

**P051** A role for syntenin in syndecan 1 mediated formation of filopodia

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The HSPG receptor syndecan-1 interacts with the carboxy-terminal LG4/5 domain in laminin-332 to participate in keratinocyte migration. Our recent experiments demonstrate that syndecan-1 mediated cell adhesion to the LG4/5 fragment induces a cytoskeleton organization in arrays of microspikes and filopodia-like structures, the cortical actin cytoskeleton being organized in stable, radial spikes, containing F-actin and the actin cross-linking protein fascin. In addition, cell adhesion to the LG4/5 fragment triggers the activation of Rac1 and Cdc42, two GTPases regulating the formation of lamellipodia and filopodia. Here we show that syndecan-1 is constitutively phosphorylated on tyrosine residues and that an initial event upon cell adhesion is the rapid tyrosine dephosphorylation of syndecan-1. The kinetics of this phenomenon is comparable to that of LG4/5 attachment to syndecan-1 and is completed within 5 minutes, suggesting the involvement of an active tyrosine phosphatase recruited upon LG4/5 ligation. The link between syndecan-1 phosphorylation and cell adhesion is also reinforced by the use of orthovanadate, which by inhibiting phosphatases, dramatically prevents cell adhesion to the LG4/5 fragment. By searching potential intracellular partners of tyrosine-dephosphorylated syndecan-1, we have identified the cytosolic protein “syntenin-1” as a major downstream effector of tyrosine-dephosphorylated syndecan-1. While syntenin-1 is known as a syndecan-associated protein, its potential involvement in microspike formation has never been shown. The present study demonstrates that the cytoskeleton protein syntenin-1 could act as a molecular switch essential in the formation of syndecan-1 mediated filopodia.