Andy (Qigui) Yu, J Vaccines Vaccin 2012, 3:4
http://dx.doi.org/10.4172/2157-7560.S1.007

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference on
Vaccines and Vaccination

August 20-22, 2012 Hilton Chicago/Northbrook, USA

Molecular adjuvants for therapeutic HIV-1 vaccines

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Globally, the human immunodeficiency virus type 1 (HIV-1, the causative agent of AIDS) pandemic has claimed over 20 million lives with 42 million people worldwide currently infected. The majority affected have minimal access to therapy necessitating an urgent need for effective preventive and therapeutic vaccines. In addition, the advances seen with the use of antiretroviral therapy (ART), also known as highly active antiretroviral therapy (HAART), against HIV-1 are limited today by the cost and toxicity of lifelong administration of the drugs. An innovative therapeutic strategy has been proposed to boost the immune system of infected patients with HIV-1 vaccines and to help limit the use of HAART. However, the concept of therapeutic vaccination implies that the host immune system is still competent for eliciting an immune response after vaccination. Patients suffering from HIV-1 infection usually exhibit impaired immune defenses caused by the loss of the CD4+ T cells that are essential for mounting both the cell-mediated and antibody-mediated immune responses. To overcome this challenge for current immunotherapeutic HIV-1 vaccine development, we have developed a heterologous prime-boost vaccine approach with the addition of CD40 ligand (CD40L), a member of the tumor necrosis factor superfamily (TNFSF) of co-stimulatory molecules, in both the prime and boost phases of vaccination to increase antiviral responses in an immunocompromised host with deficiency of CD4+ T cell help. Recent studies in murine systems have demonstrated that CD4+ T cell help is required for antiviral CD8+ cytotoxic T lymphocyte (CTL) response through interactions with dendritic cells (DCs). Furthermore, the help from CD4+ T cells can be replaced or bypassed by ligation of CD40L with CD40 on DCs. We demonstrated that co-immunization of mice with CD40L-expressing canarypox virus (ALVAC) and the ALVAC-based HIV-1 vaccine, vCP1452, augmented HIV-1 specific CTL responses in terms of frequency, polyfunctionality and IL-7 receptor α chain (IL-7Rα or CD127) expression. In addition, ALVAC-expressing CD40L significantly enhanced HIV-1 specific CTL responses in mice depleted of CD4+ T cells. Taken together, our results suggest that CD40L incorporation into ALVAC could be used as a strategy to enhance HIV-1 vaccine immunogenicity in the presence or absence of CD4+ T cell help.

Biography

Andy (Qigui) Yu has completed his M.D./Ph.D from universities in China and postdoctoral studies from University of Toronto, Canada. He is currently an assistant professor in the Department of Microbiology and Immunology, Indiana University School of Medicine. He has published more than 50 papers in peer-reviewed journals. He has recently received the Grand Challenges Explorations (GCE) Phase II grant from the Bill & Melinda Gates Foundation.

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