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# Protective autoimmunity in acute and chronic CNS disorders: Therapeutic vaccines

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Participation of the immune system is of critical importance for processes of maintenance and recovery from injuries and disorders of the central nervous system (CNS). Such participation can be viewed as the body's own mechanism of repair, which can be boosted for therapeutic purposes. We have shown that the innate immune response (involving macrophages), if well-controlled, can promote the post-traumatic process of healing in CNS axons.

The adaptive immune response (involving T cells) has long been viewed as an immune activity evoked with the purpose of enabling the organism to defend itself against invading pathogens such as bacteria and viruses. Accordingly, it was believed that an adaptive immune response would not be evoked unless the pathogen is recognized as non-self. Our rodent studies of the crush-injured optic nerve, the contused spinal cord, and retinal gangion cell damage induced by glutamate toxicity suggest that CNS insults stimulate the recruitment of autoreactive T cells (directed against myelin-associated proteins and peptides), and that these T cells have a protective effect in that they help reduce the neuronal losses resulting from secondary degeneration after the insult. The ability to sustain an autoreactive T cell-dependent protective immune response was found to be genetically controlled and inversely related to the individualĺs susceptibility to autoimmune disease. Spontaneous recovery from CNS insults was better in rats and mice endowed with the ability to sustain a beneficial autoimmune response, and worse if such animals were devoid of T cells. We further showed that the physiological T cell-dependent neuroprotective response can be intensified by a T cell-based therapeutic vaccination. These findings suggest that autoimmunity, at least in the CNS, is a purposeful response designed to help the individual cope with insult-induced stress.

Protective autoimmunity is found to be a complex cellular immune response in which both autoimmune T cells and regulatory T cells participate. Lack of the relevant physiological machinery may predispose an individual to the development of an autoimmune disease. We recently demonstrated that a T cell-based vaccination, using safe (modified) anti-myelin self-antigens or safe synthetic antigens (such as Cop-1), reduces the loss of retinal ganglion cells in a rat model of chronic glaucoma. This finding appears to have immediate clinical applicability for glaucoma treatment. The T-cell-based vaccination can also be used as a post-traumatic treatment for the contused spinal cord, where it reduces the post-traumatic loss of neurons and thus attenuates functional loss.

Research in this laboratory is currently focused on: (a) optimizing the route of vaccination for glaucoma; (b) seeking optimal peptides to be used in post-traumatic vaccination for spinal cord injury, (c) understanding the mechanism of protective autoimmunity at the immunological, molecular, and cellular levels, (d) finding out what determines the difference between destructive and protective autoimmunity, and (e) applying the therapeutic approach of protective autoimmunity to other neurological disorders such as ALS, Parkinsonĺs and Alzheimerĺs diseases.

***Selected Publications***

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