A011 The expression level of Eps8 modulates the migratory activity of neural progenitors expressing ErbB4

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The expression of the tyrosine kinase receptor ErbB4 confers to the neural progenitor cell line ST14A increased migratory activity. By gene expression profiling analysis, we examined the transcriptional changes associated with higher migratory activity mediated by specific ErbB4 isoforms, and found up-regulation of Eps8, a multimodular regulator of actin dynamics. Through in vitro experimental manipulation of the Eps8 expression level, we showed that Eps8 synergizes with ErbB4 to confer increased migratory capability to ST14A cells, whereas siRNA mediated Eps8 silencing impairs both basal and neuregulin1 (NRG1) stimulated migration.

In vivo, ErbB4 is involved in regulating the migratory behaviour of a subpopulation of medial ganglionic eminence derived interneurons migrating towards the cortex, and of olfactory bulb neural precursors migrating from the subventricular zone (SVZ) towards the olfactory bulb (OB). We focused our attention on the SVZ-OB system, showing that Eps8 and different ErbB4 isoforms are expressed. We thus tested, in this model system, whether down-regulation of Eps8 would affect neural precursor migration. Using transient knockdown of Eps8 by in vivo siRNA electroporation, followed by primary cultures of SVZ explants, we demonstrated that Eps8 down-regulation inhibits migration of OB precursors. These findings demonstrate that Eps8 is a key regulator of neural progenitor motility and underline the importance of proper actin remodeling in neuronal migration.