ImmunoTools *special* Award 2015

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Position: Associated Research

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Immunomodulatory and antiviral effect of salivary extract of *Aedes aegypti*

Dengue virus is an arthropod-borne virus affecting tropical and sub-tropical areas of the world. Nowadays dengue affects more than 100 countries, around 390 million cases and 25,000 deaths are confirmed each year. Currently, none antiviral drug or vaccine are available for dengue treatment and/or prevention.

Dengue virus belongs to the *Flaviviridae* family and flavivirus genus, presenting a positive-strand RNA genome coding for three structural proteins (C, prM/M and E) and seven non-strucutral proteins (NS2A, NS2B, NS3, NS4A, NS4B and NS5). The virus infects human through the bite of infect *Aedes aegypti* female (in Asia *Aedes albopictus* is also involved in dengue transmission). The first target cells for dengue virus infection are Langerhans cells in the Dermis, however, monocytes are also infected by the virus.

Aedes aegypti mosquitos are contaminated during the blood feeding of a patient in the viremic period, the virus replicates at the mesentery, reaches the haemocele and finally the salivary gland, were it replicates and could be transmitted to another vertebrate host. Recently, it was demonstrated that saliva from arthropod vectors has an important role in the infectious process, once contains several compounds with relevant biologically functions that affects homeostasis, inflammation and immune response. Saliva also contains pharmacologically substances controlling the haemorrhage (an important pathological consequence of dengue virus infection), like inhibition of platelet aggregation, coagulation cascade and vasoconstriction. Those effects could contribute to the blood feeding in the vertebrate and consequently, virus transmission.

The role of *Aedes aegypti* saliva during infection is generally neglected by researches working on the dengue field. In the past, some researches evaluated the role of *Aedes aegypti* saliva on dengue infection, with contradictory results, probably

due to the use of adapted laboratory strains of dengue virus. Additionally, little is known about the immunomodulatory effect of *Aedes aegypti* saliva on dendritic cells (DCs) and monocytes (MΦ). Although being target cells for dengue, DCs and MΦ are crucial cells in the processing and antigen presentation for lymphocytes, and consequently, for the development of the adaptive immune response.

Finally, the aim of this project is to evaluate the role of the extract of the *Aedes aegypti* saliva (EGS) in the dengue virus infection, and also the immunomodolatory function of EGS on human and mice DCs and MΦ. The main questions that we intend to answer are:

1) Does *Aedes aegypti* EGS have a role on dengue virus infection, using clinical isolates from the four dengue virus serotypes?
2) *Aedes aegypti* EGS presents immunomodulatory activity on primary human monocytes and monocyte derived dendritic cells (mdDCs), isolated from healthy volunteers?
3) Does *Aedes aegypti* EGS affect the immunomodulatory response of mice monocytes and monocyte derived dendritic cells (mdDCs), isolated from mice bone marrow?

Selected reagents from ImmunoTools would be used for differentiation of mdDCs from human monocytes or mice bone marrow, and for phenotyping and analyzes of response to *Aedes aegypti* EGS.

ImmunoTools *special* AWARD for **Juliano Bordignon** includes 25 reagents

FITC - conjugated anti-human CD1a, CD16, CD80, CD86, HLA-DR, Control-IgG2a, Annexin V,

PE - conjugated anti-human CD11c, CD14, CD15, Control-IgG1,

APC - conjugated anti-human CD40, Control-IgG1,

human ELISA-set for 96 wells, human IL-12p40 total (detect IL-23 as well), human sCD147 (sEMMPRIN) (each 3 reagents),

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

FITC - conjugated anti-mouse CD11b, isotype control IgG2b,

recombinant mouse cytokines: rm GM-CSF DETAILS more AWARDS