IN BRIEF

CELL SIGNALLING

How Notch gets selective

The Notch receptor, the extracellular domain of which is composed of epidermal growth factor (EGF) repeats, is activated by Delta and Serrate. How Notch discriminates between these ligands is poorly understood. This study identifies an amino acid in Notch EGF repeat 8 that is essential for the binding of Serrate but not Delta. Val to Met mutation at residue 361 in *Drosophila melanogaster* EGF repeat 8 (*Notch*^{jigsaw}) caused similar phenotypes to loss of Serrate function. Further analysis revealed that *Notch*^{jigsaw} is defective in Serrate–Notch signalling, but not in Delta–Notch signalling, and that this mutation reduces Serrate–Notch binding. Val to Met mutation at residue 327 in mouse Notch 2 decreased its interaction with the Serrate homologue Jagged 1 and also Jagged 1–Notch 2 signalling, whereas Delta-like 1–Notch 2 signalling was unaffected. Thus, the specificity of this Val residue is conserved in Serrate–Notch signalling.

ORIGINAL RESEARCH PAPER Yamamoto, S. *et al.* A mutation in EGF repeat-8 of Notch discriminates between Serrate/Jagged and Delta family ligands. *Science* **388**, 1229–1232 (2012)

CALCIUM

Helping Ca^{2+} into mitochondria

The mitochondrial calcium uniporter (MCU) was recently identified as the ion-conducting pore through which mitochondria are likely to take up Ca^{2+}. Mallilankaraman *et al.* now identify CCDC90A, which they name mitochondrial calcium uniporter regulator 1 (MCUR1), as "an integral membrane protein required for MCU-dependent mitochondrial Ca^{2+} uptake." In an RNAi screen of mitochondrial membrane proteins, the authors found that MCUR1 depletion inhibited mitochondrial Ca^{2+} uptake. Further characterization of this protein revealed that it interacts with the MCU, and that this interaction is necessary for MCU-mediated mitochondrial Ca^{2+} uptake. Finally, the authors found that cells depleted of MCUR1 had abnormal bioenergetic properties similar to those observed in cells in which Ca^{2+} uptake is blocked by established mechanisms. Thus, MCUR1 is necessary for the MCU to efficiently promote mitochondrial Ca^{2+} uptake and to ensure normal mitochondrial bioenergetics.

ORIGINAL RESEARCH PAPER Mallilankaraman, K. *et al.* MCUR1 is an essential component of mitochondrial Ca^{2+} uptake that regulates cellular metabolism. *Nature Cell Biol.* **14**, 1336–1343 (2012)

CYTOSKELETON

Determining optimal length of cilia

Motile cilia on ciliated epithelial cells generate fluid flow in the brain ventricles, trachea and oviduct, which is essential for the proper function of these organs. Fluid flow is a function of ciliary length, but the molecular mechanisms that regulate the optimal length of motile cilia in mammals are unclear. This study shows an important role for the kinesin 8 family member KIF19A in preventing abnormally long cilia. *Kif19a*$^{-/-}$ mice had hydrocephalus, and female *Kif19a*-knockout mice were infertile owing to oviduct obstruction. This was associated with increased ciliary length on all ciliated epithelial cells, which resulted in abnormal ciliary waveforms and an inability to generate proper fluid flow. KIF19A was shown to be a ciliary tip protein that negatively regulates the length of microtubules polymerized from axonemes (which form the cytoskeleton of motile cilia) by causing ATP-dependent depolymerization from the plus end.

ORIGINAL RESEARCH PAPER Niwa, S. *et al.* KIF19A is a microtubule-depolymerizing kinesin for ciliary length control. *Dev. Cell* 15 Nov 2012 (doi:10.1016/j.devcel.2012.10.016)