P006 Activation of syndecan-4 reconstitutes cell spreading and triggers dynamic regulation of Rho-family GTPases

Mark D. Bass, Zohreh Mostafavi-Pour and Martin J. Humphries
University of Manchester

Fibroblasts plated onto a recombinant ligand of integrin alpha5beta1 spread but fail to form vinculin-containing adhesions until stimulated with a ligand of the transmembrane proteoglycan, syndecan-4. Ligation of syndecan-4 stimulates the sequential formation of focal complexes behind leading lamellae followed by focal adhesions and stress fibres. This process resembles the formation and maturation of adhesion complexes seen during adhesion to whole fibronectin, and is regulated by signalling proteins commonly associated with integrin-mediated adhesion. The formation of focal complexes and lamellipodia following syndecan-4 activation coincides with activation of Rac1 and suppression of RhoA immediately after stimulation, whereas the subsequent formation of focal adhesions and stress fibres depends upon the activation of RhoA and the downstream effector Rho kinase. Furthermore, the early suppression of RhoA is mediated by activation of p190RhoGAP through tyrosine phosphorylation and recruitment to the membrane. p190RhoGAP has previously been shown to be responsible for RhoA suppression during integrin-mediated adhesion to fibronectin. Thus, the engagement of syndecan-4 reconstitutes many of the signalling processes activated during cell spreading and, in co-operation with alpha5beta1, makes a major contribution to cyotskeletal regulation during spreading on fibronectin.