

PWE-101

**HEPATOCTE NUCLEAR FACTOR 4 A (HNF4A)
PROVOKES INTESTINAL GENES IN SQUAMOUS
OESOPHAGEAL CELLS**

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Introduction Barrett's metaplasia, a precursor of oesophageal adenocarcinoma, is characterised by a change of the distal squamous oesophagus to a columnar/intestinal phenotype. The molecular mechanisms responsible for the phenotypic change seen in Barrett's metaplasia are not known. Hepatocyte nuclear factor 4 α (HNF4 α) is a transcription factor originally identified in hepatoma cells, but with essential functions in gastrointestinal tract development and function. HNF4a is not normally found in squamous epithelium but is identified in Barrett's metaplasia. The objectives of this research was to examine the utility of HNF4a in inducing a columnar/intestinal phenotypic change in squamous oesophageal epithelium following ectopic expression.

Methods Ectopic HNF4a expression was induced in a mouse model of squamous epithelium using adenoviral vectors. The intestinal markers, cytokeratin 8 (K8), villin, trefoil factor 3, alkaline phosphatase and mucin2, along with the squamous epithelial proteins p63 and K14 were examined using immunohistochemistry or PCR following HNF4a expression.

Results Three days of ectopic HNF4a is sufficient to provoke the expression of intestinal markers villin, trefoil factor 3 and K8 in squamous oesophageal cells. The expression of the squamous transcription factor p63 is down regulated following HNF4a expression. Interestingly ectopic HNF4a provokes the expression of E-cadherin in squamous oesophageal cells grown under low calcium conditions.

Conclusion HNF4a is a new candidate factor for the induction of Barrett's metaplasia. Ectopic expression is sufficient to provoke a change in the phenotype of squamous cells consistent to that seen in Barrett's metaplasia. These experiments demonstrate for the first time the expression of columnar intestinal markers (K8, villin and trefoil factor 3) in squamous oesophageal cells following forced HNF4a induction. Understanding the molecular steps that regulate the induction of HNF4a in squamous epithelium will provide further insight to the early initiation of Barrett's metaplasia and may provide therapeutic opportunities.

Competing interests None.

Keywords Barrett's oesophagus.