Gland phenotype evolution within Barrett’s

- Non-dysplastic surveillance Barrett biopsy
- Immunohistochemistry for MUC2 and MUC5AC
- LCM sequencing for mtDNA mutations

MUC2+ MUC5AC+ share a common mutation with MUC2+ MUC5AC- glands

Evans et al., Unpublished
A range of sources have been proposed including:
1) Native squamous stem cells
2) Deep submucosal gland or duct stem cells
3) Gastric glands
The ‘stereotypical’ Barrett’s gland

Gastric glands with intestinal metaplasia?

McDonald et al., Nat Gastro 2015

Foveolar cell (MUC5AC)

Goblet cell (MUC2+)

Mucous secreting Cell (MUC6+)
Gene expression in Barrett glands mimics that of pyloric stomach glands

MUC5AC

Barrett’s

Pylorus

Barrett’s

Pylorus

Barrett’s

MUC2

Lavery et al., Gut 2014
Trefoil factor expression in Barrett’s and pyloric glands

Lavery et al., Gut 2014
Stem cell identification: *LGR5* mRNA in situ hybridization

Lavery et al., Gut 2014
Proliferative zones: Barrett’s vs gastric glands

Lavery et al, Gut 2014
IdU infusion

- 200mg/m² body surface area up to 400mg max
- 30 min infusion at diagnosis followed by resection
- Pan et al., Gastroenterology 2013;144(4):761-70
Bidirectional cell migration in Barrett glands

C

Surface

Middle

Base

% IdU-positive cells

Days

% IdU-positive cells

Days

% IdU-positive cells

Days
Proposed model of the development of Barrett’s oesophagus

Non-diseased individual

Acid reflux

Initial wound repair

Migration of acid-resistant columnar epithelium from stomach

Barrett’s oesophagus

McDonald et al., CMGH 2015
Phenotypic glandular diversity in Barrett’s

A broad range of gland ‘phenotypes’ encountered in Barrett’s oesophagus

Possibly a phenotypic gradient between proximal and distal regions

McDonald et al. CMGH 2015
Barrett’s glands and non-goblet glands show similar functional organisation

<table>
<thead>
<tr>
<th>H&amp;E</th>
<th>MUC5AC</th>
<th>MUC6</th>
<th>VILIN</th>
<th>Ki67</th>
<th>LGR5 CISH</th>
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<tbody>
<tr>
<td>NON-GOBLET CYLINDER EPITHELIUM</td>
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<td>NON-DYSPLASTIC BARRETT'S</td>
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Marnix Jansen (unpublished)
Non-goblet cell gland evolution to cancer

Macroscopy opened specimen

H&E overview

Enzymatic CCO stain

Multibiopsy sampling with absolute anatomic information

Lavery et al., Gut 2016