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

In vivo dynamics of follicular helper CD4 T cells and the induction of SIV antibodies

Constantinos Petrovas

NIAID-NIH, USA

Abstract

Upon early viral infection, highly specialized anatomical sites known as germinal centers (GC) are formed within the secondary lymphoid organs where the interactions between follicular helper CD4+ T cells (T_{FH}) and B cells results in the generation of memory B cells and plasma cells capable of antibody secretion. These interactions can be occurred at different anatomical sites within the lymph node and mediated by surface receptors (i.e. PD-1, ICOS) and soluble factors (i.e. IL-21, IL-4). Therefore, the detailed characterization of the phenotype, location and function of CD4 T cell populations within the LN is necessary for the understanding of the development of antigen-specific B cell responses. We have found a shared phenotype between non-human primate and human T_{FH} cells characterized by increased expression of PD-1, ICOS, CTLA-4, BTLA, CD69 and low expression of CCR7 and CD127. Quantitative imaging analysis further supports the nature of lymph node PD-1^{high} CD4 T cells as T_{FH}. $CD150^{low}$ T_{FH} cells express a distinct molecular gene signature and cytokine function. Chronic SIV infections results in accumulation of T_{FH} cells, a process associated with altered gene signature, increased Bcl-6 expression, low in vivo cycling and increased in vitro apoptosis. Furthermore, increased frequency of T_{FH} was associated with general immune activation, a skewed IL-6 signaling favoring the development of T_{FH} and most importantly with increased frequency of memory-GC B cells and circulating SIV-specific immunoglobulins. Our findings support a model of T_{FH} cell dynamics where a constant flow of activated CD4 T cells enter the T_{FH} compartment followed by further differentiation to a status ($CD150^{low}$) characterized by a polarized cytokine profile and reduced survival ability. SIV does not lead to their specific depletion, and often results in their accumulation. This is likely because of the diverse populations of CD4 T cells that can serve to continually replenish this population, thereby assuring their persistence late into SIV infection.

Biography:

Constantinos Petrovas is currently a Staff Scientist at the Immunology Laboratory, Vaccine Research Center, NIAID, NIH, Bethesda, USA. His major scientific objective has been the understanding of the cellular and molecular mechanisms of the development of virus-specific responses, as well as the manipulation of these responses, in the settings of vaccination with specific antigens. His work has revealed an alternative strategy that HIV may employ to counterattack the immune system by affecting the survival of HIV-specific CD8 T cells and could lead to novel therapeutic interventions promoting an effective, long-lasting cellular immune response. More recently, his work was the first to describe the phenotype, localization, molecular profile and dynamics of TFH cells in acute and chronic SIV infection. He is a member of the Editorial Board of "ISRN AIDS" and "International STD Research & Reviews". He has been serving as ad hoc reviewer for several journals, including the Journal of Experimental Medicine, Blood, Journal of Immunology, Plos Pathogen and Journal of Virology.