expression is low and GD3 synthase expression is high) had experienced a longer median survival than patients with tumors showing lower levels of GM3 and GD3. Oblinger *et al.* conclude that systematic quantitative real-time RT-PCR of glycosyltransferase transcripts could provide information of both diagnostic and prognostic value.

Original article Oblinger JL *et al.* (2006) Diagnostic and prognostic value of glycosyltransferase mRNA in glioblastoma multiforme patients. *Neuropathol Appl Neurobiol* **32:** 410–418

A molecular biomarker for the diagnosis of Alzheimer's disease

Inflammatory signaling pathways mediated by protein kinase C (PKC) have been suggested to be involved in the pathogenesis of Alzheimer's disease (AD). PKC-mediated Erk1 and Erk2 phosphorylation has also been implicated by Alkon and colleagues in the storage of memory, deficits of which often occur at onset of AD. Khan and Alkon, therefore, investigated Erk1 and Erk2 phosphorylation in fibroblast cell lines from patients with AD in response to bradykinin, an activator of PKC pathways. They found that bradykinin-induced Erk1 and Erk2 phosphorylation differed between AD and control fibroblasts, providing a molecular biomarker for AD.

The level of intrinsic Erk1 and Erk2 phosphorylation was higher in control than in AD fibroblasts, suggesting that Erk signaling pathways are dysfunctional in AD. Stimulation with bradykinin caused an increase in Erk1 and Erk2 phosphorylation levels in AD fibroblasts, but not in control cells. An index derived from the change in the phosphorylated Erk1:Erk2 ratio produced by bradykinin stimulation accurately distinguished AD cell lines ($n = 31$) from age-matched controls and non-Alzheimer's dementia patients. In cases in which the diagnosis of AD had been confirmed by autopsy ($n = 23$), the index was 100% specific and 100% sensitive in distinguishing AD from both controls and non-Alzheimer's dementia. Of 20 cases in which clinical diagnosis of AD was in agreement with the index, 19 were confirmed by autopsy. There was an inverse correlation between index values and disease duration.

The authors conclude that the Erk1/Erk2 index could be an important aid to the accurate diagnosis of AD, particularly in the early stages of the disease when diagnosis is more uncertain.

Original article Khan TK and Alkon DL (2006) An internally controlled peripheral biomarker for Alzheimer's disease: Erk1 and Erk2 responses to the inflammatory signal bradykinin. *Proc Natl Acad Sci USA* **103:** 13203–13207

Endocannabinoids target glutamatergic neurons to protect against seizures

The endocannabinoid system is known to play an important role in the control of neuronal excitability through its modulatory effects on γ-aminobutyric acid (GABA)-releasing neurons and glutamatergic neurons. Monory *et al.* investigated the mechanism by which the system exerts this function on glutamatergic neurons. Their findings indicate that glutamatergic neurons located in the hippocampus are directly targeted by endocannabinoids via CB_1 receptors located on glutamatergic terminals.

Using mice in which cannabinoid receptor genes could be deleted in specific cell populations, the authors carried out a series of experiments to examine the role of the endocannabinoid system in the hippocampus during kainic-acid-induced seizures. They developed a mouse strain (Glu-$CB_1^{-/-}$) in which the cannabinoid CB_1 receptor was selectively deleted in cortical glutamatergic neurons located in the hippocampus, neocortex and amygdala, while its expression was maintained in GABAergic interneurons and subcortical neurons.

Seizures evoked in Glu-$CB_1^{-/-}$ mice were found to be stronger than those evoked in wild-type littermates or other mutant mice in which the deletion of CB_1 receptors was specifically limited to GABAergic neurons, thus demonstrating that CB_1 receptors located on cortical glutamatergic neurons play an essential role in protecting these neurons against kainic-acid-induced seizures.

The authors conclude that their results indicate a mechanism through which the endocannabinoid system directly protects the brain against epileptiform seizures in an 'on-demand' manner. They suggest that the CB_1 receptor on hippocampal glutamatergic neurons represents a novel potential target for pharmacological interventions against abnormal neuronal excitation.

Original article Monory K *et al.* (2006) The endocannabinoid system controls key epileptogenic circuits in the hippocampus. *Neuron* **51:** 455–466