Discovery of a novel immune pathway with implications to HIV/AIDS and cancer immunotherapy

by

Prof. Zhiwei Chen

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Abstract

The innate immune cells underlying mucosal inflammatory responses and damage during acute HIV-1 infection remain incompletely understood. Here, we report a Vδ2 subset of gut-homing γδ-T cells with significantly upregulated Δ42PD1 (a PD1 isoform) in acute (~20%) HIV-1 patients compared to chronic HIV-1 patients (~11%) and healthy controls (~2%). The frequency of Δ42PD1+Vδ2 cells correlates positively with plasma levels of pro-inflammatory cytokines and fatty acid binding protein before detectable lipopolysaccharide in acute patients. The expression of Δ42PD1 can be induced by in vitro HIV-1 infection and is accompanied by high co-expression of gut-homing receptors CCR9/CD103. To investigate the role of Δ42PD1+Vδ2 cells in vivo, they were adoptively transferred into autologous humanized mice, resulting in small intestinal inflammatory damage, probably due to the interaction of Δ42PD1 with its cognate receptor TLR4. In addition, blockade of Δ42PD1 or TLR4 successfully reduced the cytokine effect induced by Δ42PD1+Vδ2 cells in vitro, as well as the mucosal pathological effect in humanized mice. Our findings have therefore uncovered a Δ42PD1/TLR4 pathway exhibited by virus-induced gut-homing Vδ2 cells that may contribute to innate immune activation and intestinal pathogenesis during acute HIV-1 infection. Δ42PD1+Vδ2 cells may serve as a target for the investigation of diseases with mucosal inflammation.

Biography:

Dr. Zhiwei Chen is the founding director of the AIDS Institute at The University of Hong Kong. He graduated from the Aaron Diamond AIDS Research Center of the Rockefeller University, and obtained his Ph.D. degree from New York University School of Medicine in 1996. He is currently a tenured full professor in Microbiology with great interests in HIV vaccine and cure research as well as immunotherapy against cancer. He has published over 100 SCI papers and received numerous research grants as a PI from NIHR32, amFAR, NIHR01, Gates Foundation in US; RGC, HMRF and ITF in Hong Kong, as well as a project leader of 973, 11th- and 12th-Mega grants in Mainland China. He serves as an editorial board member for AIDS, JAIDS, and JNIP, and the only researcher from China in generating the “International AIDS Society global scientific strategy: towards an HIV cure 2016” (Nat Med 2016). He will present his discovery on a novel immune regulatory pathway, which has just been published in Nature Microbiology in October 2017.

Date : 4 October 2017 (Wednesday)
Time : 10:30 a.m. – 11:30 a.m.
Venue : Lecture Theater C

(Host faculty: Prof. Ning Li)

All are Welcome!!