

Astrocytic α 5 β 3 integrin inhibits neurite outgrowth and promotes retraction of neuronal processes by clustering Thy-1

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Thy-1 is a membrane glycoprotein suggested to stabilize or inhibit growth of neuronal processes. However, its precise function has remained obscure, because its endogenous ligand is unknown. We previously showed that Thy-1 binds directly to α 5 β 3 integrin in trans eliciting responses in astrocytes. Nonetheless, whether α 5 β 3 integrin might also serve as a Thy-1-ligand triggering a neuronal response has not been explored. Thus, utilizing primary neurons and a neuron-derived cell line CAD, Thy-1-mediated effects of α 5 β 3 integrin on growth and retraction of neuronal processes were tested. In astrocyte-neuron co-cultures, endogenous α 5 β 3 integrin restricted neurite outgrowth. Likewise, α 5 β 3-Fc was sufficient to suppress neurite extension in Thy-1(+), but not in Thy-1(-) CAD cells. In differentiating primary neurons exposed to α 5 β 3-Fc, fewer and shorter dendrites were detected. This effect was abolished by cleavage of Thy-1 from the neuronal surface using phosphoinositide-specific