SL08 **Clofazimine Is a Novel Inhibitor of Human Kv1.3 Potassium Channel and Calcium Signaling in T Lymphocytes**

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The Kv1.3 potassium channel plays an essential role in effector memory T cells and has been implicated in a number of important autoimmune diseases including multiple sclerosis, psoriasis and type 1 diabetes. A number of potent small molecule inhibitors of Kv1.3 channel have been reported, some of which were found to be effective in various animal models of autoimmune diseases. We report herein the identification of clofazimine, a known anti-mycobacterial drug, as a novel inhibitor of human Kv1.3. Clofazimine was initially identified as an inhibitor of intracellular T cell receptor-mediated signaling leading to the activation of transcription of human interleukin-2 gene in T cells from a screen of the Johns Hopkins Drug Library. A systematic mechanistic deconvolution revealed that clofazimine selectively blocked the Kv1.3 channel activity, thus perturbing the oscillation frequency of the calcium-release activated calcium channel, which in turn led to the inhibition of the calcineurin-NFAT signaling pathway. Importantly, clofazimine was found to be effective in blocking human T cell-mediated skin graft rejection in an animal model *in vivo*. Together, these observations suggest that clofazimine is a promising immunomodulatory drug candidate for treating a variety of autoimmune disorders.