1098-92-168 **Margaret Watts*** (margaret.watts@nih.gov), **Ofer Kimchi** and **Arthur Sherman**. *Modeling the Pancreatic-α-cell: Paracrine versus Intrinsic Regulation of Glucagon Secretion.*

It has been proposed that glucagon secretion is under paracrine control; however, there is evidence that α-cells also possess an intrinsic glucose-sensing mechanism. We consider two intrinsic mechanisms of glucagon secretion: ATP-sensitive potassium channels and a store operated current. Using a mathematical model of glucagon secretion in α-cells, we show that both mechanisms can suppress glucagon secretion, but both have to work together to reproduce the glucose dose response curve seen experimentally. We also investigate how paracrine effects in the form of insulin regulate glucagon secretion. By adding the inhibitory effect of insulin on glucagon secretion, we can model the anti-synchronous pulses of insulin and glucagon observed in elevated glucose. It is also known that α-cells are extremely heterogeneous and not coupled by gap junctions like β-cells. Therefore, we conclude that the paracrine effects modulate the intrinsic mechanisms and overcome the heterogeneity of the α-cells. (Received January 24, 2014)