ImmunoTools *special* Award 2015

Leonardo Fainboim, MD
Position: Professor, Head of Immunogenetics Division

Hospital de Clinicas, University of Buenos Aires, INIGEM
CONICET-UBA, Buenos Aires, Argentina

Study of a novel CD8$^+$HLA-DR$^+$ T cell in the intrahepatic immune response

The aim of the study is to characterize the phenotype and the function of two new actors present in the human liver: 1- A subset of CD8$^+$ cells expressing HLA-DR was recently described in peripheral blood with a strong suppressor capacity [1], In this study we attempt to identify the functional role of this regulatory T cells within the normal or pathological livers and their associated lymph nodes. With this porpoise in the first place we will perform a wide phenotypic analysis of this T cell subset within the liver and the associated lymph nodes. Once we established the complete phenotype of this Treg cells, and their frequencies in normal livers, we will perform a suppressor assay to confirm their function in the liver.

The liver is known to possess strong immunoregulatory capacity[2]. During transplantation, a donor liver is capable to induce systemic tolerance , particularly through the effect of immature dendritic cells with tolerogenic capacity[2]. However, these models show differences between murine and human models. In these context, we want to analyze the role play by the classic CD4$^+$ FOXP3 Tregs and the CD8$^+$HLA-DR$^+$ T cells in the modulation of liver immune responses.

Specific Objectives:
A recent report from our lab described this new subset of CD8$^+$HLA-DR$^+$ Treg cells, where we revealed this this subset is already detectable in cord blood, suggesting that they represent a population of natural Tregs with a strong suppressor activity. Our working hypothesis support the concept that this CD8$^+$ Tregs could play a central role in the liver tolerogenica response, because preliminary results indicated that their frequency is increased in the liver, and may be related with the success of liver transplantation. To perform this study we will take advantage of a novel technique where a high number of liver mononuclear cells can be obtained from healthy donor

and diseased explants livers that are perfused during the implant. Within the liver, $CD8^+$T cells represent the most frequent T cell, allowing the differentiation with blood contamination in liver samples.

References

[1] Arruvito L, Payaslian F, Baz P, Podhorzer A, Billordo A, Pandolfi J et al. Identification and clinical relevance of naturally occurring human $CD8^+HLA\text{-}DR^+$ regulatory T cells. J Immunol, 2014;193:4469-76.

[2] Morelli AE, Thomson AW. Tolerogenic dendritic cells and the quest for transplant tolerance. Nat Rev Immunol, 2007;7:610-21.