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**BIOGRAPHICAL SKETCH**  
**Senior Trainer**

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NAME: Davis, Dawn Belt

eRA COMMONS USER NAME: ddavis3

POSITION TITLE: Section Chief, Endocrinology, William S. Middleton Memorial VA Hospital; Associate Professor, Division of Endocrinology, University of Wisconsin-Madison

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**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**

My primary research goal is centered on pancreatic beta cell biology, with the aim to increase the number of functional beta cells in patients with diabetes. We specifically examine adaptation of beta cells to various stressors, to identify novel pathways important in beta cell proliferation and survival. We are interested in the adaptive responses of the maternal beta cells during pregnancy as well as the impact of the intrauterine environment on beta cell growth and development. I am well versed in diverse fields of biological research including physiology, genetics, molecular biology, cellular biology and bioinformatics, which we can combine to answer complex biological questions. Using models of obesity and diabetes, including in rodents, I have been able to identify regulatory pathways that drive beta cell proliferation and play a role in preventing apoptosis. In addition, my clinical experience provides me with both the inspiration and the knowledge of diabetes necessary to translate my work at the bench into improvements in patient care. 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**

2003–2005 Internal Medicine Residency - Categorical, Research Pathway; University of Washington, Seattle, WA

2005–2006 Clinical Fellowship in Endocrinology, Diabetes, and Metabolism; University of Wisconsin, Madison, WI

2006–2008 Clinical Research Fellow – Section of Endocrinology; Mentor: Alan Attie, PhD, Department of Biochemistry, University of Wisconsin, Madison, WI

2008–2009 Clinical Instructor/Research Associate - Section of Endocrinology; Mentor: Alan Attie, PhD, Department of Biochemistry, University of Wisconsin, Madison, WI

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

**Other Experience and Professional Memberships**

**Peer Review**

2010–present University of Wisconsin Department of Medicine Research Day Committee

2010 Research Grants Council – Hong Kong – ad hoc reviewer

2011–2012 UW Institute for Clinical and Translational Research Pilot Grants – ad hoc reviewer

2011 UW College of Agriculture and Life Sciences Hatch Grants – ad hoc reviewer  
 2012–2016 *PLOS One, J Clin Endocrin & Metab, JOVE, AJP-Endocrin and Metab, Endocrinology, Diabetes, Diabetologia, Mol Endo, Islets, Nature:Scientific Reports* – ad hoc reviewer  
 2012–2016 Midwest Islet Club – poster session judge, oral session judge  
 2013, 2016 Ad Hoc Reviewer – Diabetes UK RD Lawrence Fellowships  
 2014, 2015 American Diabetes Association Scientific Sessions abstract reviewer  
 2010-2017 NIDDK Study Sections: NIDDK-B (K awards), UC4 Human Islet Research Network- Consortium on Targeting and Regeneration, Diabetes Research Centers, CADO (R01/R21), F31/32 Training Grant Awards, Special Emphasis Panel R01- “Early-Stage Preclinical Validation of Therapeutic Leads”, UC4 Human Islet Research Network – “Competitive Collaborative Projects for Human Islet Biology”

#### Editorial Boards

2007–pres. *Endocrine Today*  
 2015-pres. *Journal of Investigative Medicine*

#### 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-pres Chair-Midwest and National Council Member - AFMR  
 2016-pres Program Planning Committee – Midwest Islet Club – Host of 2017 meeting at UW-Madison

#### Invited Presentations

2008, 2009 American Diabetes Association 68<sup>th</sup> 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 71<sup>st</sup> 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 73<sup>rd</sup> Annual Scientific Sessions – invited symposium speaker  
 2014 American Diabetes Association 74<sup>th</sup> 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 Medical College of Wisconsin – Biochemistry Seminar – invited 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  $\beta$ -cell proliferation and increased  $\beta$ -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 studies. Therefore, our initial identification of this as a potential key transcriptional regulator of  $\beta$ -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  $\beta$ -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, Kendzioriski 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  $\beta$ -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"(2014) *Advances in Nutrition*, 5(3):278-88. PMC4013180

### 3. Analysis of the expression and role of Cholecystokinin in the $\beta$ -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  $\beta$ -cell. We initially thought that CCK may play a role in  $\beta$ -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  $\beta$ -cell mass secondary to increased  $\beta$ -cell apoptosis. This ultimately resulted in diabetes. I set out to further understand how CCK is upregulated in the  $\beta$ -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  $\beta$ -cell apoptosis was dependent on CCK signaling, suggesting that these two hormones cooperate to increase  $\beta$ -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  $\beta$ -cell mass by increasing  $\beta$ -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  $\beta$ -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  $\beta$ -cell leads to increased  $\beta$ -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", (2016), *Journal of Diabetes Investigation*, 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" (2010) *Molecular Endocrinology*, 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", (2016), *Diabetes*, 65(1):25-33. PMC 4686949

**5. Identification of endocrine and metabolic changes in human subjects with obesity and glucoregulatory 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. The initial hypothesis in the literature was that these individuals had beta cell overgrowth and hyperinsulinemia, so I endeavored to find which hormones were altered in this condition that could drive this proliferative response. 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. In another project, we have also looked at circulating factors that may impact insulin secretion and/or 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. Papanicolaou, M. Ahmed, **D.B. Davis**. "Laparoscopic reversal of Roux-en-Y Gastric Bypass: Technique and Utility for Treatment of Endocrine Complications" (2014) *Surg Obes Relat Diseases*, 10(1):36-43. (PMID 24120983. PMC n/a).
2. **D. B. Davis** and G. M. Campos. "Postprandial Response to Altered Feeding Routes and Reversal Surgery in Roux en Y Gastric Bypass-Related Hypoglycemia" (2014) *J Invest Medicine* 62(4):708.
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.

For all citations, please see the following:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/dawn.davis.1/bibliography/40752392/public/?sort=date&direction=descending>

## D. Research Support

### Ongoing Research Support

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"

Department of Medicine Pilot Award Davis (co-PI, with Lamming) 8/1/16-7/31/17  
 "Stopping Obesity and Diabetes by Amino Acid Reduction"

Veterans Affairs Merit Review Award Davis (PI) 04/01/13–03/31/17  
 "Transcriptional Regulation of Pancreatic Beta Cell Mass" 1I01BX001880

### Pending Research Support

Wisconsin Partnership Program Davis (co-PI) 10/17-9/20  
 "Building a Research Pipeline to Personalize Diabetes Prevention and Treatment"

Veterans Affairs Merit Review Award (renewal) Davis (PI) 10/01/17–09/30/21  
 "Transcriptional Regulation of Pancreatic Beta Cell Mass" 1I01BX001880

### Completed Research Support

Wisconsin Partnership Program Education & Research Committee  
 New Investigator Program Davis (PI) 02/01/13–06/30/15  
 "Cholecystokinin in the Survival of Human Pancreatic Islets"

NIDDK K08DK083442 Davis (PI) Attie (Mentor) 07/01/09–06/30/14  
 "Mechanisms of Beta Cell Proliferation in Mouse and Human Islets"