Abstract

The pancreatic islet secretes the hormones insulin and glucagon to regulate glucose metabolism. To generate an adequate secretory response that contributes to glucose homeostasis, activity in islet endocrine cells is coordinated via paracrine signaling. Several neurotransmitters have been suggested to work as signaling molecules in the islet (acetylcholine, serotonin, GABA). We are deploying a battery of techniques to determine which molecules are released from endocrine cells to activate neighboring cells and alter hormone secretion. The neurotransmitter GABA is secreted by islet beta cells and was shown to protect mouse beta cells from immune attack, make them proliferate, and to reverse diabetes in mice. Little is known, however, about the basic physiological role GABA plays in the islet. Our findings indicate that GABA is secreted from beta cells in robust pulses, suggesting that GABA signaling could serve as a pacemaker by imposing its rhythm on endocrine cells within the islet. Interestingly, we also found that GABA signaling is deranged in type 2 diabetes, which may help explain abnormal, irregular hormone secretion. Ultimately, our goal is to understand how islets function in the living organism. Toward this aim, we established an animal model that allows manipulating and visualizing islet function non-invasively. In this model, islets are transplanted into the anterior chamber of the mouse eye for in vivo monitoring. By moving our in vitro studies into real time, in vivo physiology we expect to obtain data not predicted by in vitro studies.