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The ERK MAP kinase-PEA3/ETV4-MMP-1 axis is operative in oesophageal adenocarcinoma

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Many members of the ETS-domain transcription factor family are important drivers of tumorigenesis. Their activation by Ras-ERK pathway signaling is particularly relevant to the tumorigenic properties of many ETS-domain transcription factors. The PEA3 subfamily of ETS-domain transcription factors have been implicated in tumor metastasis in several solid tumors. We have studied the expression of the PEA3 subfamily members PEA3/ETV4 and ER81/ETV1 in oesophageal adenocarcinomas and determined their role in oesophageal adenocarcinoma cell function. PEA3 plays an important role in controlling both the proliferation and invasive properties of OE33 oesophageal adenocarcinoma cells and a key target gene is *MMP-1*. The ERK MAP kinase pathway activates PEA3 subfamily members and also plays a role in these PEA3 controlled events, establishing the ERK-PEA3-MMP-1 axis as important in OE33 cells. PEA3 subfamily members are upregulated in human adenocarcinomas and expression correlates with MMP-1 expression and late stage metastatic disease. Enhanced ERK signaling is also more prevalent in late stage oesophageal adenocarcinomas. This study shows that the ERK-PEA3-MMP-1 axis is upregulated in oesophageal adenocarcinoma cells and is a potentially important driver of the metastatic progression of oesophageal adenocarcinomas.

Biography

Yeng S Ang has an international professional standing and research expertise to enhance clinical interventions in Barrett's oesophagus and oesophageal cancer. He is a Member of the BSG/National Clinical Research Institute Upper GI early cancer prevention research subgroup. He is a peer reviewer for the NIHR RFPB programme and a member of the Research Steering Board of Manchester Cancer Research Centre (Cancer Research UK Manchester Institute). These research initiatives have shaped his contribution for the management of GORD, Barrett's oesophagus and oesophageal cancer. He has published over 45 articles and he is a Supervisor for PhD and MD students in the molecular cancer group of the University of Manchester.

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