DEVELOPMENT

Cell patterning by preferential adhesion

A new study shows how dynamic interactions between two cell-adhesion molecules, Roughest and Hibris, determine the precise patterning of the developing *Drosophila* eye.

Cell–cell adhesion is essential for morphogenesis, the process by which single cells are shaped and assembled into complex tissues and organs. But it is not clear how the multitude of cell surface molecules involved in cell adhesion influences cell fates and tissue patterning.

Bao and Cagan looked at adhesion processes in *Drosophila* eye development. At late larval stages, the eye disc, a monolayer epithelium, differentiates to form an array of ‘unit eyes’ or ‘ommatidia’, each of which contains photoreceptor cells, lens-secreting cone cells and primary pigment cells. Undifferentiated cells between these ommatidia, the interommatidial precursor cells (IPCs), then undergo morphogenetic movements and differentiate to create a hexagonal lattice of secondary and tertiary pigment cells and mechanosensory bristles.

Two proteins that are required for this process are Roughest and Hibris, mutations of which lead to abnormally patterned eyes and defects in the axons that project from the eye to the brain. Bao and Cagan show that these proteins are expressed by complementary cells types, and that Hibris serves as a Roughest-binding protein. IPCs expressing Roughest are attracted to Hibris-expressing primary pigment cells, and because Roughest binds more strongly to Hibris than to itself, IPCs compete for contact with ommatidia, which leads to a progressive reduction in IPC–IPC contacts. IPCs that lose out in the competition for contact with ommatidia — those with lower levels of Roughest — eventually die, whereas those expressing high levels of Roughest form long-lasting junctions with primary pigment cells. The authors argue that as successful IPCs maximize their contact with ommatidia, they form a shape with the lowest possible surface free energy — a hexagon.

So, preferential adhesion mediated by heterophilic cell-adhesion molecules seems

Interommatidial cells (artificially coloured green) form a hexagonal pattern around ommatidia in the *Drosophila* pupal eye. Image courtesy of S. Bao and R. Cagan, Washington University in St Louis, Missouri, USA.

to be the driving force behind the elaborate patterning of the *Drosophila* eye. It will be interesting to learn whether preferential adhesion can explain pattern formation in other tissues and organs.

Rebecca Craven

References and links

ORIGINAL RESEARCH PAPER Bao, S. & Cagan, R.

Preferential adhesion mediated by Hibris and Roughest regulates morphogenesis and patterning in the *Drosophila* eye. *Dev. Cell* **8**, 925–935 (2005)

FURTHER READING Hayashi, T. & Carthew, R. Surface mechanics mediate pattern formation in the developing retina. *Nature* **431**, 647–652 (2004)

SYNAPTIC PLASTICITY

A balancing act

Cell-adhesion molecules have a central role in synaptic plasticity, but their mechanisms of action have remained enigmatic. Ashley and colleagues have now identified the signalling machinery responsible for the effects of one cell-adhesion molecule — Fasciclin II (FASII) — on synaptic remodelling at the neuromuscular junction of *Drosophila* larvae.

FASII — a transmembrane protein of the immunoglobulin superfamily of cell-adhesion molecules — regulates expansions in synaptic arbors and bouton formation at the *Drosophila* neuromuscular junction to maintain synaptic efficacy when muscle fibres are enlarged. It is thought that amplifying FASII-mediated cell adhesion blocks synaptic growth, whereas weakening it diminishes this restriction, thereby enabling the growth of new synapses. However, evidence for this proposal is lacking, and little is known about the downstream pathways that are regulated by FASII.

Consistent with this proposal, Ashley and colleagues report that in *Drosophila* larvae, overexpression of FASII either pre- or postsynaptically led to a significant decrease in bouton number. Unexpectedly, however, simultaneous pre- and postsynaptic elevation of FASII resulted in a striking increase in the number of synaptic boutons. Moreover, concurrent pre- and postsynaptic reduction in FASII levels led to a small but significant increase in bouton number.

These results indicate that FASII is effective in synaptic formation only if it is evenly distributed between the pre- and postsynaptic neurons. Moreover, disruption of this balance led to abnormalities in synaptic bouton formation, including a significant decrease in bouton number, abnormal bouton formation with deposits of APPL (the *Drosophila* homologue of amyloid precursor protein) and microtubule tangles surrounding these deposits, which resembled the amyloid- β accumulation of Alzheimer's disease.

Intriguingly, the effect of simultaneously increasing or decreasing FASII pre- and postsynaptically was abolished when APPL

expression was eliminated. These data are consistent with FASII regulating its effects on synaptic bouton formation by signalling through APPL.

Immunocytochemistry and biochemical studies showed that at the neuromuscular junction, FASII and APPL form a biochemical protein complex. The *Drosophila* scaffold protein X11 was also present in this complex and its regulation of APPL was necessary for the action of FASII–APPL signalling on synaptic growth.

These findings point to a role for FASII in synaptic growth beyond its function as a cell-adhesion molecule between pre- and postsynaptic membranes. They implicate FASII in a signal transduction pathway, with APPL and X11, that regulates synaptic remodelling. Moreover, these results show that normally functioning APPL is involved in synapse formation, and might provide clues to the pathological changes seen in Alzheimer's disease.

Alison Rowan

References and links

ORIGINAL RESEARCH PAPER Ashley, J. *et al.* Fasciclin II signals new synapse formation through amyloid precursor protein and the scaffolding protein dX11/Mint. *J. Neurosci.* **25**, 5943–5955 (2005)