

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Tony K.T. Lam	POSITION TITLE John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Canada Research Chair (Tier 1) in Diabetes and Obesity Professor, Physiology and Medicine, University of Toronto Senior Scientist, Toronto General Hospital Research Institute, UHN Associate Director, Banting and Best Diabetes Centre
ADDRESS 101 College Street, MaRS Centre TMDT-10 th floor Rm 705 Toronto, Ontario Canada, M5G 1L7	

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

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, brain, and the kidney 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 pathway to lower hepatic glucose production and plasma glucose levels, and is necessary for the anti-diabetic effect of gut microbiota, metformin therapy, and bariatric surgery. 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. Lastly, we have discovered that changes in gut microbiome as well as the kidney regulates feeding, body weight and glucose homeostasis. In summary, our discoveries reveal molecular targets in the kidney, gut and the brain that may carry therapeutic potential to lower body weight as well as blood glucose and lipid levels in diabetes and obesity.

B. Positions and Honors

Academic & Hospital appointments:

2019-pres	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Canada Research Chair (Tier 1) in Diabetes and Obesity Professor, Departments of Physiology and Medicine, University of Toronto
2012-pres	Senior Scientist, Toronto General Hospital Research Institute, UHN
2011-pres	Associate Director, Banting and Best Diabetes Centre
2014-2018	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Canada Research Chair (Tier 2) in Obesity Professor, Departments of Physiology and Medicine, University of Toronto
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 (Tier 2) in Obesity Associate Professor, Departments of Physiology and Medicine, University of Toronto
2010-2013	Visiting Professor, Shanghai Jiaotong University School of Medicine, Shanghai
2006-2012	Scientist, Toronto General Hospital Research Institute, UHN
2006-2010	John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research Assistant Professor, Departments of Physiology and Medicine, University of Toronto

Professional Awards and Honors:

- 2024 Plenary Lecture, 3rd Taiwan Society for Neuroscience Congress, Taipei, Taiwan
- 2024 Keynote, Hong Kong Institute of Diabetes and Obesity 20th Anniversary Distinguished Lecture Series on Diabetes, The Chinese University of Hong Kong, Hong Kong
- 2021 Plenary Lecture, Endocrine Society's Annual Meeting, San Francisco
- 2021 Guest Editor, *Cell Metabolism*, Special Issue: 100th Anniversary of insulin discovery
- 2020 Primary organizer, Keystone Symposium: "A Gut-Systemic perspective for metabolic diseases"
- 2019-pres Canada Research Chair (Tier 1) in Diabetes and Obesity
- 2006-pres John Kitson Mclvor (1915-1942) Endowed Chair in Diabetes Research, UHN
- 2018 State-of-the-Art Lecture, American Diabetes Association 78th Scientific Sessions, Orlando
- 2018 Memorial Seminar for Academician Zhijun Wang, Peking University
- 2016-2019 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
- 2013-2023 Scientific Advisory Board, Keystone Symposia
- 2013 Endocrine Society Richard E. Weitzman Memorial Laureate award (under the age of 50)
- 2013 Canadian Diabetes Association Young Scientist Award (under the age of 45)
- 2013-16 Editorial Board Member, *Diabetes*
- 2012 Bela Issekutz Jr Memorial Lecture, Dalhousie University
- 2012 Primary organizer, Keystone Symposium: "Neuronal Control of Appetite, Metabolism and Weight"
- 2010-18 Tier 2 Canada Research Chair in Obesity
- 2010 Faculty of Medicine Graduate Teaching Award for Excellence in Graduate Teaching
- 2009-14 Early Researcher Award, Ministry of Research and Innovation, Ontario, Canada
- 2008-10 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 101 publications)

- 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**).
- 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.
- 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** 7:13501, Nov 22 2016.
- Winer D, Winer S, Dranse H & Lam TKT: Immunological impact of the intestine in metabolic disease. **J Clin Invest** 127(1):33-42, 2017.
- Filippi B, Abraham M, Siva P, Rasti M, LaPierre M, Bauer P, Rocheleau J & Lam TKT: Dynamin-related protein 1-dependent mitochondrial fission changes in the dorsal vagal complex regulate insulin action. **Cell Rep** 18(10):2301-2309, 2017.
- Bauer P, Duca F, Waise TMZ, Rasmussen B, Abraham M, Dranse H, Puri A, O'Brien C & Lam TKT: Metformin alters upper small intestinal microbiota that impact a glucose-SGLT1 sensing glucoregulatory pathway. **Cell Metab** 27(1):101-117, 2018.
- Bauer P, Duca F, Waise TMZ, Dranse H, Rasmussen B, Puri A, Rasti M, O'Brien C & Lam TKT: Lactobacillus gasseri in the upper small intestine impacts an ACSL3-dependent fatty acid sensing pathway regulating whole-body glucose homeostasis. **Cell Metab** 27(3):572-587, 2018.
- Dranse H, Waise TMZ, Hamr S, Bauer P, Abraham M, Rasmussen B & Lam TKT: Physiological and therapeutic regulation of glucose homeostasis by upper small intestinal PepT1-mediated protein sensing. **Nature Commun** 9(1):1118, 2018.
- Waise TMZ, Rasti M, Duca F, Zhang SY, Bauer P, Rhodes C & Lam TKT: Inhibition of upper small intestinal mTOR lowers plasma glucose levels by inhibiting glucose production. **Nature Commun** 10(1):714, 2019.
- Zhang SY, Bruce K, Danaei Z, Li R, Barros D, Kuah R, Lim Y, Mariani L, Cherney D, Chiu J, Reich H & Lam TKT: Metformin triggers a kidney GDF15-dependent area postrema axis to regulate food intake and body weight. **Cell Metab** 35(5):875-886, 2023
- Yue J, Garrido AN & Lam TKT: A metabolic balance of GLP1 and NMDA receptors in the brain. **Cell** 187(15):3854-56, 2024
- Li R, Barros D, Kuah R, Lim Y, Gao A, Beaudry J, Zhang SY & Lam TKT: Small intestinal CaSR-dependent and CaSR-independent protein sensing regulates feeding and glucose tolerance in rats. **Nature Metab** 6(1):39-49, 2024