

## BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.  
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NAME Tony K.T. Lam	POSITION TITLE
ADDRESS 101 College Street, MaRS Centre TMDT-10 <sup>th</sup> floor Rm 705 Toronto, Ontario Canada, M5G 1L7	John Kitson Mclvor Endowed Chair (1915-1942) in Diabetes Research Canada Research Chair in Obesity Full Professor, University of Toronto Senior Scientist, Toronto General Research Institute Associate Director, Banting and Best Diabetes Centre

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

INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	MM/YY	FIELD OF STUDY
McMaster University, Hamilton, Canada	B.Sc.	1994-1998	Biochemistry (Hons.)
University of Toronto, Toronto, Canada	Ph.D.	1998-2003	Physiology
Albert Einstein College of Medicine, NYC	Post-doc Fellow	2003-2006	Medicine and Molecular Pharmacology

### A. Personal Statement

My laboratory has been working on the mechanisms underlying the regulation of glucose, lipid and energy homeostasis and their roles in diabetes and obesity. Our main focus has been to elucidate nutrient and hormone sensing mechanisms in the gut and the brain that regulate hepatic glucose production, hepatic VLDL-TG secretion and food intake to maintain glucose, lipid and energy homeostasis. We have discovered that nutrient sensing in the small intestine triggers hormonal signaling and a gut-brain-liver neuronal pathway to lower hepatic glucose production and plasma glucose levels, and is necessary for the anti-diabetic effect of bariatric surgery and metformin therapy. The Canadian Institutes of Health Research (CIHR) has named our discoveries as a Milestone in Canadian Health Research. In parallel, we have unveiled insulin, glucagon and nutrient signaling pathways in the brain that regulate hepatic glucose production, VLDL-TG secretion and food intake. In summary, our discoveries reveal molecular targets in the gut and the brain that may carry therapeutic potential to lower blood glucose and lipid levels and body weight in diabetes and obesity.

### B. Positions and Honors

#### Academic & Hospital appointments:

2014-pres	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Canada Research Chair in Obesity Full Professor, Departments of Physiology and Medicine, University of Toronto
2012-pres	Senior Scientist, Toronto General Research Institute, UHN
2011-pres	Associate Director, Banting and Best Diabetes Centre
2014-2016	Visiting Professor, Asan Medical Centre, Seoul, South Korea
2010-2014	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Canada Research Chair in Obesity Associate Professor of Physiology and Medicine, University of Toronto
2010-2013	Visiting Professor, Shanghai Jiaotong University School of Medicine, Shanghai
2006-2012	Scientist, Toronto General Research Institute, UHN
2006-2010	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Assistant Professor of Physiology and Medicine, University of Toronto

## Professional Awards and Honors:

- 2016-pres Institutes Advisory Board Member, Canadian Institutes of Health Research (CIHR)  
2015 Simon Pierre Noel Award Lectureship, Canadian Lipoprotein Conference  
2014 Joseph and Mable Meites Lectureship, Michigan State University  
2013 Canadian Diabetes Association Young Scientist Award (under the age of 45)  
2013 Endocrine Society Richard E. Weitzman Memorial Laureate award (under the age of 50)  
2013-pres Scientific Advisory Board, Keystone Symposia  
2013-2016 Editorial Board Member, *Diabetes*  
2012 Bela Issekutz Jr Memorial Lecture, Dalhousie University  
2012-13 Primary organizer, Keystone Symposium: "Neuronal Control of Appetite, Metabolism and Weight"  
2010-pres Canada Research Chair in Obesity (Tier II)  
2006-pres John Kitson McIvor (1915-1942) Endowed Chair in Diabetes Research  
Toronto General Research Institute & University of Toronto  
2010 Faculty of Medicine Graduate Teaching Award for Excellence in Graduate Teaching  
2009-2014 Early Researcher Award, Ministry of Research and Innovation, Ontario, Canada  
2008-2010 Reuben & Helene Dennis Scholar in Diabetes Research, University of Toronto  
2005 Albert Einstein College of Medicine Outstanding Postdoctoral Research Scholar  
2005 National Institute of Health (NIH) Post-Doctoral Fellowship  
2005 American Diabetes Association (ADA) Trainee Travel Grant  
2002 Canadian Institute of Health Research (CIHR) Doctoral Award

## **C. Selected Publications** (in chronological order; out of 73 publications)

- Lam TKT, Gutierrez R, Pocai A, Rossetti L: Regulation of blood glucose by hypothalamic pyruvate metabolism. **Science** 309(5736):943-947, 2005.
- Caspi L, Wang P & Lam TKT: A balanced of lipid sensing mechanisms in the brain and liver. **Cell Metab** 6(2):99-104, 2007.
- Wang P, Caspi L, Lam C, Chari M, Li X, Light P, Gutierrez R, Ang M, Schwartz GJ & Lam TKT: Upper intestinal lipids trigger a gut-brain-liver circuit to regulate glucose production. **Nature** 452:1012-16, 2008.
- Cheung G, Kokorovic A, Lam C, Chari M & Lam TKT: Intestinal cholecystokinin controls glucose production through a neuronal network. **Cell Metab** 10(2):99-109, 2009 (**Cover Story**).
- Lam TKT: Neuronal regulation of homeostasis by nutrient sensing. **Nature Medicine** 16(4):392-395, 2010.
- Yue J, Mighiu PI, Naples M, Adeli K & Lam TKT: Glycine normalizes hepatic triglyceride-rich VLDL secretion by triggering the CNS in high-fat fed rats. **Circ Res** 110(10):1345-1354, 2012.
- Yue J & Lam TKT: Lipid sensing and insulin resistance in the brain. **Cell Metab** 15(5):646-655, 2012.
- Breen DM, Rasmussen BA, Kokorovic A, Wang R, Cheung GW & Lam TKT: Jejunal nutrient sensing is required for duodenal-jejunal bypass surgery to rapidly lower glucose levels in uncontrolled diabetes. **Nature Medicine** 18(6):950-955, 2012.
- Filippi BM, Yang CS, Tang C & Lam TKT: Insulin activates Erk1/2 signaling in the dorsal vagal complex to inhibit glucose production. **Cell Metab** 16(4):500-510, 2012.
- Mighiu PI, Yue JT, Filippi BM, Abraham MA, Chari M, Lam CK, Yang CS, Christian NR, Charron MJ & Lam TKT: Hypothalamic glucagon signaling inhibits hepatic glucose production. **Nature Medicine** 19(6):766-772, 2013.
- Rasmussen BA, Breen D, Duca F, Cote C, Zadeh-Tahmasebi M, Filippi B & Lam TKT: Jejunal leptin-PI3K signaling lowers glucose production. **Cell Metab** 19(1):155-161, 2014.
- Yue JT, Abraham M, LaPierre M, Mighiu P, Light P, Filippi B & Lam TKT: A fatty acid-dependent hypothalamic-DVC neurocircuitry that regulates hepatic secretion of VLDL-TG. **Nature Commun** 6:5970, Jan 12 2015.
- Cote C, Rasmussen B, Duca FA, Zadeh-Tahmasebi M, Baur J, Daljeet M, Breen D, Filippi B & Lam TKT: Resveratrol activates duodenal Sirt1 to reverses insulin resistance in rats through a neuronal network. **Nature Medicine** 21(5):498-505, 2015
- Duca FA, Cote C, Rasmussen B, Zadeh M, Rutter G, Filippi B & Lam TKT: Meformin activates a duodenal AMPK-dependent pathway to lower hepatic glucose production in rats. **Nature Medicine** 21:506-11, 2015
- Duca FA, Bauer PV, Hamr SC & Lam TKT: Glucoregulatory relevance of small intestinal nutrient sensing in physiology, bariatric surgery, and pharmacology. **Cell Metab** 22(3):367-380, 2015.

LaPierre MP, Abraham M, Yue J, Filippi B & Lam TKT: Glucagon signaling in the dorsal vagal complex is sufficient and necessary for high-protein feeding to regulate glucose homeostasis in vivo.

**EMBO Rep** 16(10):1299-307, 2015

Winer D, Winer S, Dranse H & Lam TKT: Immunological impact of the intestine in metabolic disease.

**J Clin Invest**, in press

Yue JT, Abraham MA, Bauer P, LaPierre M, Wang P, Duca F, Filippi B, Chan O & Lam TKT: Inhibition of glycine transporter-1 in the dorsal vagal complex improves metabolic homeostasis in diabetes and obesity.

**Nature Commun**, in press

#### **D. Operating / Infrastructure Funding** (Current; in Canadian Dollar)

- 2016-2019 Canadian Diabetes Association Operating Grant: Insulin and leptin action in the brain. (Principal Investigator, \$300,000; Renewable)
- 2015-2022 Canadian Institutes of Health Research (CIHR) Foundation Grant: Metabolic impact of nutrient sensing-dependent neuronal mechanisms in the gut and the brain (Principal Investigator, \$2,514,077; Renewable)
- 2014-2016 Canada Foundation For Innovation (CFI)-ORF Leaders Opportunity Fund – The in vivo metabolic characterization laboratory (Principal Investigator, \$1,917,912-Infrastructure for the Lam Lab)
- 2010-2020 Canada Research Chair in Obesity (\$1,000,000; Renewable-Operating portion \$400,000)
- 2006-pres John Kitson Mclvor Endowed Chair, Toronto General Research Institute & University of Toronto (\$2,500,000 Endowment + \$700,000 cash operating funds)

#### **E. Invited Lectures and other academic activities**

Dr. Lam was invited to speak at international scientific conferences and institutional seminars (>190) hosted in Australia, Austria, Brazil, China, France, Germany, Japan, Netherlands, Singapore, South Korea, Spain, Switzerland, Taiwan, the United Arab Emirates, the United Kingdom and the United States. Specifically, he was invited by Proc Natl Acad Sci USA Chief Editor, Dr. Inder Verma, to speak at the Foundation IPSEN and Nature Symposium hosted in the Salk Institute, and by the Chair of the Nobel Prize Committee for Physiology or Medicine, Dr. Juleen Zierath, to lecture at the Karolinska Institutet. Dr. Lam was also invited to lecture at Harvard, Stanford and Yale as well as University of Cambridge and Oxford. Dr. Lam is a scientific advisory board member of Keystone Symposia, an Institutes Advisory Board Member of the Canadian Institutes of Health Research, a frequent reviewer for Nature, Science, Cell, Nat Med, Cell Metab, an ad hoc editor for PNAS, an editorial member of Diabetes and Mol Metab, and serves on boards and councils in an advisory capacity including the American Diabetes Association, the Austrian Science Fund, the Canadian Diabetes Association, CIHR, the French National Research Agency, the NIH, the Research Grants Council of Hong Kong, the Society for Endocrinology and Diabetes UK.