novel sequences whose function remains to be discovered, opening new avenues of research. Other genes could help to refine the results from quantitative trait loci analysis, in which large chromosomal regions are linked to specific phenotypes. Finally, the existence of regionspecific genes should lead to the identification of the sequences that regulate their restricted expression, which could then be used to drive the region-specific expression of any transgene.

The differences in gene expression might be subtle but they provide some valuable signposts for future work.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Sandberg, R. et al. Regional and strain-specific gene expression mapping in the adult mouse brain. Proc. Natl Acad. Sci. USA 97, 11038–11043 (2000) FURTHER READING Lipshutz, R. J. et al. High density synthetic oligonucleotide arrays. Nature Genet. 21, 20–24 (1999) [Crawley, J. N. et al. Behavioral phenotypes of inbred mouse strains: implications and recommendations for molecular studies. Psychopharmacology 132, 107–124 (1997) WEB SITE C. Barlow's laboratory

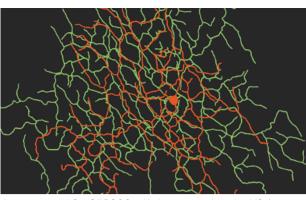
that a lower level of oscillatory activity is preserved in spite of the drugs. Could these remaining oscillations be related to the statedependent retrieval that is observed (so they tell me) after drug intake? *Juan Carlos López*

(3) References and links

ORIGINAL RESEARCH PAPER Hajos, N. et al. Cannabinoids inhibit hippocampal GABAergic transmission and network oscillations. *Eur. J. Neurosci.* **12**, 3239–3249 (2000) FURTHER READING Felder, C. C. & Glass, M. Cannabinoid receptors and their endogenous agonists. *Annu. Rev. Pharmacol. Toxicol.* **38**, 179–200 (1998) | Freund, T. F. & Buzsaki, G. Interneurons of the hippocampus. *Hippocampus* **6**, 347–470 (1996)

WEB SITE Tamas Freund's department





A reconstructed On–Off DSGC, with the soma and proximal (On) dendrites in red and distal (Off) dendrites in green. Image supplied by David Vaney, University of Queensland, Australia.

VISION

A sense of direction

Horace Barlow and William Levick first described the properties of the direction-selective ganglion cells (DSGCs) in the retina way back in the mid-1960's. They reported that the most common type of DSGC, which is activated by the onset and termination of light (On–Off DSGC), responds preferentially to image motion, the direction of which is aligned with one of four axes (up, down, forward or backward). Despite the intervening years and the relative simplicity of the retinal system (the DSGCs are located only two or three synapses from the photoreceptors), the precise locus and mechanism of direction selectivity in the retina has remained elusive.

Although image motion in both the preferred direction and the opposite 'null' direction activates interneurons that excite the DSGCs, electrophysiological evidence indicates that the excitation in the null direction is cancelled by spatially offset input from inhibitory interneurons. Conversely, in the preferred direction, the excitation and inhibition are not spatially and temporally coincident, and the excitation therefore escapes the inhibition. This circuitry therefore provides a mechanism for direction selectivity. But where and how does the interaction between excitation and inhibition occur?

Logically, the null-direction inhibition could act either presynaptically on the excitatory inputs to the DSGCs or postsynaptically on the dendrites of the DSGCs. A report in the September 29 issue of Science suggests that spatially asymmetric inhibition acts postsynaptically. Recordings made in rabbit retina whole-mounts by Taylor, He, Levick and Vaney showed that the DSGCs responded strongly to a stimulus moving in the preferred direction and only weakly to a stimulus moving in the null direction or orthogonal directions. However, when the patch clamp was used to load the DSGC with chloride, thereby preventing the excitatory and inhibitory channels in the DSGC membrane from interacting, the difference between the synaptic currents elicited by image motion in the preferred and null directions disappeared, consistent with a postsynaptic site. These results show that direction selectivity is conferred by nulldirection inhibition, acting postsynaptically on ganglion cell dendrites. The simplicity of this system should now allow the precise characterization of the computational properties of dendrites, and this may have far-reaching implications for our view of computation in the brain.

References and links

ORIGINAL RESEARCH PAPER Taylor, W. R., He, S., Levick, W. R. & Vaney D. I. Dendritic computation of direction selectivity by retinal ganglion cells. *Science* 289, 2347–2350 (2000) ENCYCLOPEDIA OF LIFE SCIENCES Dendritic Spines

WEB SITES Rowland Taylor | David Vaney

HIGHLIGHTS

DEVELOPMENT

Sim and Sonic

The patterning of embryonic neural tissue provides the template for development of the mature nervous system and consequently must proceed with remarkable precision. Sonic Hedgehog (Shh), a protein secreted by the axial mesoderm and the ventral midline of the developing central nervous system, is a key regulator of these patterns of cellular growth and differentiation. Along the dorsoventral axis, a gradient of Shh activity guides the establishment of a variety of cell fates. The role of Shh seems to be more complex along the anteroposterior axis and is thought to depend on interactions between Shh and other signalling pathways, although the genes coordinating Shh expression are poorly understood.

A report from Epstein et. al. in Development demonstrates that within the ventral areas of diencephalon, members of the basic helix-loophelix-PAS (bHLH-PAS) protein family could activate Shh transcription. By assessing the temporal and spatial overlap between known transcription factors and an Shh reporter construct expressing *lacZ* in rostal regions, this group revealed that Sim2, a member of the bHLH-PAS family, may function as a Shh activator in developing ventral diencephalon. Moreover, misexpression of Sim2 in transgenic mice led to ectopic expression of Shh. Although Shh expression was maintained in Sim2-/- mutants, it was absent from rostral midbrain and caudal diencephalon of embryos carrying a dominant-negative transgene that disrupts the function of bHLH-PAS proteins. These results indicate that Sim2 and possibly other members of the bHLH-PAS family may be important new regulators of Shh expression.

Peter Collins

(3) References and links ORIGINAL RESEARCH PAPER Epstein, D. J.

Peter Collins

et al. Members of the bHLH–PAS family regulate shh transcription in forebrain regions of the mouse CNS. Development **127**, 4701–4709 (2000) **ENCYCLOPEDIA OF LIFE SCIENCES** Neural development: bHLH genes | Vertebrate central nervous system: pattern formation **WEB SITES** Douglas Epstein | Alexandra Joyner