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Bolstering the number and function of hsv-1-specific cd8+ TEM and TRM cells in latently infected trigeminal ganglia reduces recurrent ocular herpes infection and diseases

Herpes simplex virus type 1 (HSV-1) is a prevalent human pathogen that infects over 3.72 billion individuals worldwide and can cause potentially blinding recurrent corneal herpetic disease. HSV-1 establishes latency within sensory neurons of trigeminal ganglia (TG) and TG-resident CD8+ T cells play a critical role in preventing its reactivation. The repertoire, phenotype and function of protective CD8+ T cells are unknown. Bolstering the apparent feeble numbers of CD8+ T cells in TG remains a challenge for immunotherapeutic strategies. In this study, a comprehensive panel of 467 HLA-A*0201-restricted CD8+ T cell epitopes were predicted from the entire HSV-1 genome. CD8+ T cell responses to these genome-wide epitopes were compared in HSV-1 seropositive symptomatic (SYMP) individuals (with a history of numerous episodes of recurrent herpetic disease) vs. asymptomatic (ASYMP) individuals (who are infected but never experienced any recurrent herpetic disease). Frequent polyfunctional HSV-specific effector memory IFN-+CD107a/b+CD44highCD62LlowCD8+ TEM cells were detected in ASYMP individuals and were mainly directed against three "ASYMP" epitopes. In contrast, SYMP individuals have more mono-functional central memory CD44highCD62LhighCD8+ TCM cells. Furthermore, therapeutic immunization with an innovative prime/pull vaccine, based on priming with multiple "ASYMP" epitopes (prime) and neurotropic TG delivery of the T-cell attracting chemokine CXCL-10 (pull), boosted the number and function of CD44highCD62LlowCD8+ TEM and tissue-resident CD103highCD8+ TRM cells in TG of latently infected HLA-A*0201 Tg mice and reduced recurrent ocular herpes following UV-B induced reactivation. These findings have profound implications in the development of T-cell-based immunotherapeutic strategies to treat blinding recurrent herpes infection and disease.

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Biography

BenMohamed is a Professor of Immunology, the founder and the head of the Laboratory of Cellular and Molecular Immunology in the Department of Ophthalmology at the University of California. He also holds a joint appointment with the Center of Immunology at UC Irvine and with Chao Family Comprehensive Cancer Center UCI Medical center. Dr. BenMohamed received his Ph.D. in Immunology from the Pasteur Institute, Paris, France in 1997 where he worked as the key developer and co-inventor of a new promising vaccine strategy that uses mucosal delivery of clinically approved lipopeptide molecules. Dr. BenMohamed has been involved in clinical immunology, humoral and cellular immune responses, epitope mapping, epitope improvement, and the development and optimization of sub-unit vaccines against several infectious diseases including malaria Plasmodium falciparum, human immunodeficiency virus (HIV), human cytomegalovirus (HCMV) and herpes simplex virus type 1 and type 2 (HSV-1 and HSV-2). Dr. BenMohamed is an independent immunologist, with a national and international reputation in vaccine development against both infectious diseases and cancer. Dr. BenMohamed is well integrated into the scientific community within the United States as well as Europe and is actively involved in a number of professional societies including American Association of Immunologists (AAI), American Society for Microbiology (ASM), American Society for Hematology (ASH), Association for Research in Vision and Ophthalmology (ARVO).

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