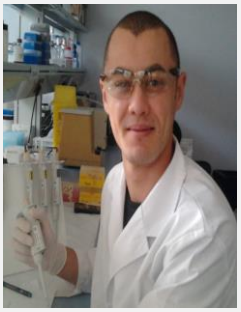
ImmunoTools *special* Award 2014



Jamal Qualai, PhD-student

Supervisor: Dr. Meritxell Genescà Ferrer

Unitat d'Immunologia de les Mucoses, Institut Germans Trias i Pujol (IGTP) Edifici de Recerca, Planta 1 Ctra Can Ruti, camí de les escoles s/n, 08916 Badalona

Novel NKT modulators as adjuvants for sexually transmitted disease vaccine development

Rational design of immunogens against sexually transmitted infections (STI) requires knowledge of different aspects of the immune response that contribute to protection in the genital mucosa. Although effective vaccines exist for human papilloma virus and hepatitis B virus, efforts to develop vaccines against herpes simplex virus-2, HIV and other bacterial STI that can elicit cellular immune responses in the female genital tract have been hampered by an inability to successfully induce immune responses in such mucosa. Effective vaccines against STI should generate localized immune responses at sites of potential exposure to provide faster and stronger control of infection. Basic knowledge of the female genital tract immune system and new methods to measure and manipulate immune responses are required to develop effective STI vaccines.

In general, mucosal T cells play a critical role in the clearance of sexually transmitted intracellular pathogens. Further, to induce long-term protection and generate a quick response at the mucosal level, induction of a resident memory T cell phenotype may be a desirable goal. Certain vaccines types, such as subunit vaccines, need potent adjuvants to initiate and maintain strong immunological memory. Similarly, vaccines directed to the epithelium also require a potent adjuvant to overcome the induction of tolerance that occurs upon mucosal exposure to an antigen. Thus, identification of adjuvants that elicit a protective immune response is one of the main challenges for the development of an effective vaccine against most STI. Adjuvants that not only optimize the immune response to pathogen-derived antigens, but also can target the vaccine-specific immune responses at the infected mucosa will be critical to develop effective vaccines against STIs.

Invariant natural Killer T (iNKT) cells are major immune regulators, bridging innate and adaptive immunity and responding within hours after activation. They have become an attractive target for vaccine development since, when activated, these cells trigger downstream activation of antigen presenting dendritic cells, antibody producing B cells, NK cells and T cells. These cells constitute a unique subset of T cells that use their T cell receptors to recognize self and foreign lipids presented by the non-classical major histocompatibility complex I molecule, CD1d, as cognate antigens. Moreover, since CD1d is codified by a non-polymorphic gene, any molecule capable to activate iNKT through CD1d will represent a universal adjuvant.

The aim of this project is to address the benefit of novel iNKT modulators as potential vaccine adjuvants against female reproductive tract infections. To this aim we will first screen a library of glycolipid compounds for their capacity of inducing cytokine secretion in human peripheral blood (i.e. IFNg, IL-4 and IL-12) to select the most promising compounds.Then, selected compounds will be tested for their capacity to properly activate the innate and the adaptive mucosal immune system in a model of human cervical explant and in a pre-clinical mouse model of a chlamydia vaccine.

The ImmunoTools award would benefit this project by providing ELISA plates for the screening process and antibodies for human and mouse phenotyping:

ImmunoTools *special* AWARD for **Jamal Qualai** includes 25 reagents

FITC - conjugated anti-human CD14, CD19, C3/C3b/iC3b,

PE - conjugated anti-human CD8, CD56, Granzyme K,

PerCP - conjugated anti-human CD3,

APC - conjugated anti-human CD11c,

human ELISA-set for 96 wells: IFNg, IL-4, IL-10, IL-12p40 differential, (each 3 reagents),

FITC - conjugated anti-mouse NK-cells, CD8a,

PE - conjugated anti-mouse gdTCR,

APC - conjugated anti-mouse CD19, Gr-1 DETAILS more AWARDS