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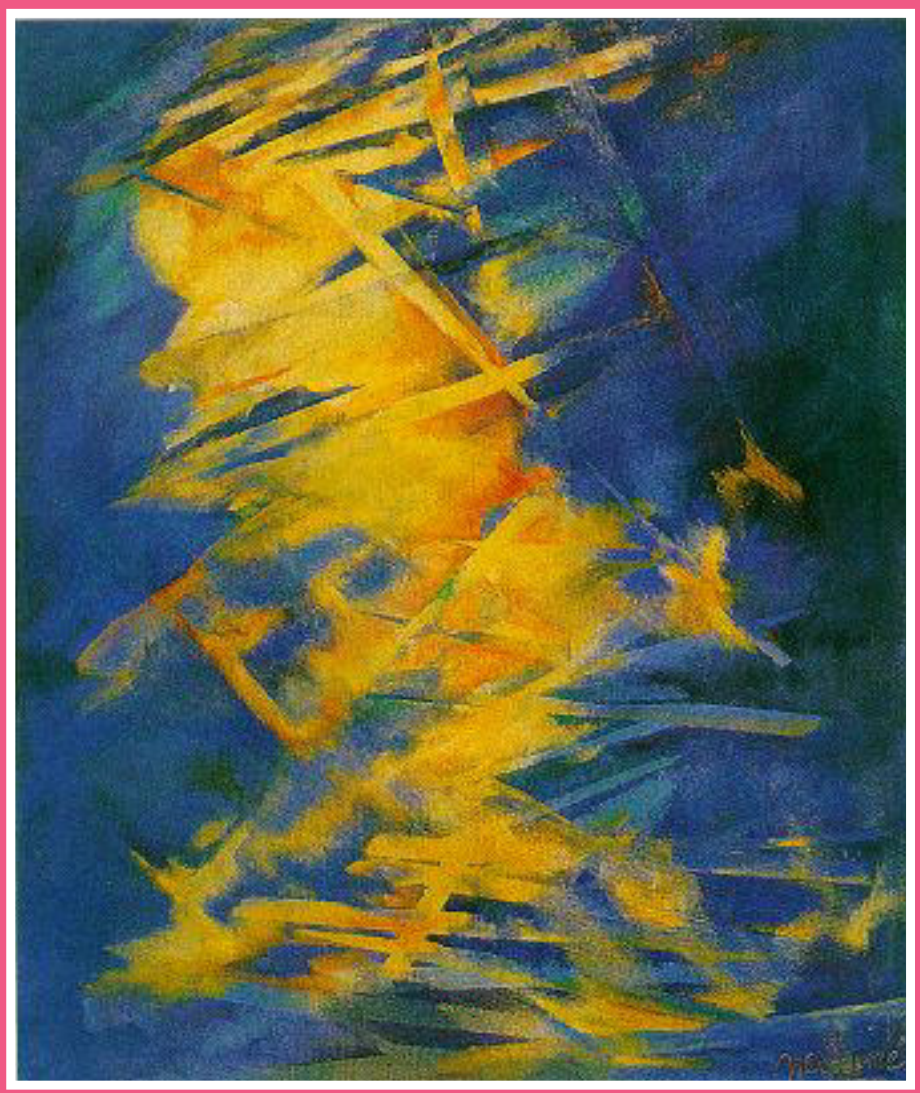

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13-17 de noviembre de 2017
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JOINT MEETING OF BIOSCIENCE SOCIETIES

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MEETING OF ARGENTINE SOCIETY OF HEMATOLOGY (SAH)

XXIX ANNUAL MEETING OF ARGENTINE SOCIETY OF PROTOZOOLOGY (SAP)

November 13 -17, 2017
Palais Rouge– Buenos Aires

(678) ***B. abortus* RNA INDUCES MHC-I RETENTION IN THE GOLGI APPARATUS VIA TLR8 AND BY DISRUPTING THE ACIDIFICATION OF THIS COMPARTMENT**

María Ayelén Milillo (1), Aldana Trotta (1), Fàbio Vitarelli Marinho (2), María Victoria Delpino (3), Lis Noelia Velásquez (1), Monica Vermeulen (1), Sergio Costa Oliveira (2), Guillermo Giambartolomei (3), Paula Barrionuevo (1)
(1) IMEX (CONICET-Academia Nacional de Medicina). (2) Departamento de Bioquimica e Imunologia, Universidade Federal de Minas Gerais. (3) INIGEM-CONICET.

Despite the cytotoxic $CD8^+$ T cell responses elicited by *Brucella abortus*, this pathogen is able to survive inside macrophages and generate a chronic infection. *B. abortus* infection of human monocytes down-modulates the IFN-γ-induced MHC-I cell surface expression by retaining these molecules in the Golgi apparatus (GA). We have recently demonstrated that *B. abortus* RNA is the bacterial component involved in this phenomenon. Thus, the aim of this study was to further characterize the receptor and mechanisms implicated in MHC-I down-modulation. Endo/phagolysosomal Toll-like receptors (TLR) 3, 7 and 8 are the most known receptors capable of recognizing RNA. We had previously discarded TLR3 consequently, to study whether TLR7 and/or TLR8 were involved in the *B. abortus* RNA-mediated MHC-I down-modulation, THP-1 cells or murine bone marrow macrophages (BMM) were treated with human TLR-7 or TLR-8 agonists in the presence of IFN-γ for 48 h. Then, the expression of MHC-I molecules was evaluated by flow cytometry. Surpringsily, TLR8 ($p<0.05$) but not TLR7 was the receptor involved in this phenomenon. Mice do not have a functional TLR8 instead TLR7 performs its function. To confirm that TLR7/8 was the receptor linked to MHC-I down-modulation, TLR7 KO BMM were infected with *B. abortus* or treated with its RNA. In both cases, MHC-I down-modulation was abolished as well as the antigen presentation to $CD8^+$ T cells. Concerning the retention mechanism, we confirmed that neither MHC-I protein degradation nor a modification of its mRNA expression was involved. Rather, we demonstrated that the ionophore monensin (which impedes the proper acidification of GA cisternae) mimicked *B. abortus* RNA-induced retention of MHC-I in GA ($p<0.05$). Overall, these results indicate that *B. abortus* RNA, viaTLR8 and probably due to an inhibition of Golgi acidification, inhibits MHC-I expression. Thus, bacteria can hide within infected cells and avoid the immunological surveillance of cytotoxic $CD8^+$ T cells.

Keywords: *B. abortus*, RNA, MHC-I, Golgi apparatus, Evasion strategies

(1438) **NONALCOHOLIC FATTY LIVER DISEASE: RESISTIN DIFFERENTIALLY REGULATES T CELL ACTIVATION AND REACTIVE OXYGEN SPECIES LEVELS**

Cecilia Claudia Garcia (1), Nadia Soledad Alegre (1), Plácida Baz (1), Javier Benavides (2), Luis Colombato (2), Daniel Poncino (3), Daniel Garcia (3), Alejandra Claudia Cherñavsky (1)
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Resistin (RES) is a cytokine which plasma concentration has been found elevated in Nonalcoholic Fatty Liver Disease (NAFLD) patients. Although human RES is produced by immunological cells, its effect on them is poorly understood. We have previously demonstrated that RES decreases CD69 expression in activated T cells from controls (Co) but not from NAFLD patients. We aimed to evaluate RES-mediated modulation of CD25 in T cells from NAFLD patients and Co and RES ability to modulate reactive oxygen species (ROS) production in peripheral blood mononuclear cells (PBMC). PBMC were obtained from NAFLD (n= 9) patients and Co (n= 14). Isolated T cells were activated with coated anti-CD3 (3 ug/ml) +/- RES (10 ng/ml) for 72 h, stained with anti-CD4, -CD8 and -CD25 mAbs and evaluated by flow cytometry (FC). To evaluate ROS levels, PBMC were incubated with or without RES (20 ng/ml) for 24 h, stained with 2´7´-dichlorofluorescin diacetate (DCFH-DA) and anti-CD3, -CD4, -CD8, -CD14 mAbs and studied by FC. As a preliminary approach, monocytes oxidative burst was stimulated with PMA (100 ng/ml) +/- RES and ROS production was evaluated by DCFH-DA. Mann-Whitney and Wilcoxon paired tests were used. RES decreased CD25 expression in activated T cells from Co but not from NAFLD patients. As a result, CD25 expression is higher in CD4+ ($p<0.01$) and CD8+ ($p<0.05$) activated T cells from NAFLD patients. RES decreased ROS levels in monocytes (p= 0.031), CD4+ (p= 0.014) and CD8+ (p= 0.008) T cells only from Co. NAFLD patients showed higher ROS levels than Co in CD4+ ($p<0.05$) and CD8+ ($p<0.05$) T cells. The presence of RES prevented ROS production when oxidative burst was induced by PMA stimulation. Similar to CD69 activation marker, RES can modulate CD25 expression and ROS levels in T cells from Co but not from NAFLD patients. Thus, NAFLD patients may have an alteration in RES signaling pathway which might contribute to NAFLD progression through ROS production and/or T cell-mediated injury.

Keywords: Resistin, Nonalcoholic Fatty Liver Disease, T cell activation markers, ROS.

IMMUNOLOGY (IMMUNOTHERAPY) 3

(68) **THE GLYCOSYLATION OF A CHIMERIC anti-rhIFN-α2b ANTIBODY PRODUCED IN DIFFERENT CELL LINES INFLUENCES ITS NEUTRALIZING ACTIVITY**

Carolina V. Attallah, María Fernanda Aguilar, Marina Etcheverrigaray, Marcos R. Oggero
UNL, CONICET, FBCB, Laboratorio de Cultivos Celulares.

The monoclonal antibodies constitute a large subset of the marketed biotherapeutics, most of which are glycosylated, and thus produced in mammalian cells. These molecules are bifunctionals, since the variable (V) regions are responsible of antigen binding and the constant (C) regions confer effector properties. However, this immunological dogma is in revision because several studies suggest that C regions of different class or subclasses of antibodies with identical V regions, influence the antigen binding activity Also, despite the glycosylation pattern strongly influences the antibody effector functions, this feature always was considered not to be important for binding antigen ability. In this work, we studied the impact of the different cell lines on the the affinity constant and antigen neutralizing ability of a chimeric anti hIFN α2b murine single chain Fv fused to Fcg1 (scFv Fc). The proteins, produced by CHO K1, HEK293 and NS0 cells showed no significant differences in the affinity constant measured by competitive ELISA. In spite of this parameter, the in vitro IFN neutralizing ability of the antibodies was higher for the molecule produced by CHO cells. In fact, the neutralizing activity of the same deglycosylated protein was considerably reduced. The present study invites us to critically discuss the choice of the cell line to produce biotherapeutic antibodies.

Keywords: antibody constant region; neutralizing activity; affinity constant; different producing cell lines, glycosylation

(341) **THE ANTI-MELANOMA THERAPEUTIC VACCINE CSF-470 CAN BE CRYOPRESERVED WITH TREHALOSE PLUS HUMAN SERUM ALBUMIN FOR LONG TERM STORAGE**

Ivana Jaqueline Tapia (1), Paula Blanco (1), José Mordoh (1, 2), María Marcela Barrio (1)
(1) Centro de Investigaciones Oncológicas, Fundación Cáncer. (2) Fundación Instituto Leloir.

The therapeutic vaccine CSF-470 is a mixture of four lethally irradiated melanoma cell lines administered with BCG and GM-CSF, that has demonstrated a significant benefit in the distant metastasis-free survival for high risk melanoma patients in a phase II Clinical Trial as compared to IFN-α2b (CASVAC-0401). Currently, CSF470 vaccine irradiated cells are frozen using dimethyl sulfoxide as a cryoprotectant and stored in liquid N_2 (DMSO) until its use. Prior to inoculation, vaccine doses must be thawed under sterile conditions, washed to remove DMSO and resuspended until clinical administration. *Methods:* To facilitate CSF-470 pharmaceutical production and distribution we designed an alternative preservation of CSF470