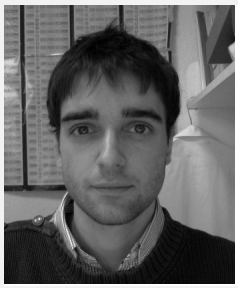
ImmunoTools IT-Box-Cy55M-Award 2013



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The implication of skin epidermal and dermal antigen-presenting cells in T follicular helper cell polarization

T follicular helper cells (T_{FH}), a lineage of $CD4^+$ T cells, play a pivotal role in differentiation of B cells to plasma cell and isotypic switch of immunoglobulin (Ig) after interaction with professional antigen-presetting cells. Using poly-lactic acid nanoparticles (NPs), coated with the HIV-derived p24 protein, we have shown that intradermal injection induced both seric IgG and mucosal IgA responses (C. Liard et al. Vaccine (2011)). The skin contains several types of DCs, such as epidermal Langerhans cells (LC) and dermal $CD207^+$ dendritic cells ($CD207^+$ dDC), specialized in the capture and presentation of antigens administered by vaccination. As T_{FH} are highly implicated in IgA class switching we thus questioned the role of epidermal Langerhans cells and dermal DC to induction of T_{FH} and investigated molecular signalling leading to CD4 polarization and IgA production.

Our results demonstrate the high efficacy of intradermally-injected NPs-HIV-p24 to polarize the development of $CD4^+$ cells into T_{FH} cells and induce the expansion of IgA-secreting B cells in dLNs. However, deficiency in skin LCs and $CD207^+$ dDCs affect the polarization of T_{FH} cells.

Interleukin-6 (**IL-6**) is described to be highly engaged in the T_{FH} polarization, so we evaluate currently the IL-6 production by LCs and CD207 dDCs *in-vivo*. In addition we look at the implication of **IL-21** and TGF beta produce by activated T_{FH} to induce B cells activation and Ig class switch. In parallel, and to confirm the interaction of skin DCs cells, CD4 T cells and B cells, we are designing an *in-vitro* experiment of co-culture and determine the requirement of cytokine to induce T_{FH} cells (**IL-6**) leading to IgA calss switch (**IL-21** and TGF beta) but also CD8 cytotoxic cells (**IFNgamma; IL2**) and thus decrypt the cytokinic interaction that elicit a specialize immune response. This work highlights the importance of skin DCs in eliciting a strong antibody response and contributes to our knowledge of the complex cellular mechanisms orchestrating intradermal vaccination.

ImmunoTools IT-Box-Cy55M for Charles Nuttens

includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS