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The role of complement in spongiform encephalopathies

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Agents of transmissible spongiform encephalopathies (TSEs) usually enter the body via a peripheral route and replicate in lymphoreticular tissues before moving into the brain. Any impairment of the lymphoreticular system slows transfer of the TSE agent to the brain and delays the clinical onset of symptoms. In the April *Nature Medicine*, Klein et al and Mabbott et al show that complement factors are involved in the uptake of TSE-inducing agents by the lymphoreticular system and that their absence can delay CNS invasion.

In the two independent studies on mouse models of scrapie, Klein *et al* from The University of Zurich, and Mabbott *et al* from Institute for Animal Health in Edinburgh, showed that depletion of either one of the early complement factors (C1q, Bf/C2 and C3) or the complement receptor (CR1/2) significantly delays the onset of disease symptoms in mice injected with limiting doses of the scrapie strains RML and ME7 (*Nat Medicine* 2001, **7**:485-487 and *Nat Medicine* 2001, **7**:488-492).

Both teams suggest that complement proteins may be a target for treatment of TSEs. But it is still the case that even if the onset of symptoms is delayed in complement-deficient animals, they will eventually succumb to the disease.

In an accompanying News and Views article Franco Cardone and Maurizio Pocchiari from the Laboratory of Virology, Istituto Superiore di Sanitô Rome suggest that the results indicate the existence of multiple, non-exclusive pathways of neuroinvasion. Consequently a complement-targeted strategy for TSE therapy may only be effective in treating low-level infections.

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