EGF modulates the β-catenin/α-catenin Membrane Complex in Oesophageal Squamous Carcinoma Cells

L.J.G. Jones, D.J. Schnugh and R.B. Veale

School of Molecular and Cell Biology, University of the Witwatersrand

Central to the adhesion complex of epithelial cells is the association between E-cadherin and β-catenin, which in turn binds to actin-bound α-catenin. Activated EGF receptor phosphorylates β-catenin on Tyr654, which is thought to decrease β-catenins affinity for α-catenin. Such a decrease would seriously compromise intercellular adhesion, which is implicated in tumour invasion and metastasis. We therefore determined the effect of EGF on the membrane-associated β-catenin adhesion complex in five moderately differentiated oesophageal squamous cell carcinoma (OSCC) cell lines.

Under standard conditions, both α-catenin and β-catenin were shown to be localised mainly at the plasma membrane, with weaker cytoplasmic/nuclear staining (indirect immunofluorescence and densitometric analysis of western blots). At 0-1 hour of EGF treatment, membrane and cytoplasmic/nuclear levels of β-catenin appeared not to change, although cytoplasmic α-catenin showed a slight increase during this time. EGF exposure for 3-6 hours showed a small decline of β-catenin levels in the cytoplasm/nuclear fraction, while α-catenin levels were increased significantly in this fraction.

Thus, EGF phosphorylation of β-catenin appears to provide the dissociation of β-catenin/α-catenin complex, with α-catenin translocating away from the membrane into the cytoplasm and nucleus. This has implications for i) the turnover of these proteins by making them available to the degradation pathway, ii) effecting their role in adhesion by destabilising the adhesion complex, and iii) in gene regulation via the Lef1/TCF transcription complex.