

Transforming growth factor-beta enhances invasion and metastasis in Ras-transfected human malignant epidermal keratinocytes

Type: Article

Abstract:

Transforming growth factor- beta(TGF-beta) is known to act as a tumour suppressor early in carcinogenesis, but then switches to a pro-metastatic factor in some late stage cancers. However, the actions of TGF-beta are context dependent, and it is currently unclear how TGF-beta influences the progression of human squamous cell carcinoma (SCC). This study examined the effect of overexpression of TGF-beta 1 or TGF-beta 2 in Ras-transfected human malignant epidermal keratinocytes that represent the early stages of human SCC. In vitro, the proliferation of cells overexpressing TGF-beta 1 or TGF-beta 2 was inhibited by exogenous TGF-beta 1; cells overexpressing TGF-beta 1 also grew more slowly than controls, but the growth rate of TGF-beta 2 overexpressing cells was unaltered. However, cells that overexpressed either TGF-beta 1 or TGF-beta 2 were markedly more invasive than controls in an organotypic model of SCC. The proliferation of the invading TGF-beta 1 overexpressing cells in the organotypic assays was higher than controls. Similarly, tumours formed by the TGF-beta 1 overexpressing cells following transplantation to athymic mice were larger than tumours formed by control cells and proliferated at a higher rate. Our results demonstrate that elevated expression of either TGF-beta 1 or TGF-beta 2 in cells that represent the early stages in the development of human SCC results in a more aggressive phenotype.

Author	<ul style="list-style-type: none">• Davies, M.• Prime, S. S.• Eveson, J. W.• Price, N.• Ganapathy, A.• D'Mello, A.• Paterson, I. C.
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