ImmunoTools *special* Award 2014

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Immunological reactions triggered by *Trypanosoma cruzi*

American trypanosomiasis or Chagas' disease, caused by the protozoon *Trypanosoma cruzi*, affects 10 million people in Latin America (WHO). Other regions of the world are also affected by this disease due to emigration of infected individuals. Main routes of transmission are vectorial, transfusional and congenital.

Previous work in our lab showed that T.cruzi-infected cord blood mononuclear cells (CBMCs) accumulate IL-12 and produce IFN-γ. Use of surface cell markers by flow cytometry to identify responding cells indicates that IL-12 accumulates in monocytes and that IFN-γ is rapidly released by NK cells, especially $CD56^{bright}$NK cells (*Guilmot et al. 2013, Plos NTDs*). We currently do not know the mechanisms leading to IL-12 and IFN-γ productions in response to the parasite in our conditions.

The aim of our work is to characterize immunological reactions triggered by *T. cruzi* in CBMCs and compare it to adult peripheral blood mononuclear cells (PBMCs), knowing that newborn and adult immune system react differently against pathogens (*Prabhudas et al. 2011, Nature Immunology*).

For example, previous work in our lab showed that NK cells of newborns congenitally infected by *T. cruzi* show phenotypical and functional changes, suggesting their previous activation *in utero* (*Hermann et al. 2006, Pediatric Research*). Besides, T cells from congenitally-infected newborns produce IFN-γ. This is interesting because healthy newborns have physiological difficulties to produce this cytokine, while this cytokine is essential to fight infections caused by intracellular pathogens.

To decipher the mechanism of NK cell IFN-γ response, we will first investigate the expression of IL-12 receptor on leucocytes (formed by 2 chains, β1 and β2) to identify responding cells to this cytokine. For this aim, several surface markers will be used as: CD1a, CD141, CD11c, CD123, HLA-DR, CD34 and "Lin neg" for dendritic cells,

CD3 for ~~all~~ T cells, CD4 and CD8 to discriminate cytotoxic T lymphocytes and helper T cells, CD16 and CD56 to identify NK cells subsets, CD14 for monocytes and CD19 for B cells, as well as CD62L and CD69 as activation markers on lymphocytes. In our model, IL-15 is used to maintain NK cells alive and synergize with *T.cruzi* for NK cells IFN-γ production.

We shall next study the signalling cascade downstream IL-12R to assess that this receptor is engaged. We will therefore at least study the expression of Jak 2, Tyk 2 and STAT 4 known to be involved in IL-12R signalling. Parallely, expression of IL-15R will also been studied to decipher which cells are important to deliver co-signals in response to *T. cruzi* in our conditions (IL-15 stimulates growth of T cells and of NK cells among leukocytes).

Finally, we intend to study the expression of various receptors on NK cells susceptible to be engaged by crosstalk with accessory cells such as monocytes and dendritic cells, since we know that *T. cruzi* activates NK cells mainly through an indirect pathway (*Guilmot et al. 2013, Plos NTDs*). We will pay attention to NKp30, NKp44, NKp46 and CD27 receptors.

References

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