

**P030** The regulation of Pancreatic Duodenum Homeobox-1 (PDX-1) by Per-Arnt-Sim (PAS) kinase  
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Background. PDX-1 is a key transcription factor involved in pancreatic  $\beta$ -cell development and function. We have previously reported that purified **per-arnt-sim (PAS) kinase efficiently phosphorylates** recombinant PDX-1 *in vitro* on a single site (Thr-152) within the DNA binding homeodomain. Here, we sought to determine the role of this phosphorylation event. . Results. We generated adenoviruses to allow the expression of wild-type or mutant forms of *c-myc*-tagged PDX-1 (T152A, T152D, T152E) in both clonal MIN6  $\beta$ -cells and in INSr $\alpha\beta$  cells, which have properties of both  $\alpha$ - and  $\beta$ -cells. **These approaches demonstrated** that phosphorylation at Thr-152 (a) is likely to significantly decrease the nuclear accumulation of PDX-1, (b) decreases binding of PDX-1 to the preproinsulin promoter A3 box, and (c) directs islet precursor cells from a  $\beta$ - towards an  $\alpha$ -cell fate. However, PASK over-expression had little impact on PDX-1 phosphorylation at Thr-152 as assessed either by mass spectrometry or by monitoring the subcellular localisation of wild-type PDX-1. Conclusions. Phosphorylation of PDX-1 at Thr-152 may play an important role in controlling the transcriptional activity of this factor. However, kinases other than PASK may play a more important role in mediating Thr-152 phosphorylation *in vivo*.