Thomas A. Lagace

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Citizenship: Canadian and U.S.

Education

1999-2004 **Doctor of Philosophy, Department of Biochemistry and Molecular Biology, Dalhousie University**, Halifax, Nova Scotia
Supervised by Dr. Neale Ridgway
"Regulation of CTP:phosphocholine cytidylyltransferase-α by substrate availability and enzyme localization"

1982-1988 **Bachelor of Science, Major in Biochemistry, University of New Brunswick**, Fredericton, New Brunswick

Research Experience

2009-present **Assistant Professor, Department of Pathology and Laboratory Medicine, University of Ottawa Heart Institute,** Ottawa, Ontario
Research focus: cellular and molecular mechanisms that regulate cholesterol homeostasis and circulating low-density lipoprotein (LDL) levels

2004-2008 **Postdoctoral Fellow, Department of Molecular Genetics, University of Texas Southwestern Medical Center,** Dallas, Texas
Supervised by Dr. Jay Horton

- Identified and characterized structural/functional aspects of a direct protein-protein interaction between the LDL receptor and PCSK9, a central regulator of plasma LDL-cholesterol levels and heart disease risk
- Demonstrated that PCSK9 functions as a secreted factor in mediating LDL receptor degradation in hepatic cells

1999-2004 **Graduate Research, Department of Biochemistry and Molecular Biology, Dalhousie University**, Halifax, Nova Scotia
Supervised by Dr. Neale Ridgway

- Demonstrated that CCTα, the rate-limiting enzyme in phosphatidylcholine synthesis, is a target of apoptotic cell-death signaling
- Identified a role of nuclear CCTα in the proliferation of tubular nuclear envelope invaginations, collectively termed the nucleoplasmic reticulum

1992-1998 **Research Technician, Atlantic Research Centre, Dalhousie University**

1991 **Research Technician, Department of Biology, Dalhousie University**

Research and Academic Awards

2006 **Postdoctoral Fellowship,** Canadian Institutes of Health Research

2004-2005 **Postdoctoral Fellowship,** Natural Sciences and Engineering Research Council of Canada

April 2005 **Graduate Thesis Award,** Department of Biochemistry and Molecular Biology, Dalhousie University

Oct. 2004 **Oral Presentation Award,** Canadian Lipoprotein Conference

2002-2005 **Doctoral Award,** Canadian Institutes of Health Research / K.M. Hunter Foundation,

2001-2002 **Graduate (PhD) Award,** Cancer Research and Education (CaRE) in Nova Scotia,

2000 **Phyllis Horton Bursary,** Alzheimer's Society of Nova Scotia

Research Funding Awards

2010-2012 **Operating Grant,** Canadian Institutes of Health Research

2010 **Medical Research Grant,** J.P. Bickell Foundation

2010-2014 **Discovery Grant,** Natural Sciences and Engineering Research Council of Canada,

2009-2011 **Grant-In-Aid,** Heart and Stroke Foundation of Canada

2009 **Leaders Opportunity Fund Award,** Canadian Foundation for Innovation,

Professional Activities

Manuscript Review:
The Journal of Lipid Research

Peer-Reviewed Publications (past 5 years)

Susan G. Lakoski, **Thomas A. Lagace**, Jonathan C. Cohen, Jay D. Horton, and Helen H. Hobbs (2009) Plasma levels of PCSK9 in a large multiethnic population. ***Journal of Clinical Endocrinology and Metabolism*** 94(7), pp. 2537-2543.

Markey C. McNutt, Hyock Joo Kwon, Chiyuan Chen, Justin R. Chen, Jay D. Horton and **Thomas A. Lagace** (2009) Antagonism of Secreted PCSK9 Increases Low-Density Lipoprotein Receptor Expression in HepG2 Cells. ***Journal of Biological Chemistry*** 284, pp. 10561-10570.

Karsten Gehrig, **Thomas A. Lagace** and Neale D. Ridgway (2009) Oxysterol activation of phosphatidylcholine synthesis involves CTP:phosphocholine cytidylyltransferase alpha translocation to the nuclear envelope. ***Biochemical Journal*** 418(1) pp.209-217.

Aldo Grefhorst, Markey C. McNutt, **Thomas A. Lagace**, and Jay D. Horton (2008) Plasma PCSK9 Functions to Preferentially Reduce Liver LDL Receptors in Mice. ***Journal of Lipid Research*** 49, pp. 1303-1311.

Hyock Joo Kwon, **Thomas A. Lagace**, Markey C. McNutt, Jay D. Horton, and Johann Deisenhofer (2008) Molecular basis for LDL receptor recognition by PCSK9. ***Proceedings of the National Academy of Sciences*** 105, pp.1820-1825.

Markey C. McNutt, **Thomas A. Lagace**, and Jay D. Horton (2007) Catalytic Activity is Not Required for Secreted PCSK9 to Reduce LDL Receptors in HepG2 Cells. ***Journal of Biological Chemistry*** 282, pp. 20799-20803.

Da-Wei Zhang, **Thomas A. Lagace**, Rita Garuti, Zhenze Zhao, Meghan McDonald, Jay D. Horton, Jonathan C. Cohen and Helen H. Hobbs (2007) Binding of Proprotein Convertase Subtilisin/Kexin Type 9 to Epidermal Growth Factor-like Repeat A of Low Density Lipoprotein Receptor Decreases Receptor Recycling and Increases Degradation. ***Journal of Biological Chemistry*** 282, pp. 18602-18612.

Thomas A. Lagace, David E. Curtis, Rita Garuti, Markey C. McNutt, Sahng Wook Park, Heidi B. Prather, Norma N. Anderson, Y. K. Ho, Robert E. Hammer, and Jay D. Horton (2006) Secreted PCSK9 Decreases LDL Receptors in Hepatocytes and in Livers of Parabiotic Mice. ***Journal of Clinical Investigation*** 116(11) pp. 2995-3005.

Zhenze Zhao, Yetsa Tuakli-Wosornu, **Thomas A. Lagace**, Lisa Kinch, Nicholas V. Grishin, Jay D. Horton, Jonathan C. Cohen, and Helen H. Hobbs (2006) Molecular Characterization of Loss-of-Function Mutations in *PCSK9* and Identification of a Compound Heterozygote. ***American Journal of Human Genetics*** 73(9) pp. 514-523.

Thomas A. Lagace and Neale D. Ridgway (2005) Induction of apoptosis by lipophilic activators of CTP:phosphocholine cytidylyltransferase alpha (CCTalpha). ***Biochemical Journal*** 392(3) pp.449-456.

Thomas A. Lagace and Neale D. Ridgway (2005) The Rate-limiting Enzyme in Phosphatidylcholine Synthesis Regulates Proliferation of the Nucleoplasmic Reticulum. ***Molecular Biology of the Cell*** 16(3) pp.1120-1130.

Invited Contributions

Thomas A. Lagace (2009) PCSK9 and heart disease: quieting an outdated metabolic moderator. ***Clinical Lipidology*** 4(4), pp. 407-410.