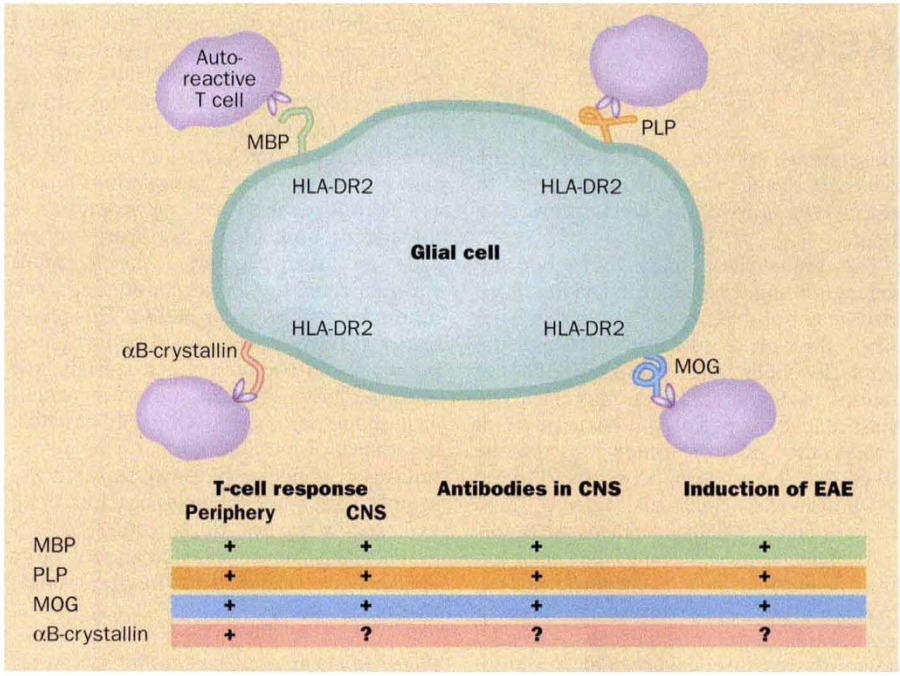

Recruitment of autoreactive T cells by different components of the myelin sheath (dark green) in white matter from MS brain (MBP, myelin basic protein; PLP, proteolipid protein; MOG, myelin oligodendroglial glycoprotein), and the immune responses triggered by these components in MS patients and in laboratory animals. EAE, experimental allergic encephalomyelitis.

cyclic nucleotide 3′-phosphodiesterases, as well as two members of the immunoglobulin supergene family found in the myelin sheath (myelin oligodendroglial glycoprotein and myelin-associated glycoprotein) all trigger immune responses in MS patients[2]. When they are injected into laboratory animals, these myelin components cause allergic encephalomyelitis, with inflammation and demyelination in the central nervous system (see figure). In addition, other inducible heat-shock proteins can be detected in glial cells in MS lesions and can stimulate an immune response in MS patients[3–5]. The large number of antigens capable of eliciting an immune response in MS patients may represent the intermolecular dispersion of an immune response that arose initially against a single component of myelin. Immune reaction to different components of a supramolecular structure, such as the myelin sheath in MS or the mitochondrion in primary biliary cirrhosis, is common in individuals with autoimmune disease that involves a discrete organ.

We cannot yet say which of these antigens is most important in the pathogenesis of MS. Strong evidence is emerging that an immune response to certain regions of myelin basic protein and proteolipid protein could be critical in MS (see figure). The major T- and B-cell response in the central nervous system of MS patients who carry the human leukocyte antigen HLA-DR2 (about two-thirds of patients) is directed to a region between residues 84 and 103 of myelin basic protein[6,7]. The principal antibody response in the lesions of MS patients is also directed against this region[8] and microbes that share critical sequence homologies with it can provoke a response to this myelin peptide[9]. Increased numbers of T cells reactive to proteolipid protein are also found in the spinal fluid of patients with MS[7]. The response to αB-crystallin has not yet been checked for T and B cells in the brain.

These efforts to determine which antigens trigger the pathological response in MS brain have very practical consequences. It is now possible to induce immunological tolerance to specific proteins using a variety of strategies, including the alteration of peptide ligands that bind to the T-cell receptor and the blockade of costimulatory molecules on T cells[2,10]. All of these approaches have been effective in suppressing animal models of MS. Identification of the critical proteins involved in MS permits the testing of these strategies for the induction of tolerance in patients suffering from this perplexing disease. □

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DAEDALUS

Plain polymer

LAST week Daedalus was studying the reaction of graphite to the linear carbon polymer, carbyne. He is now musing on its reaction with fluorine. This gives the saturated polymer, graphite fluoride — infinite sheets of carbon hexagons, with a fluorine on each carbon atom.

In principle, hydrogen should react with graphite in the same way. The result would be a novel hydrocarbon sheet polymer, a sort of two-dimensional polyethylene. This doesn't happen; even at high temperatures hydrogen merely etches graphite away into hydrocarbon vapours. Daedalus reckons that the saturation of graphite must go via negative ions. Fluorine is a ready source of the F^- ion, whereas hydrogen is a very poor source of H^-. To make the reaction go, extra electrons must somehow be pumped into the graphite.

Chemically, this might perhaps be done by electrolysing molten lithium hydride with a graphite anode. But Daedalus has a bolder scheme. Graphite is a conductor; raise it to a high enough negative voltage and its electron density should increase to the point where it reacts with hydrogen.

Charge concentrates at the surface of a conductor, and its density is greatest on a sharply curved surface. So Daedalus is taking very fine carbon fibres, and raising them to enormous negative voltages in an atmosphere of hydrogen, pressurized to inhibit sparking or corona discharge. Graphite hydride should form on the fibres.

The new polymer may adhere as a strong coating, gradually thickening as the reaction proceeds inwards. If so, a carbon fibre continuously moving through the reaction chamber will be converted into one of graphite hydride. But the charged product may instead be blown off the fibre by strong electrostatic repulsion as fast as it forms; in this case it will accumulate as a powder.

Like graphite itself, graphite hydride should slowly anneal at high temperature and pressure to a well formed crystalline product. It will be a sort of organic mica: infusible, lamellar, unreactive, very tough in the plane of the molecular sheets and very impermeable at right angles to it. Daedalus expects its major impact to be on food packaging. The tin can, that ancient invention, survives only because no present-day plastic film is quite impermeable to air. But graphite hydride, with its monolithic sheet molecules, will be a perfect gas barrier. Soup, beans, sardines, beer, all will be sold in flexible pouches of thin-film graphite hydride, while cans and can-openers are relegated to museums of technology.

David Jones