ICGEB International Centre for Genetic Engineering and Biotechnology | Developing Knowledge

ICGEB International SEMINAR PROGRAMME 2018

Wednesday, 10 January 2018 | 3:00 pm | ICGEB Seminar Room, W building | Padriciano, 99, Trieste, ITALY

Alexis KALERGIS

Profeseor and Director, Millennium Institute Immunology and Immunotherapy, Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, CHILE

Human Respiratory Syncytial Virus (hRSV) is the leading cause of bronchiolitis and pneumonia in young children worldwide. The recurrent hRSV outbreaks and reinfections are the cause of significant public health burden and associate with an inefficient viral immunity, even after disease resolution. Furthermore, hRSV can also cause severe symptoms, such as dyspnea and chest wall retractions. Recently, neurological symptoms have also been associated with hRSV- respiratory infection and include seizures, central apnea, lethargy, feeding or swallowing difficulties, abnormalities in muscle tone, strabismus, abnormalities in the CSF and encephalopathy. Although several mouse- and human cell-based studies have shown that hRSV infection prevents naïve T cell activation by antigen-presenting cells, the mechanism underlying such inhibition remains unknown. We have shown that the hRSV nucleoprotein (N) could be at least partially responsible of inhibiting T cell activation during infection by this virus. Early after infection, the N protein is expressed on the surface of epithelial and dendritic cells, after interacting with trans-Golgi and lysosomal compartments. Further, experiments on supported lipid bilayers loaded with peptide-MHC complexes, showed that surface-anchored N protein prevented immunological synapse assembly by naive CD4+ T cells. Synapse assembly inhibition was in part due to reduced TCR signaling and pMHC clustering at the T cell-bilayer interface, suggesting that protein N interferes with pMHC-TCR interactions. Moreover, N protein co-localized with the TCR independently of pMHC, consistent with a possible interaction with TCR complex components. Based on these data, we conclude that hRSV N protein expression at the cell surface of infected cells inhibits T cell activation. These data suggest that inhibition of synapse assembly can be a major virulence factor that contributes to impairing acquired immunity and enhances susceptibility to reinfection by hRSV. These data allowed the generation of an RSV vaccine, which showed protection in several animal models and now is about to enter evaluation in human clinical trials.

"Translational immunology: basic knowledge aimed at preventing infectious diseases and autoimmunity"

Host: M. Giacca

Registered seminars are available onYouTube, iTunes and ICGEB Podcast at:

http://www.icgeb.org/podcast-program.html

Open event - Free entrance

Download on iTunes

More information at:

seminars@icgeb.org | tel.: 040-3757377