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Role of Ndr2 kinase in substrate-specific neurite growth and spine development

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Neurons express a variety of alpha/beta integrin heterodimers, which allow them to control neurite growth on different extracellular substrates. The nuclear Dbf2-related protein kinases 2 (Ndr2) has been suggested to play an important role in such integrin-mediated neuronal development and function. However, how Ndr2 determines the substrate specificity of the neurite growth has not been resolved yet. Here we show that stable overexpression of Ndr2 in PC12 cells increases the phosphorylated beta1 integrin in the growth tips, reflecting the previously observed increase in neurite growth of primary neurons upon Ndr2 overexpression. By contrast, the expression of alpha1 integrin was markedly reduced in the growth tips of Ndr2 overexpressing PC12 cells, resulting in a reduced growth response to soluble and deposited alpha1beta1 integrin substrates. Laminin-111 is a neural extracellular matrix substrate, which can specifically bind and induce growth through a1b1 integrin dimers. By cultur
ing primary hippocampal primary neurons on PDL vs. Laminin-111 substrate, we could demonstrate that Ndr2 kinase also determines the substrate specificity of the dendritic growth of neurons, likely involving the above mentioned alpha1 and beta1 integrin subunit modulation. Whether these mechanisms also translate to changes in synapse formation and function is currently under investigation. Overall, our findings confirm the previously observed increase in dendritic growth of neurons by Ndr2 kinase and suggest that Ndr2 is also involved in determining the substrate specificity of neurite growth. Supported by the German Research Foundation (CRC779-TPB05 and STO488-4).