

The role of DRAK2 in autoimmunity of the central nervous system

Maureen A. McGargill¹, Ben G. Wen², and Stephen M. Hedrick¹

¹University of California, San Diego, La Jolla, CA 92093; ²Department of Pharmacology, Genomics Institute of the Novartis Research Foundation, San Diego, CA 92121.

DRAK2 is a serine/threonine kinase expressed exclusively in cells of the immune system. T cells from *Drak2*-deficient mice are hypersensitive to T cell receptor-mediated stimulation and exhibit a reduced requirement for co-stimulation. However, *Drak2*-deficient mice are remarkably resistant to experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis. While the autoimmune response to EAE is inhibited in the absence of DRAK2, the immune response to foreign pathogens is not dramatically altered. Thus, DRAK2 is an ideal target for treating autoimmune disorders without compromising immunity to infectious pathogens. We found that the resistance to EAE in *Drak2*-deficient mice is intrinsic to the T cells. Although autoreactive T cells are present and expand, these cells do not enter the central nervous system and cause disease. We are currently investigating whether DRAK2 plays a role in migration of T cells specifically into the central nervous system and if a deficiency in DRAK2 affects disease in other models of autoimmunity.