

P025 PAS-domain containing protein kinase (PASK) regulates glucagon secretion from pancreatic alpha-cells
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Aims: We have previously shown that PASK, first described as a regulator of sugar metabolism in *S.cerevisiae*, is also involved in glucose sensing by pancreatic β -cells. It was also recently demonstrated that glucose-regulated insulin secretion was impaired in PASK knockout mice. Here, we explore the role of PASK in the regulation of glucagon secretion from pancreatic α -cells.

Methods: PASK silencing was achieved in the mouse pancreatic α -cell line, α -TC1-9, using siRNA duplexes and transfection with TransIT-TKO™ (Mirus Corp). For over-expression, an adenovirus bearing full-length PASK cDNA was used. PASK levels were determined by western (immuno-)blotting. Glucagon secretion was followed by radioimmunoassay.

Results: Treatment of α -TC1-9 cells with an anti-PASK siRNA for 48 h led to near-complete knockdown of PASK protein. Glucagon secretion was higher after 30 min incubation at 0.5 (3.02 ± 0.11 fold) and 10 (9.88 ± 0.52) mmol/l glucose in PASK siRNA- compared to scrambled siRNA-treated cells. By contrast, over-expression of PASK led to a 58.4 ± 1.99 and 38.9 ± 2.05 % decrease in glucagon secretion at 1 and 5 mmol/l glucose, respectively (n=3).

Conclusion: We demonstrate that changes in PASK activity are able to regulate glucagon secretion in the pancreatic α -cell, suggesting a further role for PASK as a glucose sensor in the pancreatic islet.