

EGID SEMINAR

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Identification of Hypothalamic Mechanisms Controlling Glucagon Secretion: a Mouse Genetics Approach

We are interested in identifying brain hypoglycemia sensing neurons and how they control glucagon secretion by pancreatic islet alpha cells to restore normoglycemia. Our current studies have been initiated by genetic screens performed with a panel of recombinant inbred BXD mice to identify gene loci controlling glucagon secretion induced by neuroglucopenia or insulin-induced hypoglycemia. Several cQTLs have been identified and, in combination with hypothalamus RNASeq data, we identified several candidate genes. These are expressed in different hypothalamic neuronal populations and participate in the control of glucagon secretion through regulation of autonomic nervous activity or the secretion of AVP from magnocellular neurons. The glucose sensing properties and physiological role of these genes have been studied using genetically modified mice, electrophysiological techniques, and viral and chemogenetic circuit tracing approaches. Collectively, our data shed new light on the complexity of the neuronal networks activated to prevent hypoglycemia development. They will pave the way to identify the deregulations that increase the risk of hypoglycemia development in insulin-treated diabetic patients.

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