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A role for Semaphorin4D-plexin-B interactions in neuronal migration and pattern formation in the developing neocortex and sensory motor system

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The correct neuronal migration to specific cortical locations is a prerequisite for the normal patterning and function of the nervous system. Impaired neuronal migration is known to underlay a range of developmental problems, including neurodegenerative disorders. Mechanisms that regulate neuronal migration are still remaining to become elucidated.

Here we found that Sema4D, the ligand for B-type Plexins, Plexin-B1 and Plexin-B2, accelerated migration of both radially- and tangentially-migrating cells towards their correct destination zones over mock-treated, in cortical slices and ventricular zone explants, thereby suggesting a motogenic role for Sema4D.

Loss of Plexin-B1 function did not result in any developmental abnormalities in neuronal production, cortical architecture and cell morphology, indicating no essential requirement for this gene in cortical development.

In contrast, our results reveal that Sema4D/Plexin-B2 interaction regulates the migratory behaviour of neuronal precursors and newly generated neurons. Analyses of mice constitutively lacking Plexin-B2 signaling revealed a key requirement for Plexin-B2 in proliferation and migration of neuroblasts and in cortical topography. *plxnb2*$^{-/-}$ mice contained less number of cells across cerebral wall and that was accompanied with the finding that radial and tangential migrations was delayed in these animals. Consequently mutants lacking Plexin-B2 signaling demonstrated defects in early and late neuronal differentiation.

In the developing spinal cord, ligand-receptor pairs, Plexin-B1/Sema4D and Plexin-B2/Sema4C, were found to be expressed in striking and characteristic patterns during critical periods of sensory motor circuitry development. Constitutive double deletion of Plexin-B1 and Plexin-B2 resulted in defects in cell groups, such as motor neurons, and axonal bundles. These observations suggest that class 4 Semaphorins regulate cell fate, migration, layer formation and

afferent connectivity in the developing neocortex and spinal cord via activation of B-type Plexins.