Inflammation related stromal genes in the progression from Barrett’s oesophagus to oesophageal adenocarcinoma
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The stroma is implicated in the progression and metastases of cancer however, its role in the benign to malignant transition is unknown. Expression arrays from Barrett’s oesophagus (BE), dysplasia and adenocarcinoma (OAC) identified distinct stromal signatures which distinguished between disease stages. Gene ontology analyses revealed a central role of inflammation related genes including TGFβ. Expression of key genes including IL6, BCL6, COX2 and TGFβ related periostin, TSP1, TMEPAI was confirmed at the protein level. In vitro functional assays demonstrated induction of invasion by periostin as well as an IL6 mediated down-regulation of TP53. Profiling of primary fibroblasts from BE and OAC, a key stromal component, were characterized by similar inflammation related ontologies. Analysis of publically available datasets revealed enrichment of these inflammatory stromal signatures in the progression from pre-invasive to invasive disease for the colon, stomach and pancreas but not in breast cancer. Together these data suggest a contribution of stromal inflammatory pathways in the genesis of gastrointestinal cancers from pre-invasive lesions. These have implications for chemoprevention strategies in an era of drugs to target inflammation.