ABSTRACT

TITLE:	Characterization of CD9 as an Alternative Receptor for IL-16 Signaling in Cerebellar Granule Neurons
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ABSTRACT: Interleukin-16 (IL-16) was initially described as a pro-inflammatory cytokine. IL-16 has diverse immunoregulatory effects in various tissues and has recently been shown to induce neurite outgrowth in cerebellar granule neurons. In neurons IL-16 binds to the CD4 receptor, which triggers a signaling pathway that upregulates the expression of c-Fos. c-Fos transcriptionally regulates genes that promote proliferation, growth, and survival of neurons (Fenster et al., 2010). In previous studies, cerebellar granule neurons isolated from CD4 knockout mice still exhibited c-Fos expression and increased neurite outgrowth when treated with IL-16 (Fenster et al., 2010). This indicates that in cerebellar granule neurons, IL-16 could be binding to an alternative receptor in order to elicit this response. We hypothesize that the tetraspannin receptor CD9 may be the alternative to CD4 in cerebellar granule neurons. In other cells throughout the body, CD9 has been identified as an alternative receptor for IL-16 signaling. For instance, human mast cells respond to IL-16 treatment in a CD9-mediated pathway (Qi et al., 2005). Using several cellular and molecular biology techniques, we characterized the CD9 receptor in cerebral granule neurons. In this study we demonstrated that CD9 is present in high concentrations in cerebellar granule neurons as well as the whole brain. In addition, CD9 is highly dispersed throughout neurons and co-localization occurs with the synaptic protein PSD-95. Also CD9 is expressed in higher concentrations in neurons in comparison to CD4. Our data provides evidence to the support the hypothesis that CD9 acts as an alternative receptor of CD4 in cerebellar granule neurons. Our analysis will lay the foundation for further studies of IL-16-mediated signaling through CD9 in neurons.