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DEVELOPMENT

It's not just a gap

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When we look up the definition of gap junctions in a textbook, we find that they are intracellular channels that connect the cytoplasm of adjacent cells and allow the exchange of small molecules and ions. In *Nature*, Laura Elias and colleagues now describe that the adhesive, but not the channel, properties of gap junctions are essential for neural migration.

During brain development, the future pyramidal neurons migrate from their origin in the cortical ventricular zone to the cortical plate along guiding fibres that are extended by radial glia. Using immunohistochemistry, Elias *et al.* visualized the gap-junction subunits connexin-26 (CX26) and -43 (CX43) in both radial glial fibres and in the migrating neurons, and observed that the connexins often localize precisely at points of contact between the two cells. The authors then used RNA-interference technology to examine the functional effects of CX26 and CX43 silencing in the developing brain, and found marked impairment in neural migration. Furthermore, control experiments showed that this defect was not a consequence of impaired cell-cycle exit, differentiation or cell death.

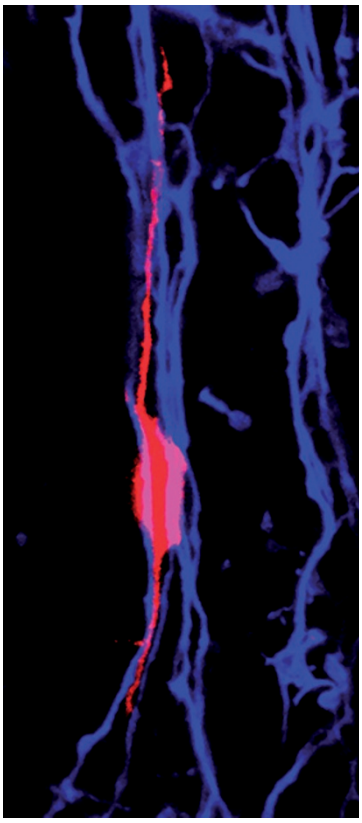
What is the molecular mechanism behind these observations? Elias *et al.* addressed this question by carrying out rescue experiments. They first used CX26 and CX43 mutants that make adhesions but have closed channels, and are therefore unable to mediate exchanges between cells. Surprisingly, the migration defect was fully rescued. Next, they tested whether waves of Ca^{2+} through the wild-type channel could be involved in the regulation of neural migration, but this was not the case. Previous studies had shown that the C-terminal domain of CX43 signals to cytoplasmic proteins and activates kinase cascades. However, Elias *et al.* found that CX43 and CX26 mutants that lacked the C-terminal domain could efficiently rescue the migration phenotype.

Only mutants that were unable to make functional adhesions failed to rescue the observed defect, thus providing for the first time strong evidence that the adhesive properties of gap junctions are necessary for neural migration. Importantly, live-imaging experiments of migrating cells further suggested that gap-junction adhesions stabilize the leading process of the migrating neurons along the radial glial fibre, which is important for determining the direction of the subsequent movement.

In the future, it will be important to investigate the role of the adhesive properties of gap junctions in the migration of other cell types during development and disease.

Francesca Cesari, Locum Editor, Nature

> "…the adhesive, but not the channel, properties of gap junctions are essential for neural migration."



A neuron migrating along a radial fibre, showing their close association. The neuron and the fibres were labelled with tomato, a red fluorescence protein, and DiD, respectively. Image courtesy of L. Elias, University of California, San Francisco, USA.

ORIGINAL RESEARCH PAPER Elias, L. A. B. *et al.* Gap junction adhesion is necessary for radial migration in the neocortex. *Nature* **448**, 901–907 (2007)
FURTHER READING Goodenough, D. A. & Paul, D. L. Beyond the gap: functions of unpaired connexon channels. *Nature Rev. Mol. Cell Biol.* **4**, 285–294 (2003)
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