ImmunoTools *special* Award 2016

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Mechanisms of B and T cell activation induced by targeting of $MSP1_{19}$ antigen to two different subsets of dendritic cells via DEC205 and DCIR2 receptors

There are mainly two Dendritic Cells (DCs) subsets in murine spleen, one that expresses the endocytic receptor CD205 (DEC205) and the alpha chain of CD8 receptor ($DEC205^+CD8\alpha^+$), and another that expresses the endocytic receptor DCIR2 but not CD8α ($DCIR2^+CD8\alpha^-$). $DEC205^+CD8\alpha^+$ DC subset is specialized in antigen cross presentation and $CD8^+$ T cells priming, while the $DCIR2^+CD8\alpha^-$ DC is associated with priming of $CD4^+$T cells *(Merad et al., 2013).*

Antigen targeting to these two DCs subsets via chimeric monoclonal antibodies (mAbs) linked to proteins derived from different pathogens is an efficient strategy to enhance the immunogenicity of such proteins *(Boscardin et al., 2006; Henriques et al., 2013).* Nevertheless, the mechanisms of B cell activation, as well as the cell-to-cell interactions induced by this strategy of vaccination, are not completely understood.

Thus, the main goal of this study is to analyse the antibody response and the cell-to-cell interactions among DCs, T and B cells induced by targeting a model antigen to the two DCs subsets. We will use chimeric αDEC205 and αDCIR2 mAbs fused with a 19 kDa fragment derived from the *Plasmodium vivax* merozoite surface protein 1 ($MSP1_{19}$). *Plasmodium* spp. are the causative agents of malaria, a disease that affects millions of people annually.

To analyse the immune response induced after immunization of mice with αDEC205-$MSP1_{19}$ or αDCIR2-$MSP1_{19}$ chimeric mAbs, we will use ImmunoTools antibodies for the immunophenotyping of different cell populations. We intend to immunize the mice with each chimeric mAb and then evaluate the expansion and/or activation of DCs, monocytes/macrophages, T, B, and NK cells. For this purpose, we will use the different population and activation markers listed below. In addition, we intend to generate DCs in vitro from bone marrows using GM-CSF plus IL-4 or Flt3L/CD135.

These DCs will be incubated with both chimeric mAbs (αDEC205-MSP1$_{19}$ or αDCIR2-MSP1$_{19}$), activated and then injected into naïve mice. The anti-MSP1$_{19}$ antibody titers, as well as the induction of T cell responses, will be accessed by intracellular cytokine staining.
With this project we intend to explore how each DC subset controls T and B cell activation.

References:

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MERAD, M. *et al*. The dendritic cell lineage: ontogeny and function of dendritic cells and their subsets in the steady state and the inflamed setting. **Annu Rev Immunol,** v. 31, p. 563-604, 2013.