WEB WATCH

In the mind of a fly

- http://flybrain.neurobio.arizona.edu/

For anyone looking for a starting point from which to find out about the anatomy of the fly brain, the aptly named Flybrain is a website worth visiting. Describing itself as "an online atlas and database of the *Drosophila* nervous system," this is a useful and comprehensive site that includes clear, well drawn schematics, as well as a range of photomicrographs.

The schematics are a good place to start. When you select a schematic of a frontal section, for example, you are presented with a colourful, clear diagram labelled with abbreviations, which you can click to go on to pages containing micrographs and information about the structure in question. The amount of information provided varies, but the micrographs are of uniformly excellent quality and are provided at a large enough size to be really useful.

The site also includes summary pages on each of the main structures of the fly nervous system — the antennal lobes, mushroom bodies and so on. These will be a particularly helpful resource for students, or for those who want a quick reminder or overview of the anatomy and function of one of these structures. There are also sections devoted to three-dimensional models of the fly brain, neural development in *Drosophila*, and different types of staining, including immunocytochemistry.

The main limitation of this site is that it has not been updated recently. There are one or two places where material has still to be added, and it is clear that a resource of this kind must be maintained if it is to remain useful.

Rachel Jones

restricting the growth of midline tissues and promoting cortical progenitor cell fate. Intriguingly, although there were virtually no cortical plate neurons in the *Lhx2* mutant brain, preplate neurons were generated, indicating that these might be derived from roof plate tissue, a theory that the authors corroborated by fate mapping of Gdf7-expressing cells.

So, this study shows that the roof plate not only controls the expansion of the cerebral cortex through the bimodal regulation of Lhx2 expression, but might also make a cellular contribution. This adds significantly to the roof plate's expanding functional repertoire, and we eagerly await further insights into its role.

Heather Wood

References and links

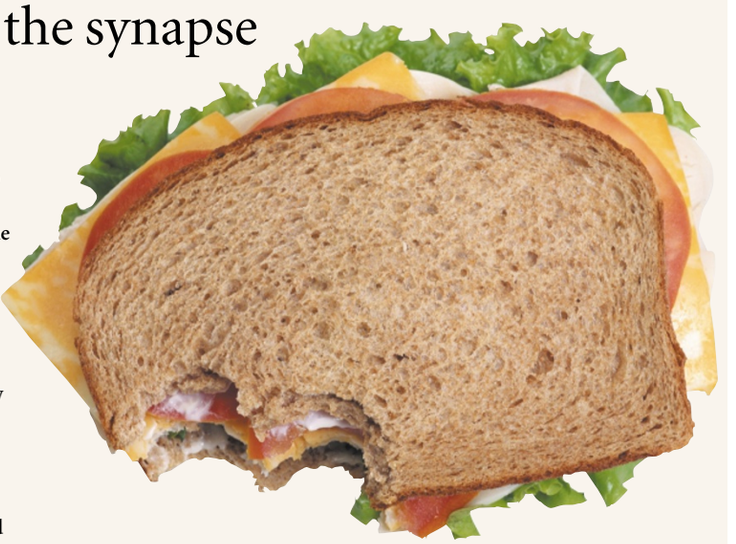
ORIGINAL RESEARCH PAPER Monuki, E. S. *et al.* Patterning of the dorsal telencephalon and cerebral cortex by a roof plate–Lhx2 pathway. *Neuron* **32**, 591–604 (2001)

FURTHER READING Lee, K. J. *et al.* Genetic ablation reveals that the roof plate is essential for dorsal interneuron specification. *Nature* **403**, 734–740 (2000) | Millonig, J. H. *et al.* The mouse *Dreher* gene *Lmx1a* controls formation of the roof plate in the vertebrate CNS. *Nature* **403**, 764–768 (2000)

WEB SITE Christopher Walsh's Lab http://www.walshlab.org/index1.html

DEVELOPMENT

Fattening up the synapse



Synapses are crucial nodes of information transfer in the brain. The pattern of these connections, which outnumber neurons by 100 to 1, is central to brain function, but little has been known about the basic molecular mechanisms that allow this intricate network to wire together. A tantalizing clue was presented by the study of purified retinal ganglion cells (RGCs) in culture, which form few synapses unless they are cultured in the presence of medium conditioned by exposure to glial cells (glial-conditioned medium; GCM). This observation indicated that a factor secreted by glial cells might be limiting for neuronal synapse formation. Now Mauch *et al.* report that they have identified the crucial glial-derived factor, and surprisingly it seems to be cholesterol.

The authors took two approaches to find the glial-derived factor. First, they performed partial purification of the synapse-inducing activity from GCM to establish the molecular weight and chromatographic properties of the active fraction. Then they ran two-dimensional silver-stained gels of RGCs grown in the absence or presence of GCM to identify proteins that transferred from the glia to the neurons. One prominent silver-stained spot was seen to correlate with exposure to glial cells. Microsequencing by nanospray mass spectrometry showed the protein to be the lipoprotein carrier ApoE, the molecular weight and chromatographic profile of which are consistent with the partially purified active fraction from GCM.

Despite this correlation, when the authors added purified ApoE back into RGC cultures, the protein had no synapse-inducing activity. However, reasoning that the function of ApoE is to deliver cholesterol to cells, the authors next tested the effects of adding purified cholesterol to the cultures, and found that cholesterol alone recapitulated all of the synapse-inducing effects of GCM. In addition, they found that the cholesterol content of RGCs rose when they were cultured with GCM, indicating that the synthesis of cholesterol within neurons might be limiting for synaptogenesis.

Although compelling, these data raise a number of questions. Is cholesterol synthesis really limiting for synaptogenesis *in vivo*, when the RGCs are in a far more enriched environment? What is the role of glial-derived ApoE, as the *in vitro* addition of cholesterol alone can induce synapses? Cholesterol is an important structural component of both presynaptic vesicles and the caveolae-like lipid rafts where many postsynaptic receptors cluster, but ApoE can also activate a large number of intracellular signalling pathways through interactions with the low density lipoprotein (LDL) family of receptors. Nonetheless, this elegant assay is supported by the observation of Ullian *et al.* that synaptogenesis of RGCs *in vivo* correlates in time with gliogenesis, indicating that further studies in animals could define a role for lipoprotein modulation of synaptogenesis in the brain.

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References and links

ORIGINAL RESEARCH PAPER Mauch, D.H. *et al.* CNS synaptogenesis promoted by glia-derived cholesterol. *Science* **294**, 1354–1357 (2001)

FURTHER READING Ullian, E.M. *et al.* Control of synapse number by glia. *Science* **291**, 657–660 (2001)