

The Maurice and Ilse Katz Professorial Chair in Neuroimmunology
Laboratory of the Immunology of the Mind in Health and Disease
Weizmann Institute of Science
Rehovot, Israel

"Protective anti-self immunity: A paradigm shift in the perception of brain inflammation in health, neurodegenerative diseases, and age-related dementia"

Friday, March 16, 2012
12:00 p.m.
Jordan Hall, Room 1-17

Neurodegenerative diseases are associated with neuronal loss occurring within the central nervous system (CNS), a compartment behind walls. Thus, it was assumed that these tissues are unable to benefit from the assistance provided by the immune system. Moreover, signs of inflammation accompanying brain pathology were believed to indicate immune cell infiltration from the circulation that should be mitigated. However, we have shown that both circulating blood macrophages and T lymphocytes are needed for recovery, and that these two cell types orchestrate neuroprotection and cell renewal. In contrast to the well-documented pro-inflammatory activity of the microglia (the CNS-resident macrophages) at the site of trauma, the infiltrating monocyte-derived macrophages express hallmarks of 'alternatively' activated (M2; resolving) phenotype. In healthy animals, we demonstrated that T cells recognizing CNS antigens reside in the CNS borders and are needed for the maintenance of brain plasticity, including cognitive ability, neurogenesis, and coping with stress. We found that such T cells, including effector CD4⁺ T cells and regulatory T cells (Treg), are part of a dynamic network that provides life-long brain maintenance. These and other studies have led us to propose that neurodegenerative diseases may remain dormant long before their onset as long as the circulating immune cells can contain the pathology-induced deviation; disease onset indicates that either the deviation overrides the ability of the immune cells to counterbalance the rise of the risk factors, or that the immune system becomes exhausted and deteriorates concomitantly with the disease process. Thus, an appreciation of the distinct temporal and spatial contributions of resident and systemic leukocytes to life-long brain plasticity is essential for CNS pathologies including neurodegenerative and mental diseases and aging.