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Trained innate immunity in vaccine protection against intrarectal AIDS virus transmission

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We have found that vaccine protection against SIV/SHIV transmission in rhesus macaques can be achieved in the absence of anti-envelope antibodies, and even without a direct role of T cells, but rather mediated by monocytic cells through trained innate immunity. In the first study, a vaccine involving an envelope construct and modified vaccinia Ankara (MVA) encoding SIV antigens was used mucosally, with TLR ligands, IL-15, and mutant E coli labile toxin as adjuvants. Protection was achieved against repeated SHIV challenge (VE= 44%) even though no anti-envelope antibodies could be detected. T cells were induced but did not correlate. Rather, protection correlated with newly migrated CD14+ monocytes. Since trained innate immunity of monocytes has been shown to involve epigenetic changes leading to increased response to exposure to the same antigens, we tested monocytes from protected or naïve macaques and found that the protected ones produce more IL-6, TNF and MIP1a than the naïve ones, and these responses correlated with the number of exposures required to infect the animals. Epigenetic changes in the IL-6 gene were detected. In the second study, animals were vaccinated with a live attenuated virus, SHIV, whose envelope does not crossreact with SIV envelope. No antibodies to SIV envelope could be detected, yet the animals had reduced risk of rectal transmission of SIVmac251 (VE = 81%). T cells were induced but did not correlate with protection. Moreover, CD8 T cell depletion of protected animals led to rebound of the original SHIV, but no infection with SIV. Transcriptomic studies suggested changes in myeloid cells from the protected animals compared to those from infected animals. This provides new approaches to AIDS vaccine development.

Keywords: AIDS vaccine, trained immuity, monocytes, rhesus macaque model

Biography:

Dr. Sui got her PhD in Pathology from Beijing Institute of Basic Medical Sciences. After two postdoctoral taining from Department of Microbiology, Immunology, and Molecular Genetics, University of Kansas Medical Center and Department of Infectious Diseases and Microbiology, University of Pittsburgh, she joined Vaccine Branch at NCI, NIH as a staff scinentist in 2008. Dr. Sui has been studying the innate and adaptive immunological mechanisms of human immunodeficiency virus/simian immunodeficiency virus (HIV/SIV) vaccine-induced control of HIV mucosal transmission using SIV/SHIV-macaque models. In addition, she is interested in exploring new technologies and novel molecular adjuvants to help prevent mucosal HIV-1 transmission.

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