NF-κB activation in oesophageal cells following acid exposure
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The early molecular pathogenesis of Barrett’s metaplasia remains unclear. In particular, how the oesophageal mucosa responds to exposure to duodenogastric refluxate has yet to be elucidated in any detail. There is increasing recognition of the importance of interactions between epithelial and stromal cells in other contexts, and it is likely that similar interactions may operate in the oesophagus. To investigate this, we exposed both primary human oesophageal squames (HOSs) and, separately, oesophageal fibroblasts (HOFs) to acid (pH7 – pH4 ≤120 minutes). Next the media conditioned by HOS exposure to acid was applied to HOFs and vice versa. Exposure of HOSs to pH4 for 60-120 minutes resulted in the activation of NF-κB whilst HOFs demonstrated a reduction in cell viability without translocating NF-κB. Interestingly however, subjecting HOSs to pulsatile pH5 led to the production of a factor which triggered paracrine NF-κB activation in HOFs. This was observed in conditions that did not cause significant NF-κB activation in HOSs themselves. This cross-talk between squamous cells and fibroblasts indicates a biological effect of relatively modest acid exposure and suggests that signalling between epithelial and stromal compartments may indeed be of relevance in the development of Barrett’s oesophagus.