Identification of stem cells of the human squamous oesophageal epithelium.

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Barrett’s could arise from abnormally differentiating epithelial stem cells, but their location is still controversial. Identifying these cells would improve our understanding of Barrett’s development and provide important research tools. Previous studies on 2D tissue sections may lead to errors in interpretation.

We aimed to characterise the cell proliferation and locate the stem cells in the epithelium of squamous oesophagus, using 3D epithelial wholemounts.

Quantitative analysis (4x10⁴ cells) of the cell proliferation showed a clear decrease from the inter-papillary epithelium to the top of the papillae (p<10⁻⁴), which was confirmed by quantitative analysis of mitosis (p<10⁻⁴). In keeping with this, consistent staining of epithelial stem cell markers (β1-integrin, MCSP, CD34) identified candidate stem cells at the top of the papillae. Immunofluorescence for cell lineage markers confirmed their epithelial origin.

Primary keratinocytes were sorted based on differential CD34 expression and, if cultured, the putative stem cells highly expressing CD34 showed higher self-renewal potential, compared to CD34-negative cells.

For the first time, candidate stem cells of human oesophageal epithelium have been identified using 3D imaging. Clone-size analysis and 3D in-vitro culture are currently in progress. These results have important implications for our understanding and potential future prevention of Barrett’s.