OMICS Group Conferences
Accelerating Scientific Discovery
3rd World Congress on Virology
November 20-22, 2013 DoubleTree by Hilton Baltimore-BWI Airport, USA

Therapeutic vaccination with Tat restores immune homeostasis and promotes proviral DNA decay in patients on HAART

Barbara Ensoli

Istituto Superiore di Sanita, Italy

Abstract

Tat is a key HIV regulatory protein playing a major role in virus replication, reactivation, and in immune dysregulation, still unmet needs of HAART. This provides a strong rationale for use of Tat in preventative and therapeutic HIV/AIDS vaccines (http://www.hiv1tat-vaccines.info/). This is further strengthened by the recent demonstration that anti-Tat Abs, infrequently produced upon natural infection, restore HIV neutralization, which is impaired by extracellular Tat. In fact, by binding Env spikes on R5 or X4 virus particles, extracellular Tat shields Env and forms an entry complex promoting an integrin-mediated entry and productive infection of DCs and efficient virus transmission to T cells (Monini, PLoSONE 2012).

Results from a phase II trial (ISS T-002, Clinicaltrials.gov: NCT00751595) in 168 anti-Tat Ab-neg subjects under effective HAART (Ensoli, PLoSONE 2010) indicate that vaccination with Tat was not only safe and immunogenic but reverted signs of AIDS progression, including reduction of immunoactivation, increase of T ($CD4^+$) and B lymphocytes, and restoration of functional CD4 and CD8 central memory subsets. Remarkably, proviral DNA load progressively decreased in vaccinees since week 72 after the first immunization. Reduction correlated with anti-Tat Ab titers and occurred at the highest $CD4^+$ T cell increases suggesting repopulation by virus-free $CD4^+$ T cells. In addition, sera from vaccinees efficiently blocked Env entry into DCs and cell infection. These effects were not seen in 88 individuals enrolled in a parallel prospective observational study (ISS OBS T-002). Thus, Tat immunization synergizes with HAART to restore immune homeostasis and to attack the virus reservoir.

Biography

Barbara Ensoli (MD, PhD) is the Director of the NAC. Since 1996 she is conducting an HIV Tat-based vaccine program, currently in advanced clinical phase. She has coordinated several international and national research programs in Europe and Developing countries. She has also coordinated and has been the Sponsor of 5 clinical trials with the Tat-based vaccine and 4 observational studies in Italy and South Africa. She is a member of the WHO-UNAIDS Vaccine Advisory Committee and *EMBO* and Vice-President of the National AIDS Committee of the Italian Ministry of Health. She is a member of the European Research Council (*ERC*).