The authors suggest that $CD8^+$ T cells and HLA-A3 are required for initiation of MS, but that progression to advanced disease depends on $CD4^+$ T cells. HLA-A2 protects against MS by modulating the thymic selection of autoimmune $CD8^+$ cells.

Original article Friese MA *et al.* (2008) Opposing effects of HLA class I molecules in tuning autoreactive $CD8^+$ T cells in multiple sclerosis. *Nat Med* **14:** 1227–1235

Impaired executive function in behavioral-variant frontotemporal dementia

Behavioral-variant frontotemporal dementia (bv-FTD) is a heterogeneous disease; some patients have rapidly progressing 'true' disease, whereas others show little or no progression for many years. Hornberger *et al.* tested whether performance on tests of executive function—which should be impaired in patients with progressive bv-FTD because of frontal brain atrophy—can be used to differentiate between patients with progressive bv-FTD and those with a nonprogressive variant.

In this study, 50 patients with bv-FTD were retrospectively classified as having progressive or nonprogressive disease on the basis of atrophy on MRI at presentation and cognitive decline over a 3-year period. These patients and 40 healthy controls undertook six tests of executive function.

Global cognitive function in both the progressive bv-FTD group ($n=27$) and the nonprogressive bv-FTD group ($n=23$) was worse than that of controls. The mean scores of patients with nonprogressive disease were similar to those of controls across most tests of executive function. For patients with progressive bv-FTD, however, mean scores on executive function tests were considerably worse than those of controls, in particular for the digit span test, the FAS letter verbal fluency test and the trail-making test ($P<0.0001$ for all). Approximately 80% of patients with progressive bv-FTD had abnormal executive function according to the tests.

The authors conclude that performance on executive tests can distinguish the majority of patients with progressive bv-FTD from those with a nonprogressive bv-FTD.

Original article Hornberger M *et al.* (2008) Executive function in progressive and nonprogressive behavioral variant frontotemporal dementia. *Neurology* **71:** 1481–1488

Oral fumarate reduces the incidence of brain lesions in patients with multiple sclerosis

A placebo-controlled, dose-finding, phase II trial testing the efficacy and safety of BG00012, an oral formulation of dimethyl fumarate, reports a reduced incidence of gadolinium-enhancing lesions—indicative of inflammatory activity in the CNS—in patients with relapsing–remitting multiple sclerosis (MS).

Kappos *et al.* recruited 257 patients with relapsing–remitting MS (aged 18–55 years) from 43 medical centers in Europe and Russia. For the first 24 weeks, patients were randomly assigned to receive BG00012 120 mg once daily ($n=64$), 120 mg three times daily ($n=64$), or 240 mg three times daily ($n=64$), or placebo ($n=65$). In a 24-week extension period for safety assessment, patients receiving BG00012 continued on their assigned dose and the placebo group switched to the highest fumarate dose.

Compared with placebo, treatment with the highest BG00012 dose led to a 69% reduction in the mean number of new gadolinium-enhancing lesions on brain MRI scans from weeks 12 to 24, and reductions in T_1-hypointense lesions and T_2-hyperintense lesions of 53% and 48%, respectively. High-dose BG00012 also reduced the annualized relapse rate by 32%. No significant differences were observed between the lower-dose-BG00012 and placebo groups. Safety and tolerability profiles were similar in all treatment groups.

Kappos *et al.* suggest that BG00012 has immunomodulating effects and may also activate a pathway that protects against the oxidative stress implicated in the pathology of MS. Phase III trials are underway, which are anticipated to confirm the results of this study.

Original article Kappos L *et al.* (2008) Efficacy and safety of oral fumarate in patients with relapsing-remitting multiple sclerosis: a multicentre, randomised, double-blind, placebo-controlled phase IIb study. *Lancet* **372:** 1463–1472

The tau kinase GSK3B is associated with dementia

Hyperphosphorylated tau protein deposits are a feature of Alzheimer disease (AD) and frontotemporal dementia (FTD). Mutation of the tau-phosphorylating enzyme glycogen synthase kinase (GSK3B) has been postulated as a