

## Central control of insulin secretion: roles of AMPK and LKB1.

Secretion of insulin is crucial for normal metabolic homeostasis and its disruption underlies all forms of diabetes mellitus, a disease currently affecting ~5 % of all westernised populations and expected to grow to affect more than 400 m individuals worldwide by 2025. Pancreatic islet beta cells are the body's sole source of the hormone, and respond to glucose, other nutrients and a range of circulating factors with hormone release. We have identified a fuel sensitive protein kinase, AMP-activated protein kinase, and its upstream activator LKB1, as important regulators on beta cell function and development.<sup>1-3</sup>

However, inactivation of either enzyme in the beta cell and brain leads to dramatically differing phenotypes (inhibited secretion in the former, stimulated in the latter). We wish to determine whether this difference reflects a differential activation of neuronal circuits deriving from the hypothalamus to innervate the islet and will use a variety of in vivo and ex vivo preparations to address this question.

Web pages

<http://www1.imperial.ac.uk/medicine/people/g.rutter/>

<http://www1.imperial.ac.uk/medicine/about/divisions/departamentofmedicine/diabetesendocrinologymetabolism/cellbiology/>

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### Reference List

- 1 Sun,G. *et al.* (2010) Ablation of AMP-activated protein kinase alpha1 and alpha2 from pancreatic beta-cells and RIP.Cre neurons suppresses insulin release in vivo. *Diabetologia* in press
- 2 daSilvaXavier,G. *et al.* (2000) Role of AMP-activated protein kinase in the regulation by glucose of islet beta-cell gene expression. *Proc Natl Acad Sci U S A* 97, 4023-4028
- 3 Rutter,G.A. and Leclerc,I. (2009) The AMP-regulated kinase family: Enigmatic targets for diabetes therapy. *Mol Cell Endocrinol.* 297, 41-49