ImmunoTools *special* Award 2014

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Human T- Cell lymphotropic virus type 1 (HTLV-1)infection: Study of the role of BST2 (Bone Marrow Stromal Protein 2) and in vitro studies with nanoparticles related to interferon (IFN) type 1.

Human T-cell lymphotropic virus type 1 (HTLV-1), human retrovirus that is endemic in Northwest Argentina and with high prevalence in risk groups, is the etiologic agent of Adult T-cell leukemia (ATL), lethal in the short term, and HTLV-1 Associated Mielopathy/ Tropical Spastic Paraparesis (HAM/TSP), a progressively disabling pathology. There is neither preventive vaccine for the infection, nor effective therapies available for these pathologies. HTLV-1 has tropism for $CD4^+$ T cells and is preferentially multiplied by clonal expansion of the host cell. It is transmitted cell to cell by viral synapse, a mechanism that was recently described, which involves an extracellular structure rich in carbohydrates and specific components such as collagen, galectin and BST-2 (Bone marrow stromal antigen 2, also known as "tetherin"/CD317). This structure is induced and spatially organized by viral infection, similar to bacterial biofilms, and it was observed that a higher density of BST- 2 was present in the point where infected and non-infected cells contact each other, in the $CD4^+$ T cells from individuals with HAM/TSP.

In relation to the innate response, it has been suggested that plasmacytoid dendritic cells (pDCs) infected with HTLV-1 have diminished IFN production although the mechanisms involved are not known. In viral infections, IFN production by pDC is controlled by negative feedback through the complex formed by the inmunoglobulin-like receptor transcript (ILT7) expressed in these cells and its ligand BST- 2, which strongly inhibits the production of IFN type. It has also been described that BST-2 helps to retain viral particles on the outer surface of the cell, allowing a more efficient transmission to non-infected cells. Our hypothesis is that blocking the interaction BST-2/ILT7 by anti-BST-2 monoclonal antibodies, we could trigger IFN production by pDCs, by diminishing the overexpression of BST-2 and therefore its inhibitory effect.

Furthermore, these antibodies would also be able to block the retention of viral particles in the outer surface of the cell, diminishing in a way viral cell to cell transmission.

Thus, the therapeutic options for both diseases associated with HTLV-1 include Interferon-α (IFN-α). The drug used for viral infections and various cancers was chemically modified with polyethylene glycol to create the pegylated IFN-α (PEG) in order to reduce undesired effects. While allowing a weekly dosage, the success rate in the anti-viral treatment is not optimal and in some cases severe side effects preclude their use. In this project we propose to evaluate in vitro assays by testing whether IFN-α immobilized on biodegradable nanoparticles, which showed greater benefit, produces a more efficient antiviral response in infected $CD4^+$ T cells compared with soluble IFN-α. The results provide original insights into the pathogenesis of HTLV-1, the antiviral response mounted against the infection and the possible use of nanoparticles in therapeutics.

Currently, we are beginning with the separation of $CD4^+$ and dendritic cells in order to start infecting them with HTLV-1. We would then start looking at BST-2 overexpression and its correlation with IFN production.

Get the ImmunoTools Award will be a great help to our research and will allow us to move forward with the project.

ImmunoTools *special* AWARD for **Carolina A. Berini** includes 19 reagents

FITC - conjugated anti-human CD1a, CD14, CD45RA, CD86, HLA-DR,

PE - conjugated anti-human CD4, CD40, CD62L, CD80,

PerCP - conjugated anti-human CD4,

human IL-6 ELISA-set for 96 wells, human TNFa ELISA-set for 96 wells (each 3 reagents),

recombinant human cytokines: rh GM-CSF, rh IL-2, rh IL-4

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