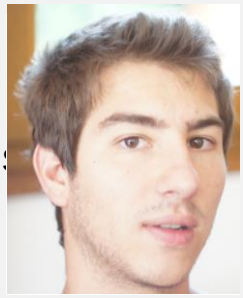
ImmunoTools *special* Award 2014



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Role of B cells and T follicular helper cells in the generation of mucosal immunity following intradermal vaccination.

Mucosal immunity, and particularly high affinity class-switched IgA and IgG antibodies are primordial for protection against invading pathogens. HIV entry and propagation takes place mainly in the vaginal and intestinal mucosa. Thus, new vaccine strategies must induce high affinity antibody-secreting B cells able to home specifically to mucosal sites in order to block virus entry.

Following isotype class-switch and somatic hypermutation that takes place in draining lymph nodes, mucosal imprinting of B cells is mediated by the chemokine receptors CCR9 and CCR10, which ligands **CCL25** and **CCL28** are produced by epithelial cells of the small intestine and other mucosa-associated tissues respectively. What are the molecular mechanisms that drive expression of these receptors is still under investigations. While some works have shown evidences that vitamin derivates secreted by dendritic cells in the gut or skin could induce such receptors expression, these do not fully explain what happens during vaccination and infection.

It has been shown that T follicular helper (T_{FH}) cells are necessary for Ig class switching and can imprint CCR10 homing receptor to B cells *in vitro*, through secretion of **TGFβ1** and **IL-21** (Dullaers et al, Immunity, 2009). However, the ability of CCR10(+) antigen-specific B cells to efficiently migrate to the gut and vagina has not yet been demonstrated *in vivo*. Anyway, promotion of T_{FH} cells should be a must-have when aiming at promoting B cell affinity maturation and class switching.

Our team has previously shown that intradermal (ID) immunization with HIV antigen-coated nanoparticles is more potent in generating antigen-specific IgAs in the vaginal mucosa and mucosal secretions than other conventional routes such as intramuscular and subcutaneous (Liard et al, vaccine, 2011). Moreover, intradermal immunization promoted T_{FH} cell polarization and isotype class switching of B cell in skin draining lymph nodes following ID immunization. We have shown that cells from the skin, and particularly Langerhans cells where involved in this process.

My work will focus on the mechanisms that are responsible for generation of antigen-specific IgA antibody-secreting B cells and their migration and homing to the gut and vaginal mucosa following intradermal vaccination. The idea of a common mucosal immunological system was first introduced by John Bienenstock nearly 40 years ago,

but has gained much attention recently (Gill et al., 2010). Indeed, the previous concept that DCs could imprint T and B cells to migrate to the tissue in which they were originally activated has been challenged. Evidences suggest that in fact DCs could mediate an immune cross-talk between mucosal compartments by inducing expression of homing receptors on primed B and T cells (Chang et al., 2008; Ruane et al., 2013). Thus, by focusing on skin dendritic cells such as Langherans cells and CD207+ dermal dendritic cells we aim at to deciphering the cellular and molecular events that can shape the immune reponse toward a class-switched and homing receptor-bearing B cells following intradermal vaccination in mice.

Antibodies from ImmunoTools would be very usefull for routine flow cytometry surface staining of B and T cells. Moreover, recombinant mouse cytokines and chemokines could be used for future *in vitro* T and B cell coculture assays.

ImmunoTools *special* AWARD for **Clément Levin** includes 20 reagents

FITC - conjugated anti-human CD33,

PE - conjugated anti-human CD56, control-IgG1, control-IgG2a, control-IgG2b,

APC -conjugated anti-human CD56, CD69, control-IgG1, control-IgG2a, control-IgG2b,

FITC - conjugated anti-mouse isotype control-IgG2b,

PE - conjugated anti-mouse CD4, control-IgG2b,

APC -conjugated anti-mouse CD19, control-IgG2b,

recombinant mouse cytokines rm IFNgamma, rm IL-16, rm IL-21, rm MCP1/CCL2, rm MIP3a/CCL20

DETAILS