Is Cdx2 sufficient to induce intestinal genes in an in vitro model of oesophagus?

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Introduction: The caudal type homeobox transcription factors 2 (CDX2), has been implicated in the pathogenesis of Barrett's metaplasia (BM). CDX2 expression is normally limited to the post pyloric epithelium of the gastrointestinal tract, but is found in BM. In mice, Cdx2 is sufficient to induce intestinal metaplasia in the stomach, but this has not been shown in the oesophagus. We have developed a novel long-term representative in vitro model of oesophagus and investigated the result of ectopic Cdx2 expression within this model.

Methods: Explants of mouse oesophageal epithelium were cultured and characterised by immunohistochemistry. We expressed transgenes (Ad-RSV-GFP and Ad-CMV-Cdx2-IRES-hrGFP) by adenoviral infection. Changes in gene expression were assessed by RT-PCR and immunohistochemistry.

Results: The explant culture model contains fibroblasts and epithelium and is viable for 6 months. The epithelial cells express markers for all stages of stratification: keratins 5, 14 and 4, involucrin, loricrin and p63. Ectopic expression of Cdx2 within the epithelium of this model did not provoke the transcription of any intestinal genes.

Conclusion: We have developed a long-term in vitro model of squamous oesophagus that is fully representative. Ectopic gene expression is obtained using adenoviral vectors. Cdx2 is not sufficient to induce intestinal genes in oesophageal cells, suggesting that other factors are required to induce an intestinal phenotype in the oesophagus. Identification of these factors has implications for understanding the pathogenesis of BM.