BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Cyphert, Holly Ann (Damron)

eRA COMMONS USER NAME (credential, e.g., agency login): Cypherha

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Concord University, Athens, WV	B.S.	2003-2007	Biology (Pre-professional)
West Virginia University, Morgantown, WV	Ph.D.	2007-2012	Biochemistry and Molecular Pharmacology
West Virginia University, Morgantown, WV	Postdoctoral fellow	2012-2013	Biochemistry and Molecular Pharmacology
Vanderbilt University, Nashville, TN	Postdoctoral fellow	2013-2015	Molecular Physiology and Biophysics

A. Personal Statement

My background has positioned me with the background and expertise to be considered as a future junior investigator for the COBRE, focused on cellular transport in obesity related disorders. Throughout my scientific career, I have focused on studying diabetes mellitus and obesity. During my undergraduate work, I participated in multiple research internships that involved studying the translocation of stress proteins in diabetic and aged rodent models. These experiences paved my way to graduate school where I trained under Dr. Brad Hillgartner and studied the anti-diabetic hormone, FGF21. During my tenure, I received an American Heart Pre-doctoral fellowship and authored/co-authored several papers. Following graduate school, I pursued further training as a postdoctoral fellow at Vanderbilt in the lab of Dr. Roland Stein where I studied transcription factors involved in pancreas development/function and pregnancy. Together, these opportunities have given me a skill set to look at diabetes at a multi-organ level. Therefore, I aim to further delineate the interaction between tissues affected during diabetes/GDM (pancreas, liver), further elaborate on the role of bile acids, and translate my work to human therapeutics. In addition, I hope to continue my studies on FGF21 and discern its role in the pancreas. Being from West Virginia and seeing firsthand the devastation of this disease, my goal was always to come back to the state and mentor future researchers to help with the ongoing epidemic. Here at Marshall, I have the ability to do cutting-edge research with the help of core facilities and mentors that are involved in the field. In addition, I have been fortunate to be more involved in clinical research that has allowed me to further my research education and enhance my skill set. Noteworthy, I am Co-PI on a grant where we are investigating metabolic risk factors in college students and providing one group with an intervention that will hopefully decrease their chances of developing diabetes and/or obesity. I hope to be part of the groundbreaking research that will lead to better treatment options for the millions of people that suffer from diabetes, especially for my fellow West Virginians.

B. Positions and Honors

Positions and Employment

2004-2007	Lab/Teaching Assistant for Introductory Biology Courses, Concord University
2004-2007	Tutor for Biology, English, and Math, Student Support Services, Concord University
2005-2006	Summer Intern, Summer Undergraduate Research Fellowship (SURF), Laboratory of Dr. Eric Blough, Project: Regulation of MAP Kinase Activity in Obese Animal Models, Marshall University
2005-2006	Volunteer, CONTACT Crisis Center for Domestic Abuse, Huntington, WV
2005-2007	Volunteer, Rural Health Education, Area Health Education Centers (AHEC), Marshall University/Concord University, Presented health lectures to rural elementary/middle school students
2005-2006	Sports Editor of the *Concordian* newspaper, Concord University
2006-2007	Summer Intern, McNair Scholars Program, Laboratory of Dr. Darla Wise, Project: Effect of Aging on the Translocation of ERK from the Cytoplasm to the Nucleus in Skeletal Muscle, Concord University
2007-2012	Graduate Research Assistant, Laboratory of Dr. Brad Hillgartner, Department of Biochemistry, West Virginia University
2009-2012	Tutor for Biomedical Science Program (cell biology, genetics, biochemistry, metabolism)
2010-2011	Student Representative – Graduate Education Recruitment, WVU School of Medicine Biomedical Sciences Program, West Virginia University
2012-2013	Writer/Contributor to *The Catalyst,* Biochemistry Newsletter, Department of Biochemistry, West Virginia University
2012-2013	Post-Doctoral Fellow, Laboratory of Dr. Brad Hillgartner, Department of Biochemistry, West Virginia University
2013-2014	Secretary – Postdoctoral Association, Vanderbilt University
2013-2014	Diabetes Research and Training Core – T32 Research Fellow, Vanderbilt University
2014-2015	Contributor to *PostDocket* Magazine. National Post Doctoral Association
2015-present	Assistant Professor, Health Sciences Department, Marshall University, Huntington, WV
2016-present	Clinical Professor, Department of Clinical and Translational Sciences, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

Other Experience and Professional Memberships

Honors

2003-2007	Health Science Technology Academy (HSTA) Undergraduate Scholarship, Concord University
2003-2007	Promise Undergraduate Tuition Scholarship, Concord University
2003-2007	Marsh Dean Tuition Scholarship, Concord University
2004-2007	Dean's List, Concord University
2005	Sports Writer of the Year, Concord University
2005	Bailey Family Essay Scholarship Award, Concord University
2006	WVIAC Track and Field Conference Champion, Concord University
2006	Selected as the Student Speaker for the Concord University Alumni Banquet, Concord University
2006-2007	Tutor of the Year, Concord University
2006-2007	Alpha Chi Honors Program, Concord University
2007	Biology Graduate of the Year, Concord University
2007	Graduated Cum Laude, Concord University
2007-2008	NANO/STEM Bridge Fellowship for First and Second Year Graduate Students, West Virginia University
2010	Van Liere Research Day Selected Speaker – Placed Third in Selected Talks, West Virginia University
2010	NANO/STEM Poster Contest Winner, West Virginia University
2010-2012	American Heart Predoctoral Fellowship Awardee, West Virginia University
2011	Selected Speaker – FASEB Nutrient Signaling Meeting, Steamboat, Colorado
2012	Van Liere Poster Winner, West Virginia University

C. Contribution to Science

1. Determine the role of FGF-19 in hepatocytes. FGF-19 is a member of the fibroblast growth factor family of proteins and is involved in regulating bile acid synthesis via CYP7A. In this work, FGF-19 administration in primary bile acids inhibited fatty acid synthesis and alter SHP protein levels. This work was completed during my graduate career at WVU.
    a. Bhatnagar, S., Damron, H. A., and Hillgartner, F. B. (2009) Fibroblast growth factor-19, a novel factor that inhibits hepatic fatty acid synthesis. *J. Biol. Chem.* 284, 10023-10033.

2. Delineate regulatory factors of FGF21. FGF-21 is a novel anti-diabetic protein that regulates fatty acid synthesis, lipogenesis, and glucose disposal. FGF-21 is regulated by nutrient state as starvation leads to an increase in both hepatic expression and plasma protein levels. In previous work, fatty acids through PPAR-alpha was identified as a signaling cascade to enhance FGF-21 levels during starvation; however, the removal of PPAR was not complete, suggesting a role of other factors. I screened for factors that are increased during the starvation state and focused in on bile acids as they accumulation in the liver during starvation following recycling after a meal. The primary bile acid, chenodeoxycholic acid, caused a large change in gene expression of FGF-21 in primary bile acids. I identified the FXR-response element in FGF-21 and showed that it was important in bile acid-mediated regulation. This information is vital to understanding FGF-21 physiologically and could be used to enhance endogenous FGF-21 to reverse diabetes.
    a. Cyphert, H.A., Ge, X., Kohan, A.B., Salati, L.M., Zhang, Y., and Hillgartner, F. B. (2012) Activation of the farnesoid X receptor induces hepatic expression and secretion of fibroblast growth factor 21. *JBC*. 287(30):25123-3.

3. Elaborate on the regulation of FGF-21. My main dissertation work focused on FXR and bile acid-regulation of hepatic FGF-21. I also screened other factors that could be involved in FGF-21 regulation. Glucagon, a hormone enhanced during starvation to stimulate glucose storage disposal, caused a decrease in gene expression short-term. However, long-term stimulation caused an increase in secreted FGF-21 from primary rat hepatocytes. This pathway was further dissected to reveal a role of PKA and EPAC in this posttranscriptional pathway. These experiments employed not only rat hepatocytes but also Ins-1 cells and HepG2 cells.
    a. Cyphert, H.A., Alonge, K.M., Ippagunta, S.M. and Hillgartner, F.B. (2014). Glucagon stimulates hepatic FGF21 secretion through a PKA- and EPAC-dependent posttranscriptional mechanism. *PLoS One*. Apr 14;9(4):e94996.

4. Identify coregulators of MAFA and MAFB. During my post doc with Roland Stein, I worked on the role of coregulators during islet enriched transcriptional events. MafA, an islet-enriched transcription factor, was first identified in the Stein lab. While we know the role of MAFA in beta cell maturation and function, little is known about the mechanism of action. Using Re-CLIP, we identified the MLL3/MLL4 methyltransferases as coregulators. Removal of NCOA6, a subunit of the complex, blocked MAFA dependent transcription events. This work required extensive work in mice and the EndoC-BH1 cell line. Given the role of MAFA in beta cell function, it is important to delineate its mechanism of action. MAFA expression/influence is lost during diabetes. Perhaps coregulator recruitment could be involved in the collapse of beta cell function during diabetes.
    a. Scoville, D.W., Cyphert, H.A., Liao L, Xu J, Reynolds A. Guo, S., and Stein, R.S. (2015). MLL3 and MLL4 methyltransferases bind to the MAFA and MAFB transcription factors to regulate islet β-cell function. *Diabetes.* 64(11):3772-83.

5. Expand on the role of islet-enriched factors during pregnancy and diabetes in multiple models. During my tenure at Vanderbilt, I was fortunate enough to collaborate with several investigators. My expertise with the EndoC-BH1 cell line and my MafB transgenic moouse line was also important in these collaborations. First, I identified roles of MAFB in alpha-cell function and further elaborated on expression of islet-enriched transcription factors in other species. I also identified Prox1, a MAFB coregulator identified by Re-CLIP, and

assisted in determining how these proteins effect maturation. Lastly, a large project of mine focused on MafB during pregnancy. MafB is only expressed during embryogenesis and pregnancy. Loss of MafB renders pregnant mice glucose intolerant. In addition, prolactin loss also results in glucose intolerance during pregnancy. Working with Dr. Banerjee, we delineated the connection between prolactin and MafB during pregnancy. This work and its outcomes sheds light on gestational diabetes and, perhaps, suggests that MafB loss in pregnant humans could lead to an increased risk of gestational diabetes. Little is known about beta cell alterations during pregnancy and this paper provides more information to better understand this delicate state. I will also be submitting my primary project at Vanderbilt that involves the MafA/MafB heterodimer and further elaborate on the role of MafB during pregnancy with a transgenic mouse model that misexpressed MafB during the adult state in the beta cell (submitted Oct 1 2016). MafB regulates proliferation and genes involved in insulin and insulin secretion.

a. Conrad, E., Dai, C., Spaeth, J., Guo, M., Cyphert, H.A., Scoville, D., Carroll, J., Yu, W.M., Goodrich, L.V., Harlan, D.M., Grove, K.L., Roberts, C.T. Jr, Powers, A.C, Gu, G., and Stein, R. (2015) The MAFB transcription factor impacts islet α-cell function in rodents and represents a unique signature of primate islet β-cells*. Am J Physiol Endocrinol Metab*. Jan 1;310(1):E91-E102.
b. Paul, L., Walker, E., Drosos, Y., Cyphert, H.A., Neale, G., Stein, R., South, Jack, G., Gerard, Herrera, P., and Sosa-Pineda, B.. 2016. Lack of Prox1 Downregulation Disrupts the Expansion and Maturation of Postnatal Murine β-cells. *Diabetes*. 65(3):687-98.
c. Ganic, I., Singh, T., Luan, C., Fadista, J., Johansson, J.K., Cyphert, H.A, Bennet, H., Storm, P., Prost, G., Ahlenius, H., Renström, E., Stein, R., Groop, L., Fex, M., and Artner, I. (2016) MafA controlled nicotinic receptor expression is essential for insulin secretion and is impaired in patients with type 2 diabetes. Cell Reports. 14(8):1991-2002.
d. Dai C., Kayton N.S., Shostak, A., Poffenberger, G., Cyphert, H.A., Aramandla, R., Thompson, C., Papagiannis, I.G., Emfinger, C., Shiota, M., Stafford, J.M., Greiner, D.L., Herrera, P.L., Shultz, L.D., Stein, R., and Powers, A.C. (2016) Stress-impaired transcription factor expression and insulin secretion in transplanted human islets. *J Clin Invest*. Epub ahead of print.
e. Banerjee, R., Cyphert, H.A., Walker, E.M., Chakravarthy, H., Peiris, H., Gu, X., Liu, Y., Conrad, E., Goodrich, L., Stein, R., and Kim, S.K. (2016) Gestational diabetes from inactivation of prolactin receptor and MafB in islet beta cells. *Diabetes*. Epub ahead of print
f. Cyphert, H.A. Walker, E. M., and Stein, R. (2017) MafB and its role in adult beta cell. In preparation – Submitting to Diabetalogia January 2017.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Cyphert%20HA%5BAuthor%5D&cauthor=true&cauthor_uid=27217483

D. Additional Information: Research Support and/or Scholastic Performance

Ongoing Research Support

Promote Committee Funding – Examining the Prevalence and Modification of Metabolic Risks in College Students Enrolled in Marshall University 2016-2019
Role: Co-Investigator

INCO Travel Grant – Marshall University Cyphert (PI) 2016
Role: PI

Faculty Resources Grant, Washington University Cyphert (PI) 08/15/09-08/14/15
Opiate Addiction Database
The goal of this project is to create an integrated database of demographic, social and biomedical information for homeless opiate abusers in two urban Missouri locations, using a number of state and local data sources.
Role: PI

Completed Research Support

Loan Repayment Program – NIH – Pediatrics Cyphert (PI) 2014-2016
NIH F32 (F32 DK102283-01A1), Vanderbilt University Cyphert (PI) 2014-2016
DRTC Training Grant Fellow, Vanderbilt University Cyphert (PI) 2013-2014