Human T Cell Immunity to Dengue Virus

Dr. Laura Rivino
Emerging Infectious Diseases
Duke-NUS Graduate Medical School

Abstract
Dengue virus (DENV) is the most prevalent mosquito-borne viral disease afflicting human populations. Up to 400 million infections occur every year with disease severities that range from asymptomatic infection, self-limiting dengue fever to severe vascular leakage and hemorrhagic manifestations. The correlates of protective immunity and in particular the contribution of the T cell response to protection and/or pathology during dengue infection are still unclear. To better understand T cell immunity to DENV we first comprehensively identify the CD4+ and CD8+ T cell epitope reactivities against DENV in patients of Asian ethnicity. Our study highlights key differences in the immunodominance of dengue proteins for CD4+ and CD8+ T cells and provides novel tools for T cell analyses. By using pentamerized peptide-HLA class I molecules we address the phenotype, functional capacity and migratory potential of virus-specific CD8+ T cells during dengue infection. We show that natural infection induces virus-specific CD8+ T cells that are highly activated and proliferating, exhibit anti-viral effector functions, and express CXCR3, CCR5, and the skin-homing marker cutaneous lymphocyte-associated antigen (CLA). The expression of CLA by dengue-specific CD4+ and CD8+ T cells correlates with their in vivo ability to traffic to the skin during acute dengue infection. Upon resolution of the infection virus-specific CLA+ T cells are undetectable in the blood but are retained in the skin tissue. Our data highlights the skin as an important site for the immune surveillance of DENV.

Selected Publications for Reference


