Protective autoimmunity in neurodegenerative and mental disorders

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Acute or chronic damage to the central nervous system (CNS) triggers self-perpetuating 'secondary degeneration', caused by cytotoxic mediators (neurotransmitters, free radicals) emanating from lesioned sites. Local and infiltrating anti-self immune cells at the injury site were long considered pathological. Our findings suggested, however, that autoimmunity is a beneficial fighting force against destructive self-derived compounds, leading us to redefine 'tolerance to self', long equated with 'nonresponsiveness', as ability to tolerate autoimmune responses without developing an autoimmune disease. We thus perceive autoimmunity as a physiological repair mechanism possessing the on/off switch needed to maintain or restore tissue homeostasis without attendant autoimmune disease, and controlled by naturally occurring CD4+CD25+ regulatory T cells (Treg), themselves controlled by brain-derived neurotransmitters/peptides. If ongoing neurodegeneration after acute injuries results from insufficiency of the endogenous fighting force, and chronic neurodegenerative diseases reflect age-related deterioration of the body's two principal regulators (CNS and immune system), restoration or boosting of immune function might bridge the gap between manifestation of CNS-related risk factors and the immune system's defensive capacity. Boosting of peripheral immunity, by vaccinating with a universal weak anti-T-cell antigen or its agonist, or by weakening suppression of autoimmunity (e.g., by eliminating Treg), might be developed as therapies to counteract multiple risk factors. T cells that home to the damaged CNS might then help restore homeostasis there by regulating glial behavior and producing neurotrophic factors, while avoiding cytotoxic inflammatory activity. Since neurodegenerative diseases possess some common features deriving from the local chaos, the same vaccine might protect against several disorders associated with impairment of brain function (motor, cognitive and mental).

Selected Publications


