Treating rhematoid arthritis with peptide-specific CD8+ regulatory T cells
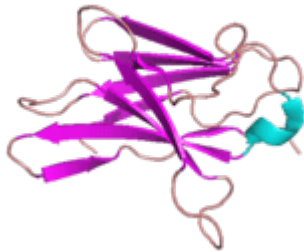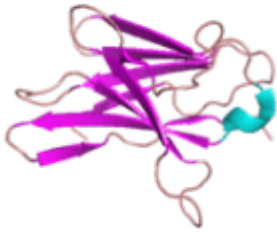

The autoimmune disorder rheumatoid arthritis (RA) is characterized by joint inflammation and erosion along with systemic involvement. Although the identification of effector cytokines, including TNF, IL-1, and IL-6, that contribute to this disease has led to improved therapies, RA has remained relatively refractory to decisive intervention. A potentially more effective approach could entail targeting autoreactive T cells that initiate the disease cascade and break self tolerance. This study therefore analysed the contribution of Treg and effector T cell subsets to autoimmune arthritis in the collagen-induced arthritis (CIA) animal model. This murine disease model shares several similarities with human RA, including breach of self tolerance and generation of autoantibodies, and has been used to establish the potential efficacy of several approved RA therapies, such as anti-TNF Ab, IL-1 antagonists, and methotrexate (MTX). The murine MHC class Ib molecule Qa-1b (HLA-E in humans) exhibits limited

polymorphisms and binds to 2 dominant self peptides: Hsp60p216 and Qdm. This study found that peptide-induced expansion of tetramer-binding CD8+ Tregs that recognize Qa-1—Hsp60p216 but not Qa-1—Qdm strongly inhibited CIA. Moreover, infusion of small numbers of Qa-1—Hsp60p216—specific CD8+ Tregs resulted in robust inhibition of autoimmune arthritis, confirming the inhibitory effects of Hsp60p216 peptide immunization. Thus suggesting that the ability to expand Qa-1—restricted CD8+ Tregs based on their TCR specificity may represent a new and effective approach to treatment of autoimmune disease.

Leavenworth, J. 2013. Amelioration of arthritis through mobilization of peptide-specific CD8+ regulatory T cells. *The Journal of Clinical Investigation.*