GLOSSARY

Tg2576 MICE

Tg(APP^{SWE})2576Kahs mice; these mice express a human amyloid- β precursor protein variant that is linked to Alzheimer's disease

MORRIS WATER MAZE

A behavioral neurological test for assessing spatial learning and memory

Kumar *et al.* carried out a series of experiments in mice with JEV or WNV encephalitis. The researchers identified a cross-species conserved sequence within the region encoding domain II of the viral envelope protein that, when targeted with a synthetic siRNA (siFvE^{JW}), resulted in protection against encephalitis from either JEV or WNV.

Mice were given a single intracranial injection of siFvE^{JW} or control siRNA (siLuc) 30 min or 6 h after intracranial injection with JEV or WNV. All control mice died, whereas all mice given an siFvE^{JW} injection 30 min after flavivirus infection survived. Of the mice injected with siFvE^{JW} 6 h after infection, 100% of those administered WNV survived, and 80% of those challenged with JEV survived.

The authors suggest that siRNA has the potential to be developed into a therapeutic drug for flavivirus-induced encephalitis. They note, however, that improved delivery methods are needed to ensure that siRNA is present throughout the brain, to combat the spread of virus that has occurred by the time clinical symptoms are evident.

Christine Kyme

Original article Kumar P *et al.* (2005) A single siRNA suppresses fatal encephalitis induced by two different flaviviruses. *PLoS Medicine* 3: e96

Safety of clopidogrel in children with arterial ischemic stroke

Antiplatelet therapy with aspirin is widely used for the secondary prevention of stroke in patients who have experienced an arterial ischemic stroke (AIS). Long-term use of aspirin, however, can cause gastric and respiratory adverse effects, and resistance to therapy often occurs. Researchers in Canada have investigated the safety and tolerability of clopidogrel, an alternative antiplatelet treatment, in children with AIS.

This study included 17 children (mean age 8.8 years) recruited at time of initial AIS diagnosis. Children in whom aspirin intolerance or failure occurred began clopidogrel therapy; eight children received clopidogrel alone and seven received clopidogrel in conjunction with aspirin.

No major side effects were reported during clopidogrel treatment alone. Complications were reported in four patients, but two of these—hand numbness and headaches—were unlikely to be clopidogrel-related, as they started before

clopidogrel treatment commenced, and persisted when clopidogrel was discontinued. Two patients on clopidogrel plus aspirin suffered intracranial hemorrhage. Both of these patients had potential risk factors for hemorrhage—one patient had undergone surgery recently and the other had hypertension, and both had cerebral atrophy.

The authors conclude that clopidogrel seems to be well tolerated in children resistant to aspirin, but that the combination of aspirin plus clopidogrel should be used with caution in children who have risk factors for hemorrhage. AIS did not recur in any patient in the study, but no conclusions can be drawn from this as the sample size was small and the study was not designed to assess effectiveness of clopidogrel in stroke prevention.

Rebecca Ireland

Original article Soman T *et al.* (2006) The risks and safety of clopidogrel in pediatric arterial ischemic stroke. *Stroke* 37: 1120–1122

An amyloid- β protein assembly in the brain is linked with impaired memory

In a letter published in *Nature*, Lesné and co-workers have described a novel mechanism of memory impairment that could contribute to the cognitive deficits associated with Alzheimer's disease. This mechanism, which involves extracellular accumulation of a 56 kDa soluble amyloid- β (A β) assembly, dubbed A β *56, has been shown to induce memory deficit in middle-aged *Tg2576* MICE, independently of plaques or neuronal loss.

The authors quantified and compared four pools of transgene-derived A β species extracted from *Tg2576* mice aged 4–25 months. A β *56 and its 40 kDa equivalent (A β *40) both appeared at 6 months of age—coinciding with onset of memory decline—and remained at stable levels in aging mice, implicating these assemblies as possible inducers of memory deficit. A β *56, however, was found at higher levels than the 40 kDa complex and correlated more strongly with memory impairment. Purified A β *56 taken from the brains of impaired *Tg2576* mice was subsequently injected into young, healthy rats, which underwent a series of tests in the MORRIS WATER MAZE. A β *56 impaired long-term memory but did not affect acquisition of spatial memory; memory impairment was reversed when A β *56