# Publications


Wrighton, LS, Bhatnager, S, Keller, MP, Chapman, ER, Attie, AD. "Synaptotagmin-11 is required for the formation of the dense core of insulin granules in pancreatic B-cells." (In preparation)

Kebede MA, Oler AT, Gregg T, Balloon AJ, Johnson A, Mitok K, Rabaglia M, Schueler K, Stapleton D, Thorstenson C, Wrighton L, Floyd BJ, Richards O, Raines S, Eliceiri K, Seidah NG, Rhodes C, Keller MP, Coon JL, Audhya A, Attie AD. "SORCS1 is necessary for normal insulin secretory granule biogenesis in metabolically stressed B-cells." *J. Clin. Invest.* 2014, 124 (10): 4240-4256.

Bhatnagar S, Soni MS, Wrighton LS, Herbert AS, Zhou AS, Paul PK, Gregg T, Rabaglia ME, Keller MP, Coon JJ, Attie AD. "Phosphorylation and degradation of tomosyn-2 depresses insulin secretion." *J. Biol. Chem.* 2014, 289 (36): 25276-25286.

Raines SM, Richards OC, Schneider LR, Schueler KL, Rabaglia ME, Oler AT, Stapleton DS, Genove G, Dawson JA, Betsholtz C, Attie AD. "Loss of PDGF-B activity increases hepatic vascular permeability and enhances insulin sensitivity." *Am. J. Physiol. Endrocrinol. Metab.* 2011, 301 (3): E517-526.


WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON


Cellular and Molecular Pathology Graduate Program, Joanne Thornton, 3170–10K MFCB, 1685 Highland Avenue, Madison, WI 53705


CMP Cellular and Molecular Pathology

# Lindsay Wrighton

Program of the Dissertation Defense Seminar
for the Degree of Doctor of Philosophy
in Cellular and Molecular Pathology

## "The role of synaptotagmin-11 in the formation of the dense core insulin granule and regulated insulin secretion"

Biochemistry Addition, Rm 175 (Khorana Auditorium)

Thursday, June 4th, 2015

10:00am

Research conducted in the lab of
Alan Attie, PhD
Department of Biochemistry

UNIVERSITY OF WISCONSIN – MADISON

# Lindsay Wrighton

## Education

**University of Wisconsin-Madison**
Doctor of Philosophy
PhD in Cellular and Molecular Pathology

**Colgate University**, Hamilton, NY, 2005-2009
Bachelor of Arts in Molecular Biology

## Research Experience

University of Wisconsin-Madison, Graduate Research Assistant, Advisor: Alan Attie, Investigated the role of atypical synaptotagmins in insulin secretion. (2009 – present)

Life Technologies-Lab Technician (Research and Development), Cellular Assay Division/Biochemical Assay Division, Advisors: David Piper and Robert Horton, Produced GPCR-specific baculovirus for use in high throughput toxicological screens and validated co-factors required for kinase-based assay systems. (2008-2009)

Invitrogen Corporation, Research and Development Intern, Advisors: David Piper and Beth Frey, Utilized MultiSite Gateway® technology to produce expression clones for use in drug discovery using high throughput calcium-response assays. (2008)

Colgate University, Undergraduate Research Assistant, Advisor: Nancy Pruitt, Utilized cDNA subtractive hybridization to probe freeze tolerance and freeze susceptibility of *E. solidaginis* larvae. (2007-2008)

## Presentations

The Midwest Islet Club 8th Annual Meeting, Poster Presentation, May 2015, Chicago, IL

University of Wisconsin 1st Annual Metabolism Symposium, Poster Presentation, August 2014, Madison, WI

1st – 3rd Annual Michael N. Hart Pathology Research Symposium, Poster Presentation, 2012-2014, Madison, WI

34th Steenbock Symposium: the Metabolism of Lipids – Implications in Human Diseases, Poster Presentation, May 2011, Madison, WI



## DISSERTATION ABSTRACT

Synaptotagmins comprise a family of proteins critical for the function of secretory vesicles. Seventeen synaptotagmin isoforms have been identified. Eight of these bind to calcium and are thought to function in a myriad of membrane trafficking pathways, including the acceleration of secretory granule fusion at the plasma membrane. The role of mammalian non-calcium binding synaptotagmins in exocytosis remains largely uncharacterized. Synaptotagmin-11 (Syt11) is a non-calcium binding synaptotagmin that is highly expressed in pancreatic islets. We found that its expression is reduced by ~50% in islets from diabetic mice and humans. We also observed reduced Syt11 expression in islets from pre-diabetic mice, suggesting that a decrease in Syt11 expression may contribute to diabetes. SiRNA-dependent knockdown of Syt11 in INS-1 cells resulted in >90% loss of insulin granules with a dense core and severely reduced insulin secretion. We identified a residue predicted to bind zinc, Cys-40. Mutation of Cys-40 to Ala reproduced the phenotypes elicited by knockdown of Syt11; it led to a loss of the dense core in insulin-containing granules and a decrease in insulin secretion. Our results indicate that Syt11 is necessary for normal β-cell secretory function and zinc binding is necessary for Syt11 function.