

P013 Regulation of $\alpha\text{v}\beta\text{6}$ -dependent functions
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Expression of $\alpha\text{v}\beta\text{6}$ is very low or undetectable in resting keratinocytes but is highly upregulated in squamous cell carcinoma (SCC). Thus our lab has shown that $\alpha\text{v}\beta\text{6}$ promotes invasion by modulating the production of MMP9. However the molecular mechanisms by which $\alpha\text{v}\beta\text{6}$ mediates invasion are not fully understood. Therefore we have investigated two aspects of $\alpha\text{v}\beta\text{6}$ -dependent behaviour. Firstly, to determine whether MMP9 was regulated transcriptionally, a large panel of MMPs was screened by real time RT-PCR using cell lines C1 and VB6, varying only in their expression of $\alpha\text{v}\beta\text{6}$. We discovered that more than 5 different proteases of the matrix metalloprotease (MMP) family, including MMP2, MMP9, MMP10, MMP12 and MMP13, are modulated at transcriptional level when $\alpha\text{v}\beta\text{6}$ binds to its ligand. Secondly, we also investigated the role of the growth factors in modulating $\alpha\text{v}\beta\text{6}$ functions. EGF and HGF/SF, but not KGF or PDGF, were shown to increase migration of VB6 cells in an $\alpha\text{v}\beta\text{6}$ -dependent manner. Moreover, in preliminary experiments, LY294002 was shown to inhibit the EGF-dependent but not the HGF-dependent increase in $\alpha\text{v}\beta\text{6}$ -dependent migration. Thus $\alpha\text{v}\beta\text{6}$ -dependent migration can be promoted by via PI3-kinase-dependent and -independent pathways.