

**P015** Reprogramming Gall Bladder Epithelium into Beta-like Cells  
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Our recent discovery of beta-cells within the biliary system of wild type mice has highlighted the possibility of reprogramming biliary cells into functioning beta-cells.

We have now devised a method for culturing mouse adult gall bladder epithelium using dissociation and monolayer culture, and established that adenovirus can be used for transient introduction of genes.

This system is being used to attempt to identify the key pancreatic transcription factors needed to reprogram gall bladder epithelial cells into beta-cells. One key transcription factor believed to repress the endocrine pathway in the biliary system is Hes1.

Previous Hes1 knockout studies demonstrated the development of ectopic pancreas in the region of the developing extrahepatic biliary ducts. We have made a mutant Hes1 construct with a deleted DNA binding domain ( $\Delta$ Hes1) which relieves repression of the Ngn3 promoter in an *in vitro* luciferase assay. We are currently using adenoviral vectors expressing the  $\Delta$ Hes1 construct together with other key pancreatic transcription factors to infect gall bladder epithelial cultures with a view to finding the optimal combination for insulin expression.

The cells which give most insulin output will undergo functional and morphological evaluation and their ability to cure diabetic mice when transplanted will be determined.