the number of microhemorrhage profiles in scFv-treated mice compared with controls.

The results suggest that intramuscular delivery of scFv is as effective and safe as intracranial delivery for reducing the total Aβ burden in a mouse model of AD, and that neither mode of delivery elicits an inflammatory response.

Original article Wang Y-J *et al.* (2007) Intramuscular delivery of a single chain antibody gene reduces brain Aβ burden in a mouse model of Alzheimer's disease. *Neurobiol Aging* [doi:10.1016/j.neurobiolaging.2007.06.013]

Polymorphism in 5-HT transporter gene is associated with tolerance of rotating shift work

Desynchronization of circadian rhythms from environmental conditions can have important health implications for rotating shift workers (those who work shifts that rotate or change according to a set schedule). Those individuals have a high risk of developing cardiovascular and metabolic problems. Using a cohort of 683 Argentinian men of European ancestry (437 day workers, 246 rotating shift workers), Sookoian *et al.* have explored the relationships between 5-hydroxytryptamine (5-HT; a neurotransmitter with an important role in modulating circadian rhythms), 5-hydroxyindoleacetic acid (5-HIAA; a 5-HT metabolite), functional polymorphism of the 5-HT transporter gene (*SLC6A4*), and work schedule.

Platelet 5-HT and 5-HIAA content were both greater in day workers than in shift workers. Significantly decreased platelet 5-HIAA content, but not platelet 5-HT content, was observed in individuals homozygous for the *SLC6A4* promoter short variant, relative to other genotypes. The short (deletion) variant of the *SLC6A4* promoter reduces *SLC6A4* transcription rates relative to the long (44 bp insertion) variant. Overall, *SLC6A4* allele distribution differed between day workers and shift workers, with the short allele being more prevalent in shift workers. This difference was observed in individuals with at least 5 years' exposure to their present work schedule, but not in those with shorter exposure, indicating that individuals harboring short *SLC6A4* variants (i.e. those with decreased serotonergic function) might better tolerate shift work than those with long variants.

The authors conclude that better understanding of the mechanisms underlying circadian rhythm desynchronization might aid the development of therapies to alleviate comorbidities associated with shift work.

Original article Sookoian S *et al.* (2007) Serotonin and serotonin transporter gene variant in rotating shift workers. *Sleep* **30:** 1049–1053

Neurotrophin receptor p75 regulates the invasiveness of malignant gliomas

The highly invasive nature of malignant gliomas makes them very difficult to treat. To elucidate the underlying mechanism of glioma invasiveness, Johnston *et al.* used serial *in vivo* selection to establish a mouse model of the disease. These authors subsequently identified the p75 neurotrophin receptor ($p75^{NTR}$) to be a major regulator of glioma invasion and migration. They suggest that this receptor could be targeted to prevent recurrence of malignant gliomas.

The authors isolated a population of invasive cells from a noninvasive human glioma cell line following implantation in immunocompromised mice. After reinjection into a new group of immunocompromised mice, these invasive cells migrated far from the original tumor site and formed tumors with highly infiltrative edges; by contrast, reinjected noninvasive cells resulted in large tumors with well-defined borders. Microarray analyses revealed that $p75^{NTR}$ was upregulated in the invasive cells and not expressed in tumor cells, and reverse-transcriptase polymerase chain reaction and western blot analysis confirmed that ectopic expression of $p75^{NTR}$ induced migration and invasion *in vitro*. Furthermore, upregulation of $p75^{NTR}$ in glioblastoma cells from various cell lines dramatically increased their invasiveness *in vivo*. Disruption of the ability of $p75^{NTR}$ to bind neurotrophin resulted in tumors similar to those derived from noninvasive cells, indicating that $p75^{NTR}$-induced invasiveness was neurotrophin-dependent. The authors observed that $p75^{NTR}$ results in striking actin cytoskeletal rearrangements in invading cells. Analyses of resected human tumors demonstrated that $p75^{NTR}$ is commonly expressed in glioblastoma multiforme, and that $p75^{NTR}$-positive cells migrate at a greater rate than do $p75^{NTR}$-negative cells.

Original article Johnston ALM *et al.* (2007) The p75 neurotrophin receptor is a central regulator of glioma invasion. *PLoS Biol* **5:** e212