram Nolten Award for Outstanding Endocrine Fellow–University of Wisconsin
2008 Dickie Award–Department of Medicine, University of Wisconsin–for research contributions toward advancing the field of medicine
2008 University of Wisconsin Institute on Aging Postdoctoral Fellowship (T32)
2008–2009 Pearl Stetler Award–competitive extramural fellowship support for research year
2009–2014 NIDDK Career Development Award (K08)
2010–2011 Central Society for Clinical Research–Early Career Development Award
2010 Excellence in Endocrine Teaching Award
2011 University of Wisconsin Hilldale Undergraduate/Faculty Research Award
2013 American Federation for Medical Research Scholar Award

2013 UW Health Patient Experience Physician Champion Award
2014 American Federation for Medical Research Junior Physician Investigator Award
2015 University of Wisconsin Department of Medicine Puestow Research Award

C. Contribution to Science

1. Identification and characterization of novel skeletal muscle proteins important in membrane stability
My graduate work focused on understanding the pathophysiology of muscular dystrophy and genetic cardiomyopathies. We initially sought to identify genetic modifiers that could explain the phenotypic variability in patients with limb girdle muscular dystrophy 2B, which is caused by mutations in dysferlin. I identified and cloned the novel gene, myoferlin, which is closely related to dysferlin. We ultimately found that myoferlin was not upregulated in patients with dysferlin mutations. I went on to demonstrate that myoferlin, which is a transmembrane protein that contains several calcium-sensitive C2 domains, was expressed in skeletal and cardiac muscle and mediated calcium-dependent membrane fusion events. I generated a myoferlin knockout mouse, which showed that myoferlin was critical for maintenance of skeletal muscle integrity and repair in response to injury via its role in myoblast fusion to form syncytial myotubes. Since that time, myoferlin has been found to play important roles in endothelial cell adhesion, angiogenesis, and tumor proliferation and invasion. While my career ultimately moved into a different field, this work continues to represent my scientific mission and the goals of this proposal, which is to identify the key genetic modifiers of disease and work out the role of these genes and proteins in pathophysiology.

1. **Davis DB**, Delmonte AJ, Ly CT, McNally EM. "Myoferlin, a candidate gene and potential modifier of muscular dystrophy". *Hum Mol Genet* 2000; 9(2):217-226.
2. **Davis DB**, Doherty KR, Delmonte AJ, McNally EM. "Calcium-sensitive phospholipids binding properties of normal and mutant ferlin C2 domains". *J Biol Chem* 2002; 277(5):22883-88.
3. Vainzof M, Anderson LVB, McNally EM, **Davis DB**, Faulkner G, Moreira ES, Pavanello RCM, Passos-Bueno MR, Zatz M. "Dysferlin protein analysis in Limb-Girdle muscular dystrophies". *J Mol Neurosci* 2001; 17(1):71-80.
4. Doherty KR, Cave A, **Davis DB**, Delmonte AJ, Posey A, Earley JU, Hadhazy M, McNally EM. "Normal myoblast fusion requires myoferlin". *Development* 2005; 132(24):5565-75.

2. Identification of regulators of the adaptive beta cell proliferative response in beta cells. In the setting of insulin resistance and obesity, there is an adaptive beta cell proliferative response to expand beta cell mass and allow increased insulin production. We set out to understand how this adaptive process is regulated, with the goal of identifying pathways activated in adaptive physiology that could ultimately be harnessed to drive beta cell proliferation in the setting of diabetes and beta cell decline. Using two mouse strains with differential susceptibility to diabetes, I identified a tightly coordinated group of genes whose expression pattern in the islet was upregulated in non-diabetic obesity, when beta cell proliferation was occurring. This gene set contained many known cell cycle regulators and some novel genes. I set out to identify key transcriptional regulators of cell cycle in the beta cell and pursued two candidate genes found in this gene set. FoxM1, which is a transcription factor known to regulate cell division, was an attractive candidate. I found that overexpression of FoxM1 was sufficient to stimulate beta cell proliferation in both mouse and human islets. Additionally, its expression was highly correlated with glucose and insulin levels in a genetically mixed obese mouse population and with obesity and cell cycle gene expression in human islets, suggesting that FoxM1 is likely to be a key regulator of beta cell proliferation. We next pursued a novel, uncharacterized gene, Tcf19, which encodes a putative transcription factor. We found that Tcf19 was also upregulated in non-diabetic obese mouse and human islets. Knockdown of Tcf19 resulted in reduced β-cell proliferation and increased β-cell apoptosis. Specifically, we found a downregulation of ER homeostasis genes, that are required to maintain prevent ER stress from triggering apoptosis. Notably, Tcf19 has been genetically associated with both type 1 and type 2 diabetes in GWAS studes. Therefore, our initial identification of this as a potential key transcriptional regulator of β-cell proliferation in mouse models may explain the importance of this gene in human diabetes susceptibility. Ultimately, my work has identified novel transcriptional regulators of β-cell growth, particularly in human islets and with relevance to diabetes in humans.

1. Keller MP, Choi YJ, Wang P, **Davis DB**, Rabaglia ME, Oler AT, Stapleton DS, Argmann C, Schueler KL, Steinberg HA, Neto EC, Kleinhanz R, Turner S, Hellerstein MK, Schadt EE, Yandell BS, Kendziorski C, Attie AD. "A gene expression network model of type 2 diabetes links cell cycle regulation in islets with diabetes susceptibility", *Genome Res* 2008; 18(5):706-16. PMC2336811

2. **Davis DB***, Lavine JA*, Krautkramer KA, Suhonen JI, Rabaglia ME, Sperger JM, Fernandez LA, Keller MP, Yandell BS, Keller MP, Wang I, Schadt EE, Attie AD. "FoxM1 is upregulated by obesity and stimulates beta cell proliferation", *Mol Endocrinology* 2010, 24(9):1822-34. (*co-first authors, corresponding author) PMC2940473
3. K.A. Krautkramer, A.K. Linnemann, D.A. Fontaine, T.W. Harris, A.L. Whillock, G.J. Schleis, N.A. Truchan, J.A. Lavine, O. Cleaver, M.E. Kimple, **D.B.Davis**. "Tcf19 is a novel islet factor necessary for β-cell proliferation and survival", *AJP:Endocrin & Metab,* 2013, 305(5):E600-10. PMC3761170.
4. A. K. Linnemann, M. Baan and **D.B. Davis**, "Pancreatic beta cell proliferation in response to obesity" *Advances in Nutrition* 2014, 5(3):278-88. PMC4013180

3. Analysis of the expression and role of Cholecystokinin in the β-cell and its role in apoptosis prevention. Cholecystokinin (CCK) is a peptide hormone classically produced in the intestine and brain, where it signals to increase satiety and can stimulate insulin secretion. However, we identified CCK as the most upregulated gene in obese mouse islets and found that it was expressed in the β-cell. We initially thought that CCK may play a role in β-cell proliferation, similar to the role proposed for another incretin hormone, GLP-1. However, overexpression of CCK did not stimulate proliferation in mouse or human islets. However, we found that knockout of CCK in obese mice led to decreased β-cell mass secondary to increased β-cell apoptosis. This ultimately resulted in diabetes. I set out to further understand how CCK is upregulated in the β-cell, where it seems to have an important protective role. Interestingly, we found that CCK is upregulated by GLP-1, via a cAMP/CREB pathway that stimulates both CCK transcription and secretion. This identified a novel intra-islet hormonal signaling network. We also found that GLP-1 mediated protection from β-cell apoptosis was dependent on CCK signaling, suggesting that these two hormones cooperate to increase β-cell survival. There is significant translational potential in these studies, as GLP-1 is already in wide use as a therapeutic for type 2 diabetes and CCK has been studied for diabetes treatment as well.

1. Lavine JA, Raess PW, Stapleton DS, Rabaglia ME, Suhonen JI, Schueler KL, Koltes JE, Dawson JA, Yandell BS, Samuelson LS, Beinfeld MC, **Davis DB**, Hellerstein MK, Keller MP, Attie AD. "Cholecystokinin is upregulated in obese islets and expands β-cell mass by increasing β-cell survival". *Endocrinology* 2010, 151(8):3577-88. PMC2940525
2. A.K. Linnemann, J.C. Neuman, T.J. Battiola, J.A. Wisinski, M.E. Kimple, **D.B. Davis**. "Glucagon-like peptide-1 regulates transcription and secretion of cholecystokinin from β-cells", *Mol Endocrinology* 2015, 29(7):978-987. PMC 4484781
3. J.A. Lavine, C. Kibbe, M. Baan, S. Sirinvaravong, H.M. Umhoefer, K.A. Engler, L.M. Meske, K.A. Sacotte, D.P. Erhardt, **D.B. Davis**. "Cholecystokinin expression in the β-cell leads to increased β-cell area in aged mice and protects from streptozotocin-induced diabetes and apoptosis", AJP:*Endocrinol&Metab* 2015, 309(10):E819-28. PMC 4652070.
4. A.K. Linnemann and **D.B. Davis**. "GLP-1 and CCK production and signaling in the pancreatic islet as an adaptive response to obesity", *Journal of Diabetes Investigation* 2016, Suppl 1:44-9. PMC 4854504

4. **Identification of challenges and dissemination of solutions regarding reagents that impact scientific rigor and reproducibility.** During my scientific career, I have encountered setbacks related to unforeseen challenges with reagents or mouse models. In each of these instances, I have chosen to publish and discuss these challenges so that others in the research community could be aware and ensure careful assessment of their own reagents and experimental designs. In this way, I have made important contributions to the overall rigor and reproducibility in my field. Collectively, this work highlights my commitment to performing research with rigor and integrity.

1. J.A. Lavine*, P.W. Raess*, **D.B. Davis**, M.E. Rabaglia, B.K. Presley, M.P. Keller, M.C. Beinfeld, A.S. Kopin, C.B. Newgard, A.D. Attie. "Contamination with E1A-positive wild-type adenovirus accounts for species–specific stimulation of islet cell proliferation by CCK: A Cautionary Note" *Molecular Endocrinology* 2010, 24(2):464-7. PMC2817600
2. M. Baan, J. Bushkofsky, C.R. Kibbe, T. Harris, D. Sherman, **D.B. Davis**. "Transgenic expression of the human growth hormone minigene promotes pancreatic beta cell proliferation", *AJP:Regulatory, Integrative and Comparative Physiology* 2015, 309(7):R788-94. PMC 4631542
3. D.A. Fontaine, **D.B. Davis**. "Attention to background strain is essential in metabolic research: C57BL/6 and the International Knockout Mouse Consortium", *Diabetes*, 2016, 65(1):25-33. PMC 4686949

5. Identification of endocrine and metabolic changes in human subjects with obesity and gluco-regulatory disorders. Given my interest in pancreatic beta-cell growth and survival, I have been interested in the circulating factors that may drive adaptive change in the islet. I initiated a study on patients with a history of gastric bypass surgery, who had now developed hypoglycemia. Ultimately, in collaboration with a bariatric surgeon, we discovered that pancreatic beta cell function was not altered in these subjects and restoration of normal gut anatomy and feeding routes ameliorated hypoglycemia, hyperinsulinemia and gut peptide responses. I have sinceserved as site-PI in a multicenter phase II clinical trial investigating a GLP-1R antagonist for the treatment of post-bariatric hypoglycemia. In another project, we have also looked at circulating prostaglandins that may impact response to therapies for type 2 diabetes. These accomplishments highlight my ability to translate concepts and findings from the laboratory to clinical studies that can determine the pathophysiology and identify novel treatment options for obesity and disorders of glucose metabolism.

1. G.M. Campos, M. Ziemelis, R. Paparodis, M. Ahmed, **D.B. Davis**. "Laparoscopic reversal of Roux-en-Y Gastric Bypass: Technique and Utility for Treatment of Endocrine Complications" *Surg Obes Relat* Diseases, 2014, 10(1):36-43. (PMID 24120983. PMC n/a).
2. **D. B. Davis**, J. Khoraki, M. Ziemelis, S. Sirinvaravong, JY Han, G.M. Campos. "Roux en Y gastric bypass hypoglycemia resolves with gastric feeding or reversal: confirming a non-pancreatic etiology" *Mol Metabolism*, 2018, 9:15-27 (PMID 29449181, PMC5869737).
3. A.C. Weeks, M. Dart, X. Li, **D.B. Davis**, M.E. Kimple, "The impact of prostaglandin E2 levels on glycemic control and therapeutic response in human subjects with type 2 diabetes mellitus", *J Investigative Medicine*, 2015, 63(4);667.
4. C.J.E. Lee, H.M. Lawler, M. Tan, **D.B. Davis**, J. Tong, M. Glodowski, E. Rogowitz, C.A. Lamendola, R. Karaman, M.S. Dar, L. Porter, C.M. Craig, "28-Day Dosing with Avexitide Improves Hyperinsulinemic Hypoglycemia in Patients with Severe, Refractory Post-Bariatric Hypoglycemia: The PREVENT Study", J Endo Soc, 2019, Abstract Supplement

For all citations, please see the following:
https://www.ncbi.nlm.nih.gov/sites/myncbi/dawn.davis.1/bibliography/40752392/public/

D. Research Support

Ongoing Research Support

1. NIDDK R01 (R01DK110324) Davis (PI) 10/1/16-6/30/21
   "The role of GLP-1 and CCK in the pancreatic islet to promote beta-cell survival"
   - with Admin Suppl to Promote Diversity in Biomedical Research
2. Department of Medicine Pilot Award Davis (co-I, with Lamming) 8/1/16-7/31/18
   "Stopping Obesity and Diabetes by Amino Acid Reduction"
3. UW 2020: WARF Discovery Initiative Davis (co-I, with Kimple, Cox) 6/1/18-5/31/20
   "Building a Translational Research Pipeline to Personalize Diabetes Prevention and Treatment"
4. Veterans Affairs Merit Review Award Davis (PI) 04/01/19–03/31/23
   ""Functional studies of the novel diabetes gene TCF19" 1I01BX004715
5. NIDDK F31DK120275 Kim (PI) – Davis (Sponsor) 3/1/19-2/28/21
   " Selective cholecystokinin receptor signaling in the pancreatic islet as a therapeutic target against diabetogenic stress"

Completed Major Research Support

6. Veterans Affairs Merit Review Award Davis (PI) 04/01/13–03/31/17
   "Transcriptional Regulation of Pancreatic Beta Cell Mass" 1I01BX001880
7. NIDDK K08DK083442 Davis (PI) 07/01/09–06/30/14
   "Mechanisms of Beta Cell Proliferation in Mouse and Human Islets"
8. Eiger BioPharmaceuticals, Inc. Davis (Site PI) 2/18-1/19
   "PREVENT: A Phase 2, Multicenter, Randomized, Single-Blind, Placebo-Controlled Cross-Over Study to Assess the Efficacy and Safety of Exendin 9-39 in Patients with Postbariatric Hypoglycemia"