Activation of epidermal growth factor receptor results in Snail protein but not mRNA overexpression in endometrial cancer.

Abstract:
Reduced E-cadherin expression is associated with tumour progression of many carcinomas, including endometrial cancers. The transcription factor Snail is known as one of the most prominent transcriptional E-cadherin repressors; its regulation in cancer tissues, however, still remains unclear. Here, we report that activation of epidermal growth factor receptor (EGFR) resulted in overexpression of Snail and also identified critical downstream signalling molecules. Stimulation of two endometrial carcinoma cell lines with epidermal growth factor (EGF) lead to an increase of Snail protein expression. In primary human endometrioid endometrial carcinomas Snail protein expression correlated with the activated, phosphorylated form of EGFR (Tyr1086) as revealed by profiling 24 different signalling proteins using protein lysate microarrays. In addition, we observed an inverse correlation between Snail and E-cadherin protein levels in these tumours. Most likely, p38 MAPK, PAK1, AKT, ERK1/2 and GSK-3beta are involved in the up-regulation of Snail downstream of EGFR. Snail mRNA expression did not show a correlation with activated EGFR in these tumours. Taken together, profiling of signalling proteins in primary human tissues provided strong evidence that EGFR signalling is involved in Snail protein overexpression.