In the news

SILENCING SCRAPIE

Finding a method to target the abnormal proteins that cause prion diseases, such as scrapie, bovine spongiform encephalopathy (BSE) and Creutzfeldt–Jakob disease (CJD), could lead to new treatments or prevention strategies for these fatal diseases. A recent study suggests that harnessing RNA interference (RNAi) technology could be a promising approach.

Previous work has shown that genetic deletion of the normal form of PrP^C, the protein that becomes malformed to cause scrapie, can protect against disease development. Now, Alexander Pfeifer of the University of Bonn, Germany, and colleagues have shown that knocking out the protein in only a proportion of brain cells is effective, leading Pfeifer to suggest that this might be "a promising therapeutic option" (*BBC News*, 4 December 2006).

Despite these encouraging findings, the researchers urged caution. Pfeifer says: "It will take years before the method can be used on human beings" (*University of Bonn*, 4 December 2006). Approximately two-thirds of brain cells need to carry the transgene responsible for knocking out PrP^C to prevent disease progression. Targeting this number of brain cells in adult humans could be difficult, and improving current methods of gene delivery will be necessary. As Adriano Aguzzi from the University Hospital of Zurich, Switzerland, puts it, the researchers face "an engineering problem" (*News @ nature.com*, 1 December 2006).

Other researchers have highlighted the potential adverse effects of RNAi, including off-target effects and unknown consequences of deleting normal PrP^C. Qingzhong Kong from the Case Western Reserve University, USA, says that: "Much more research is needed" (*BBC News*, 4 December 2006) and argues that other therapeutic interventions, such as a vaccine against prion proteins, would be easier to administer.

Katherine Whalley

DEVELOPMENT

Dendrites hit the spot

During development of the nervous system, countless connections must be formed between neurons. How axons and dendrites come together to make the functional circuits of the brain is a subject of endless fascination. A new insight comes from Mumm *et al.*, who have found evidence that dendrites actively seek out specific targets in the developing brain.

Developing axons use various strategies to ensure that they reach the correct target, but dendrites have generally been thought to be more promiscuous. Instead of forming selective synapses, they are believed to generate widespread arborizations and connections that are then refined through removal, or 'pruning', of the inappropriate synapses and branches.

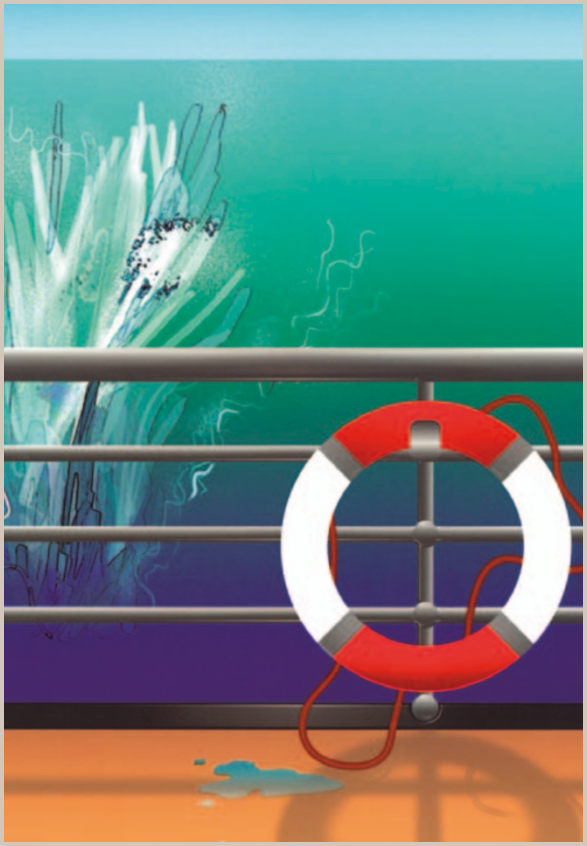
> "…retinal ganglion cells formed dendritic arborizations in a sequential pattern, targeting specific laminae…"

Mumm *et al.* used *in vivo* time-lapse imaging to investigate how the dendrites of retinal ganglion cells in the zebrafish form lamina-specific dendritic arborizations in the inner plexiform layer of the retina. Zebrafish embryos develop from an egg to a larva with a functioning visual system in just 5 days, and because they are transparent they are perfect for studying this kind of problem. By using transgenic zebrafish that expressed fluorescent dyes in specific neurons, the authors could watch as the dendritic arbor developed.

Remarkably, they found that many of the retinal ganglion cells formed dendritic arborizations in a

REPAIR

Rescue of vision



Degeneration of photoreceptors in the retina will cause irrevocable blindness and so far no treatment is available to rescue the sight of patients with this condition. Among the different treatment strategies, transplantation of retinal cells is closely pursued and investigated. In a recent study by MacLaren, Pearson *et al.*, the transplantation of photoreceptor precursor cells resulted in their functional integration into host retinas.

Previously, transplantation of either neural-derived stem cells or immature retinal cells into an adult retina has not been successful. It was believed that the mature environment prevents immature cells making appropriate connections and therefore functionally wiring up with the brain. By assessing the survival, differentiation and functional integration of photoreceptor precursor cells at different stages of differentiation, the authors have identified a time window in which these cells can be successfully transplanted and restore at least partial sight in mouse models of retinal degeneration.

Initially, the authors isolated immature mouse retinal cells on postnatal day 1 (P1), using green fluorescent protein (GFP)-expressing mice in order to discriminate between donor and host cells. Isolated P1 cells were transplanted into GFP-negative wild-type P1 littermates. The authors

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