

In the format provided by the authors and unedited.

Mechanism and effects of pulsatile GABA secretion from cytosolic pools in the human beta cell

Danusa Menegaz^{1,16}, D. Walker Hagan^{1b 2,16}, Joana Almaça¹, Chiara Cianciaruso³, Rayner Rodriguez-Diaz¹, Judith Molina¹, Robert M. Dolan², Matthew W. Becker^{1b 2}, Petra C. Schwalie^{3,4}, Rita Nano⁵, Fanny Lebreton^{1b 6}, Chen Kang^{7,8}, Rajan Sah^{7,8}, Herbert Y. Gaisano⁹, Per-Olof Berggren^{10,11,12}, Steinunn Baekkeskov^{1b 3,13*}, Alejandro Caicedo^{1b 1,10,14,15*} and Edward A. Phelps^{1b 2,3*}

¹Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL, USA. ²J. Crayton Pruitt Family Department of Biomedical Engineering, University of Florida, Gainesville, FL, USA. ³Institute of Bioengineering, School of Life Sciences, École Polytechnique Fédérale de Lausanne, Lausanne, Switzerland. ⁴Swiss Institute of Bioinformatics, Lausanne, Switzerland. ⁵Pancreatic Islet Processing Facility, Diabetes Research Institute, IRCCS San Raffaele Scientific Institute, Milan, Italy. ⁶Cell Isolation and Transplantation Center, Faculty of Medicine, Department of Surgery, Geneva University Hospitals and University of Geneva, Geneva, Switzerland. ⁷Center for Cardiovascular Research and Division of Cardiology, Department of Internal Medicine, Washington University School of Medicine, St Louis, MO, USA. ⁸Department of Internal Medicine, Division of Cardiovascular Medicine, University of Iowa, Carver College of Medicine, Iowa City, IA, USA. ⁹Department of Medicine, University of Toronto, Toronto, Ontario, Canada. ¹⁰Diabetes Research Institute, University of Miami Miller School of Medicine, Miami, FL, USA. ¹¹The Rolf Luft Research Center for Diabetes & Endocrinology, Karolinska Institutet, Stockholm, Sweden. ¹²Division of Integrative Biosciences and Biotechnology, WCU Program, University of Science and Technology, Pohang, Korea. ¹³Departments of Medicine and Microbiology/Immunology, Diabetes Center, University of California San Francisco, San Francisco, CA, USA. ¹⁴Department of Physiology and Biophysics, Miller School of Medicine, University of Miami, Miami, FL, USA. ¹⁵Program in Neuroscience, Miller School of Medicine, University of Miami, Miami, FL, USA. ¹⁶These authors contributed equally: Danusa Menegaz, D. Walker Hagan. *e-mail: sbaekkeskov@ucsf.edu; acaicedo@med.miami.edu; ephelps@bme.ufl.edu

		human			rat		
		β	α	δ	β	α	δ
GAD65	IF	+	+	+	+	-	-
	RNA seq	+	+	+	nd	nd	nd
VGAT	IF	-	-	+	-	+	-
	RNA seq	-	-	-	nd	nd	nd
GABA	IF	+	-	+	+	-	-

+	positive
-	not detected
nd	no data

Supplementary Table 1. Data summary comparing the expression of GAD65, VGAT, and GABA in human and rat islet endocrine cell subtypes. Table summarizes results obtained by immunofluorescence (our results) and the public single cell RNA-seq datasets analyzed in this paper. While VGAT was not detected by RNA-seq, it was detected by immunostaining, likely because its mRNA transcripts were below the detection threshold. VGAT mRNA has been detected by others in whole human islets by rt-PCR.