URLs

ASYMMETRIC CELL DIVISION

A different route to cell fate

Asymmetric cell division has been studied in many different organisms, and although results have indicated that a number of mechanisms might direct this process, only one pathway has been identified so far in animals — the one mediated by PAR proteins. Reporting in *Cell*, Emery and colleagues now describe an alternative pathway that involves the asymmetric distribution of RAB11 endosomes.

Asymmetric division of the *Drosophila melanogaster* sensory organ precursor (SOP) cells is under the control of PAR proteins, which control the asymmetric localization of Numb and Neuralized. These proteins are required for the establishment of distinct fates in the two daughter cells pIIa and pIIb. By controlling the endocytic trafficking of Notch-pathway components, they ensure that Notch signalling is only activated in the pIIa cell.

To understand how endocytic trafficking regulates Notch signalling, the authors expressed green fluorescent protein (GFP) fusions of different RAB GTPases that enabled them to analyse the distribution of the endocytic compartments in the two daughter cells. Time-lapse confocal microscopy revealed that although the distribution of all the markers is similar in the two cells during mitosis, only RAB11–GFP exhibits asymmetric distribution after the completion of cytokinesis — it accumulates in the perinuclear region distal to the cleavage plane

in one of the cells. But does this asymmetry also depend on the PAR–Numb–Neuralized mechanism? And if not, what generates it?

The authors compared the localization of RAB11 and Partner of Numb (PON) in different mutants and showed that RAB11 asymmetry does not depend on the PAR pathway, whereas PON asymmetry does. Next, taking advantage of a collection of mutant lines and screening for changes in RAB11 localization, they identified the *nuclear fallout* (*nuf*) gene. NUF concentrates in the centrosomes and is a known binding partner of RAB11. In fly embryos, both RAB11 and NUF are required for protein recycling. But can they also regulate Notch or Delta recycling? Image analysis, combined with a modified endocytosis assay, confirmed the idea that endocytosed Delta moves through RAB11-specific recycling endosomes only in one of the cells — pIIb.

The authors propose that two partially redundant pathways generate asymmetry in the SOP cells. In the pIIb cell, the PAR proteins, by regulating Numb and Neuralized, repress Notch or activate Delta, whereas in the pIIa cell, inhibition of NUF and RAB11 inhibits Delta, by preventing it from passing through the recycling endosomes. NUF homologues exist and bind to RAB11 in vertebrates, so the obvious next step would be to investigate whether these homo-

logues regulate Notch signalling in vertebrates and control asymmetric cell division in the mammalian brain.

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References and links

ORIGINAL RESEARCH PAPER Emery, G. *et al.* Asymmetric Rab11 endosomes regulate Delta recycling and specify cell fate in the *Drosophila* nervous system. *Cell* **122**, 763–773 (2005)

WEB SITE

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<http://www.imba.oeaw.ac.at/knoblich/index.html>