**14d The Role of Jnk Signaling in Cell-Cell Adhesion and Differentiation of Epithelial Cells: Implications for Tissue Engineering of Stratified Epithelium**

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The c-jun-N-terminal protein kinases (JNK) belong to the mitogen activated protein kinase (MAPK) group of serine/threonine protein kinases. They are primarily activated in response to stress and induce a diverse set of responses ranging from apoptosis to cell survival. Here we show that inhibition of JNK phosphorylation by the chemical inhibitor SP600125, induces cell-cell adhesion in primary keratinocytes even in low Ca2+ conditions and in serum free medium. Cell adhesion is accompanied by upregulation of integrin alpha3 (2-fold) and beta1 (1.5-fold) as well as changes in actin cytoskeleton and redistribution of integrins and E-cadherin to the cell-cell junctions on the cell surface. Interestingly, blocking integrin alpha3 did not block SP 600125-induced cell-cell adhesion but increased migration, suggesting that this integrin may stabilize cell-cell contacts by reducing cell motility. Inhibition of JNK also reduced proliferation and initiated the program of keratinocyte differentiation in cell culture and in three-dimensional bioengineered skin substitutes. We are currently investigating at the role of JNK in controlling the switch between proliferation and differentiation using dominant negative and siRNA approaches.