
Islet imaging: releasable β -cells with tight Ca^{2+} -exocytosis coupling dictate biphasic glucose-stimulated insulin secretion

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Biphasic glucose-stimulated insulin secretion (GSIS) is essential for blood glucose regulation, but a mechanistic model incorporating recently identified islet β -cell heterogeneity remains elusive. Here we show that insulin secretion is spatially and dynamically heterogeneous across the islet. Using a zinc-based fluorophore with spinning-disc confocal microscopy, we reveal that approximate 40% of islet cells, which we call readily releasable β -cells (RR β s), are responsible for 80% of insulin exocytosis events. Although glucose up to 18.2 mM fully mobilized the RR β s to release insulin synchronously (first phase), even higher glucose enhanced the sustained secretion from these cells (second phase). Release-incompetent β -cells show similarities to RR β s in glucose-evoked Ca^{2+} transients but exhibit Ca^{2+} -and-exocytosis coupling deficiency. Decreased number of RR β s and their altered secretory abilities are associated with impaired GSIS progression in ob/ob mice. Our data reveal functional heterogeneity at the level of exocytosis among β -cells and identify RR β s as a subpopulation of β -cells that make a disproportionately large contribute to biphasic GSIS from mouse islets.



Short Bio:

Liangyi Chen is a New Cornerstone Investigator, a Boya Prof. at Peking University & Deputy Dir. of the Nat. Biomed. Imaging Sci. Center at PKU. He got his B.S. in Bioeng. & Med. Instruments from XJTU ('95), M.S. in Bioelectronics ('98) & Ph.D. in Biomed. Eng. ('01) from HUST. From '01-'04, he was a postdoc at U. of Washington, USA. Later, he was an Assoc. Res. at the Inst. of Biophysics, CAS ('04-'10). Since '10, Dr. Chen has been at the Inst. of Molecular Med. at PKU. In '19, he was appointed Long-Term Prof. at PKU, & in '21, he joined the PKU-Tsinghua Center for Life Sci. He is the recipient of the National Natural Science Foundation of China's Outstanding Youth Fund.