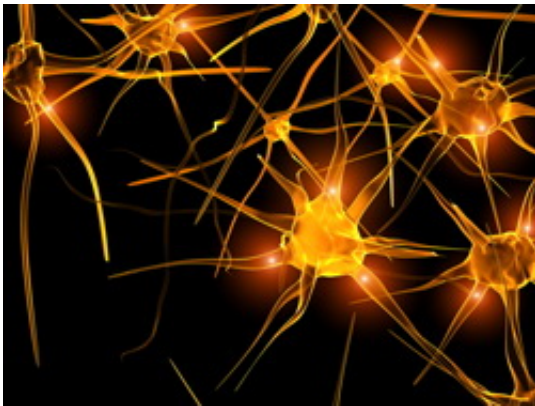


Driving developing brain neurons in the right direction

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One of the marvels of brain development is the mass migration of nerve cells to their functional position. European research has investigated the molecules required for their successful navigation.

Formation of the cerebral cortex during [embryonic development](#) requires the migration of billions of cells from their birth position to their final destination. A motile nerve cell must have internal polarity to move in the specified direction. What is more, neurons then have to extend neurites or projections from the cell body to communicate with each other.

The key to this extraordinary feat of organisation lies in cell signalling

pathways. The EU-funded Neuronal Polarity project aimed to characterise these cascades important in [cerebral cortex](#) development. At a later stage, defective cortical architecture can be responsible for brain pathologies including microcephaly, epilepsy and schizophrenia.

Project scientists showed that in vivo the guanine triphosphatase GTPase Ras-proximate-1 (Rap 1) caused an accumulation of neurons halfway to their destination. The team used time-lapse video microscopy and immunostaining to show that the problem does not lie with motility of the neurons but in a defect in their polarity. Other evidence from motility tests in vitro and the fact that some neurons do actually make it to their destination, albeit slowly, suggest Rap 1 is important for initial polarisation of the neurons.

The transmembrane receptor N-cadherin (Ncad) also has an important function in polarising cortical neurons. Experimental data confirmed that this receptor is involved downstream from Rap 1. Overall, inhibition of Rap 1 reduces Ncad presence.

Neuronal Polarity scientists suggest that Rap 1 activity is important in migrating neurons to maintain a high level of Ncad at the [plasma membrane](#) for [nerve cells](#) to polarise correctly.

Exactly how Ncad interacts with molecular cascades for neuron [polarisation](#) is still under investigation. The Neuronal Polarity project accumulated data on which to base a concrete research path for future investigation.

Provided by CORDIS

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