was driven by the simian virus 40 (SV40) promoter. The DNA was protected inside the liposome until the antibodies bound to the transferrin receptors on the blood–brain barrier and were transported across into the brain. The DNA was then taken up into brain cells by transferrin-mediated endocytosis. Because the transferrin receptor is found in other tissues as well as brain, and the SV40 promoter is not tissue-specific, the gene was also expressed in other organs that express the transferrin receptor.

In their new experiments, Shi *et al.* have taken the idea an important step further. Working in mice instead of rats, they used an antibody against the mouse transferrin receptor, so the liposomes were still targeted to a number of tissues as well as the brain. But this time, the exogenous gene was driven by the brain-specific glial fibrillary acidic protein (GFAP) promoter. The transgene — β-galactosidase — was expressed only in the brains of the mice, specifically in the astrocytes.

This work is an important proof of the principle that it might be possible to use a non-viral targeting technique, coupled with tissue-specific gene promoters, to achieve the expression of therapeutic genes specifically in the cells that are affected by a genetic disorder. Of course, these are early days; for example, the expression of the exogenous genes in these experiments lasted for only a few days. More work will be needed to find out whether that period can be extended. But it might be possible to use this gene targeting system in conjunction with transgenic mouse models of human diseases to work towards the ultimate goal of this type of study: successful, safe gene therapy in humans.

Rachel Jones

References and links

ORIGINAL RESEARCH PAPER Shi, N. *et al.* Brain-specific expression of an exogenous gene after i.v. administration. *Proc. Natl Acad. Sci. USA* **98**, 12754–12759 (2001)

FURTHER READING Somia, N. & Verma, I. M. Gene therapy: trials and tribulations. *Nature Rev. Genet.* 1, 91–99 (2000)

ENCYCLOPEDIA OF LIFE SCIENCES human gene therapy | liposomes

perform similar experiments on neurons from mice that lack the synaptobrevin partners SNAP-25 and syntaxin to test whether this intriguing proposal holds for other SNARE proteins.

Juan Carlos López

References and links

ORIGINAL RESEARCH PAPER Schoch, S. *et al.* SNARE function analyzed in synaptobrevin/VAMP knockout mice. *Science* **294**, 1117–1122 (2001)

FURTHER READING Chen, Y. A & Scheller, R. H. SNARE-mediated membrane fusion. *Nature Rev. Mol. Cell. Biol.* **2**, 98–106 (2001)

ENCYCLOPEDIA OF LIFE SCIENCES synaptic vesicle traffic

IN BRIEF

DEVELOPMENT

Control of retinal ganglion cell growth: a new role for Sonic hedgehog.

Trousse, F. *et al. Development* **128**, 3927–3936 (2001)

Trousse *et al.* report on a new role for Sonic hedgehog (Shh), a signalling molecule already known to be required for many aspects of neural ontogeny, in the developing visual system. *In vitro*, they show that Shh inhibits the growth of retinal ganglion cell axons. *In vivo*, they suggest that it is important for the initial positioning of the optic chiasm, and that its repulsive effect on ganglion cell axons might facilitate their guidance through the chiasm at later developmental stages.

SENSORY SYSTEMS

Auditory detection and discrimination in deaf cats: psychophysical and neural thresholds for intracochlear electrical signals.

Vollmer, M. *et al. J. Neurophysiol.* **86**, 2330–2343 (2001)

Cochlear implants work by providing direct electrical stimulation to the auditory nerve, bypassing the non-functional sensory cells of a deaf cochlea. How are these electrical stimuli processed and represented in the central auditory system? The authors used a deaf animal model to address this question, directly comparing behavioural and neurophysiological thresholds to intracochlear electrical signals. This model might assist in the design and calibration of cochlear implants and other speech-processing strategies.

SENSORY SYSTEMS

Induction of photoreceptor-specific phenotypes in adult mammalian iris tissue.

Haruta, M. *et al. Nature Neurosci.* 12 November 2001 (10.1038/nn762)

The gene *Crx* is crucial for photoreceptor differentiation. Haruta *et al.* show that transfecting *Crx* into cells of the iris leads to the expression of photoreceptor-specific antigens. This finding reveals an unexpected plasticity of the iris, and raises the possibility that this structure could be used as an autologous source of tissue for retinal transplants. It remains to be determined whether *Crx* is sufficient to drive the cells of the iris through the complete photoreceptor differentiation programme.

NEUROGENETICS

Chromosomal variation in neurons of the developing and adult mammalian nervous system

Rehen, S. K. *et al. Proc. Natl Acad. Sci. USA* **98**, 13361–13366 (2001)

Do all neurons in a given brain have identical genomes? Apparently not. Rehen *et al.* show that as many as one third of cortical neuroblasts might be aneuploid. They observed lagging chromosomes during neuroblast mitosis and found all kinds of related alterations — hyperploidy, monosomy, trisomy. Moreover, when looking at differentiated neurons, the authors found a subpopulation of cortical cells that were aneuploid. It remains to be seen whether this observation has a functional correlate.