A novel mechanism linking memory stem cells with innate immunity in protection against HIV-1 infection

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HIV infection affects 37 million people and about 1.7 million are infected annually. Only the RV144 vaccine phase III clinical trial elicited significant protection against HIV-1 acquisition, but the efficacy and immune memory were inadequate. To boost these two critical functions of the vaccine we studied T stem cell memory (TSCM) and innate immunity. TSCM cells were identified by phenotypic markers of CD4+ T cells and they were further characterized into 4 subsets. These consisted of IL-2/IL-15 receptors and APOBEC3G anti-viral restriction factors, which were upregulated, whereas CCR5 co-receptors and α4β7 mucosal homing integrins were decreased. A parallel increase in CD4+ T cells was recorded of the IL-15 receptors, APOBEC3G and CC chemokines, with a decrease in CCR5 expression. We suggest a novel mechanism of dual memory stem cells; the established sequential memory pathway, TSCM →Central →Effector memory CD4+ T cells and the innate pathway consisting of the 4 subsets of TSCM. Both pathways are likely to be activated by endogenous HSP70, the hallmark of cellular stress. The memory stem cells and innate immunity pathways should be optimized to boost the efficacy and immune memory of protection against HIV-1. TSCM are likely to be activated by inducible HSP70, as PES (phenylethynesulphonamide), a small molecular inhibitor induced a dose-dependent inhibition of TSCM. The link between memory stem cells and innate immunity suggests a novel mechanism of inhibiting HIV-1 acquisition, by decreasing CCR5 and α4β7, increasing IL-15/IL-2 receptors and HIV-1 restriction factors.

Recent Publications

- Wang Y, Whittall T, Neil S, Britton G, Mistry M et.al. (2017) A novel mechanism linking memory stem cells with innate immunity in protection against HIV-1 infection. Scientific reports. 7(1):1057.
- Wang Y, Rahman D, Mistry M and Lehner T (2016) The effect of cellular stress on T and B cell memory pathways in immunized and unimmunized BALB/c mice. J. Biol. Chem. 291(39):20707-20717.
- Wang Y, Lavender P, Watson J, Arno M and Lehner (2015) Stress activated DC induce dual IL-15 and IL-b mediated pathways, which may elicit CD4+ T cells and IFN stimulated genes. J. Biol. Chem. 290(25):15595-609.
- Lewis DJM, Wang Y, Huo Z, Gimza R, Babaahmady K et. al. (2014) Effect of vaginal immunization in women with HIVgp140 and HSP70 on HIV-1 replication, innate and T cell adaptive immunity in women. J. Virol. 88(20):11648-11657.
- Wang Y, Whittall T, Rahman D, Bunnik EM, Vaughan R (2012) The role of innate apobec3g and adaptive aid immune responses in HLA-HIV/SIV immunized SHIV infected macaques. PlosOne. 7(4): e34433

Biography

Thomas Lehner is a Professor of Basic and Applied Immunology from London University. He pursued MB, BS London, MD London, FDS RCS, FRC Path, F Med Sci. He has several Prizes and honors to his credit which includes: Besredka Prize of the Pasteur Institute, Lyon, France; Honorary Doctorate, Karolinska Institute, Stockholm, Sweden; Honorary Life President of the International Society for Behcet's Disease; Appointed Commander of the British Empire (CBE) and Honorary Fellow of the Royal Society of Medicine. He has few selected international appointments including: Member of NIH (NIAID), Bethesda US Review Committee Research Grants 1999-2007; Member of Scientific Committee of the International Mucosal Immunology 1997-2006 and Member of the Scientific Committee of the Institute of Virology of the University of Maryland (1998-2002). He has 265 peer-reviewed papers published in scientific journals. Over the past 20 years his research involved animals and humans, preventing HIV and SIV infections, focus on mucosal immunization, generation of CC-chemokines, CCR5 coreceptors stress agents and alloimmunization.

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