

## NEUROLOGICAL DISORDERS

Two sides to  $\beta$ -amyloid

The ability of  $\beta$ -amyloid to form amyloid plaques in the brains of patients with Alzheimer's disease has led to strenuous attempts to clear it or to block its effects. Now, it seems that the bad guy of Alzheimer's disease might be a good guy under other circumstances — in a mouse model of multiple sclerosis.

The precursor of  $\beta$ -amyloid (amyloid precursor protein (APP)) has been implicated in multiple sclerosis because it accumulates in the lesions found in the disease, and  $A\beta_{42}$ , one of the forms of  $\beta$ -amyloid, is upregulated in damaged areas. To investigate the role of  $\beta$ -amyloid in multiple sclerosis, Grant *et al.* administered  $\beta$ -amyloid ( $A\beta_{42}$  or  $A\beta_{40}$ ) by intraperitoneal

injection into mice with experimental autoimmune encephalomyelitis (EAE, a commonly used model of multiple sclerosis). To their surprise, treatment with  $\beta$ -amyloid led to a marked improvement — paralysis in the mice was reduced and inflammation in both the CNS and the lymphoid tissue was attenuated.

The beneficial effects of  $\beta$ -amyloid injection were reproduced in other forms of EAE and also in mice in which symptoms of multiple sclerosis were induced by the adoptive transfer of autoreactive T cells from mice with EAE. Furthermore, mice that lacked the gene for APP and therefore had no  $\beta$ -amyloid showed more severe effects than normal mice when EAE was induced.

To find out how  $\beta$ -amyloid ameliorated the effects of EAE, the authors looked at CD4<sup>+</sup> T cells — the subset of lymphocytes that are most involved in the pathology of EAE and multiple sclerosis. Interestingly, T cells taken from  $\beta$ -amyloid-treated mice with EAE that were adoptively transferred to untreated mice caused less severe disease than did T cells from untreated mice with EAE. Further investigation showed that treatment with  $\beta$ -amyloid decreased the proliferation of certain types of T lymphocyte and reduced the production of pro-inflammatory cytokines, such as interferon- $\gamma$ .

Although the precise effects varied between  $A\beta_{42}$  and  $A\beta_{40}$  and in different forms of EAE, these results clearly show that systemic treatment with  $\beta$ -amyloid can ameliorate symptoms in this mouse model of multiple sclerosis. As Hohlfeld and Wekerle discuss in an accompanying article, there is a long way to go in terms of mechanistic understanding and investigation of safety issues before we can think about using  $\beta$ -amyloid to treat patients with multiple sclerosis. However, this unexpected finding might lead to a new understanding of the role of  $\beta$ -amyloid in Alzheimer's disease as well as multiple sclerosis.

Rachel Jones



... these results clearly show that systemic treatment with  $\beta$ -amyloid can ameliorate symptoms in this mouse model of multiple sclerosis.



**ORIGINAL RESEARCH PAPER** Grant, J. L. *et al.* Reversal of paralysis and reduced inflammation from peripheral administration of  $\beta$ -amyloid in T<sub>H</sub>1 and T<sub>H</sub>17 versions of experimental autoimmune encephalomyelitis. *Sci. Transl. Med.* **4**, 145ra105 (2012)

**FURTHER READING** Hohlfeld, R. & Wekerle, H.  $\beta$ -amyloid: enemy or remedy? *Sci. Transl. Med.* **4**, 145fs24 (2012)