Qingsheng Li, J Vaccines Vaccin 2016, 7:3(Suppl)
http://dx.doi.org/10.4172/2157-7560.C1.039

Distinct transcriptome profiles of Gag-specific CD8+ T cells temporally correlated with the protection elicited by live attenuated SIV

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SIVmac239Δnef (SIVΔnef) live attenuated vaccine (LAV) confers the best protection among all the vaccine modalities tested in rhesus macaque model of HIV-1 infection. This vaccine has a unique feature of time dependent protection that is macaques are not protected at 3-5 weeks post vaccination (WPV), whereas immune protection emerges between 15 and 20 WPV. Although the exact mechanisms of the time dependent protection remain incompletely understood, recent studies suggested IgG antibodies specific to viral envelope glycoprotein gp41 trimers correlated spatially and temporally with the maturation of local protection against high dose pathogenic SIV vaginal challenge and SIV-specific CD8+ T cells quality rather than quantity may correlate with maturation of local protection. To further elucidate the mechanisms of protection induced by SIVΔnef vaccine, we longitudinally compared the global gene expression profiles of SIV Gag-CM9+ CD8+ (Gag-specific CD8+) T cells from peripheral blood of Mamu-A*01 rhesus macaques at 3 and 20 WPV using rhesus microarray. We found that gene expression profiles of Gag specific CD8+ T cells at 20 WPV are qualitatively different from those at 3 WPV. At 20 WPV, the most significant transcriptional changes of Gag specific CD8+ T cells were genes involved in cell activation, differentiation and maturation toward central memory cells with increased expression of CCR7, TCR-alpha, TCR-beta, CD28 and decreased expression of CTLA-4, IFN-γ, RANTES (CCL5), granzyme A and B. Our study indicates that a higher quality of SIV-specific CD8+ T cells elicited by SIVΔnef over time contributes to the maturation of time dependent protection.

Biography

Qingsheng Li is a Professor at the School of Biological Sciences and the Nebraska Center for Virology at University of Nebraska-Lincoln, USA. He is the Member of American Society for Microbiology, American Association for the Advancement of Science, Society for Mucosal Immunology and American Society for Virology. He has earned his PhD degree in 1995 from the Beijing University Medical School and completed his Postdoctoral training at University of Minnesota (1995-1998). He has more than 20 years of experience of HIV-1 research focused on prevention of HIV-1 transmission by studying early events of SIV-rhesus macaque and humanized-BLT (bone marrow liver and thymus) mouse models of HIV-1 infection. He has also published extensively on HIV/SIV transmission, pathogenesis and prevention, including one paper in Science and two papers in Nature as the leading author.

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