Alzheimer’s disease (AD) like many other neurodegenerative diseases, is a multi-dimensional disease involving numerous biological pathways and molecules that become deviated within the brain. Attempts have been made to address several factors that are considered hallmarks of the disease, with the vast majority of them focusing on amyloid beta (Aβ) peptides and plaque formation. Thus far, none of these approaches has resulted in a disease modifying therapy. Our findings over almost two decades show that immune system activity plays an essential role in maintaining life-long brain plasticity, and that following damage to the brain, immune cells are involved at all stages of tissue repair. Specifically, we identified the brain choroid plexus epithelium as an immunological interface needed for “healing” immune cell recruitment to sites of brain pathology. In mouse models of AD, recruitment of blood-borne monocyte-derived macrophages to sites of brain pathology is associated with a therapeutic effect. We recently pointed to peripheral immune suppression as a negative player which hamper this process, and showed that boosting peripheral immunity, by transiently breaking immune tolerance, can augment recruitment of immune regulatory cells to sites of brain pathology, and to support tissue repair and reduced inflammation. Immune checkpoints are regulatory pathways which maintain systemic immune homeostasis and tolerance. Among such checkpoints, PD-1 is expressed by immune cells and negatively regulates immune responses. PD-1 blockade is currently used as an effective immunotherapy in cancer. Using a similar approach in AD animal models, we reported that anti-PD-1 antibodies are effective in reversing cognitive loss, in removal of plaques, and in restoring brain homeostasis as determined by the inflammatory molecular profile. Such an approach is not meant to be directed against any disease escalating factor in AD, but rather it empowers the immune system of the individual to drive the process of repair. Moreover, based on the animal studies, in which the effect was dramatic in terms of learning and memory skills restoration, we expect to see a robust effect on the mental abilities of patients.