

# Neuronal Thy-1 induces astrocyte adhesion by engaging syndecan-4 in a cooperative interaction with $\alpha_3$ integrin that activates PKC $\delta$ and RhoA

Avalos, Ana María

Valdivia, Alejandra D.

Muñoz, Nicolás

Herrera-Molina, Rodrigo

Tapia, Julio C.

Lavandero, Sergio

Chiong, Mario

Burridge, Keith

Schneider, Pascal

Quest, Andrew F.G.

Leyton, Lisette

Clustering of  $\alpha_3$  integrin after interaction with the RGD-like integrin-binding sequence present in neuronal Thy-1 triggers formation of focal adhesions and stress fibers in astrocytes via RhoA activation. A putative heparin-binding domain is present in Thy-1, raising the possibility that this membrane protein stimulates astrocyte adhesion via engagement of an integrin and the proteoglycan syndecan-4. Indeed, heparin, heparitinase treatment and mutation of the Thy-1 heparin-binding site each inhibited Thy-1-induced RhoA activation, as well as formation of focal adhesions and stress fibers in DI TNC1 astrocytes. These responses required both syndecan-4 binding and signaling, as evidenced by silencing syndecan-4 expression and by overexpressing a syndecan-4 mutant lacking the intracellular domain, respectively. Furthermore, lack of RhoA activation and astrocyte responses in the presence of a PKC inhibitor or a dominant-negative form of PKC $\delta$  implicated PKC $\delta$  and RhoA activation in these e