# Oral presentations

## 1 THE USE OF FLUORESCENT BILE ACIDS TO CHARACTERISE UPTAKE IN OESOPHAGEAL CELLS

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**Introduction** Bile acid presence in the refluxate has been implicated in the development of Barrett's oesophagus and oesophageal adenocarcinoma. However the uptake and distribution of bile acids in the normal esophageal epithelium has not been properly characterised. The role of deoxycholic acid (DCA) in this context is especially important to understand.

**Aims/Background** To study the uptake and distribution of bile acids in normal esophageal cell lines using the fluorescent analogs. To compare the uptake of free bile acids versus conjugated bile acids. To study the uptake of bile acids in cells exposed in a pulsative manner similar to GORD. To characterize this mode of transport of both the free bile acids and the conjugated bile acid.

**Method** Bile acids analogs (10 μM) (3 mg dansyl DCA and 3 mg dansyl TDCA) were added to a chamber slide of Het1A cells and the images were obtained using a 63× objective on a Zeiss laser scanning confocal microscope. 3 mg NBD DCA was used to compare the transport of a different fluorescent bile acid and determine whether the fluorescent component affected the bile acid.

Transport Experiment: Fluorescent bile acid (10 μM) was added to each well of a 48 well plate and left for 30 min. The supernatant was removed and the cells were washed twice with PBS. Equal volume of lysis buffer was added to the well and left for 30 min. This was removed and both the lysate and supernatant were run through HPLC and the fluorescent bile acid was quantified from the chromatogram.

**Results** Fluorescent bile acids can rapidly enter epithelial cells in the oesophagus and achieve high concentration. The uptake of DCA is a mixture of active and passive transport that doesn't follow Michaelis Menten kinetics. TDCA is passively transported into the cells with a decrease in transport from normal cells to Barrett's to cancer. Bile acids accumulate to high concentration intracellularly when cells are repeatedly exposed to them at low concentrations as happens in gastroesophageal reflux disease. There is a proposed novel new mechanism of bile acid transport into epithelial cells via endocytosis through the caveolae which is influenced by EGFR.

**Conclusion** In the context of the progression from normal squamous epithelial cells to a more dysplastic morphology, bile acids have been shown to play an important role. The ease of bile acid transport and potential to accumulate in high concentrations shown in this study outline the possible long term consequences of GORD.