

P008 Engagement of syndecan-4 modulates the regulation of RhoA during cell spreading and stimulates p190RhoGAP by recruitment to the membrane

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Fibroblasts spread on a recombinant ligand of integrin alpha5beta1 but are unable to form RhoA-dependent focal adhesions or actin stress fibres unless the transmembrane proteoglycan, syndecan-4, is also stimulated. During the initial phase of cell spreading on fibronectin, RhoA activity is suppressed to allow rapid membrane protrusion, and is re-activated during the later phase to stimulate rearrangement of actin into stress fibres. Stimulation of pre-spread fibroblasts with a soluble syndecan-4 ligand reconstitutes the bi-phasic RhoA activation profile observed during cell spreading on whole fibronectin. Furthermore, both suppression and re-activation of RhoA are compromised when cells spread on an isolated alpha5beta1 ligand compared with fibronectin, indicating that syndecan-4 plays a role in this process. Previous studies have demonstrated that p190RhoGAP is one of the mediators of the early suppression of RhoA activity during spreading and is in turn regulated by tyrosine phosphorylation. We have shown that engagement of syndecan-4 not only induces a limited change in tyrosine phosphorylation, but triggers a dramatic redistribution of p190RhoGAP to the membrane during the early phase. We hypothesise that the dual-regulation of p190RhoGAP by redistribution and tyrosine phosphorylation is one of the points at which integrins and syndecan-4 cooperate to enable membrane protrusion.