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Phone: 212 305 7363**Email:** peh1@columbia.edu**Paul Harris, Ph.D.***Research Scientist**Division of Endocrinology, Department of Medicine at the
College of Physicians & Surgeons, Columbia University***Research Summary:**

We have shown that the vesicular monoamine transporter type 2 (VMAT2) is a suitable marker for imaging beta cell mass and are conducting human clinical trials to determine whether these measurements are useful for the management of type 1 and 2 diabetes. In parallel, we have explored the role of neurotransmitter substrates of VMAT2 in the control of insulin secretion by beta cells. Our most recent studies show that glucose homeostasis within the endocrine pancreas utilizes a dopaminergic circuitry similar to that found in the CNS. In this circuit, dopamine (DA), synthesized de novo or imported by dopamine (reuptake) transporter (DAT), is stored in β -cell insulin granules by the action of the vesicular monoamine transporter type 2 (VMAT2). The insulin granules also contain dopamine 2 like receptors (D2R). During GSIS, DA and insulin are released and D2R is delivered to the cell surface where it binds DA. DA signaling through D2R is a powerful inhibitor of glucose dependent insulin secretion. Since DA acts as an anti-incretin and is released with similar kinetics as GLP-1 and GIP following a mixed meal, we are following up on the hypothesis that the rapid reversal of hyperglycemia following RYGB in T2DM may be due surgical removal of dopamine producing gastrointestinal tissue.

Selected Publications:

1. Goland R, Freeby M, Parsey R, Saisho Y, Kumar D, Simpson N, Hirsch J, Prince M, Maffei A, Mann JJ, Butler PC, Van Heertum R, Leibel RL, Ichise M, Harris PE. 11C-dihydrotetrabenazine PET of the pancreas in subjects with long-standing type 1 diabetes and in healthy controls. *J Nucl Med* 2009 50: 382-389. PMID 19223416
2. Simpson, N, Maffei, A, Freeby, M, Burroughs, S, Freyberg, S, Javitch, J, Leibel, RL and Harris, PE. Dopamine Mediated Autocrine Inhibitory Circuit Regulating Human Insulin Secretion in vitro. *Molecular Endocrinology*, 2012 26(10):1757-1772 PMID 22915827.

3. Freeby, M, Goland, R, Ichise, M, Harris, PE. Vesicular Monoamine Transporter, Type 2 (VMAT2) Expression as it Compares To Insulin and Pancreatic Polypeptide in the Head, Body and Tail of the Human Pancreas. *Islets*. 2012 4(6):393-397. PMID: 23221614
4. Harris, PE, Farwell, MD, Ichise, M. PET quantification of pancreatic VMAT 2 binding using (+) and (-) enantiomers of [18F] FP-DTBZ in baboons. *Nuclear Medicine and Biology*, 2013 40(1):60-64. PMID: 23102539
5. Maffei, A., Segal, AM, Perez-Alvarez, JC, Garcia-Ocana, A. and Harris, P.E. Anti-incretin, anti-proliferative action of dopamine on β -cells. *Molecular Endocrinology*, 2015. 29(4):542–557. PMID: 25751312
6. Freeby, MJ, Kringas, P, Goland, RS, Leibel, RL, Maffei, A, Divgi, C, Ichise, M, Harris, PE. Cross-sectional and Test-Retest Characterization of PET with 18F-FP-(+)-DTBZ for β -Cell Mass Estimates in Diabetes. *Molecular Imaging and Biology*. 2015 Submitted.

More about PAUL HARRIS:

(<http://www.columbiamedicine.org/divisions/Endo/faculty/harris.html>)

(<http://www.nbdiabetes.org/our-research-faculty#7>)

