

PROPOSITION DE STAGE DE MASTER (M2) Année universitaire 2021-2022

Equipe d'accueil : Dendritic cells and B cells in their microenvironment during viral infections and cancer

Intitulé de l'unité : Université de Paris, INSERM U1016, CNRS UMR8104

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Titre du sujet de recherche : *In situ* delivery of Interleukin-7 to adjuvant pulmonary vaccines

Résumé du projet

Despite tremendous work on vaccine development over the last decades, mucosal immune responses remain difficult to trigger and we still need to propose new vaccine strategies to specifically target mucosal immunity. The main objective of the project is to investigate the capacity of IL-7 to enhance mucosal immune responses to locally administered viral antigens. Indeed, we demonstrated that this cytokine is produced in infected mucosae (Ponte et al. 2017) and is able to trigger local expression of chemokines when administered either locally (Logerot 2021) or systemically (Beq 2009), leading to massive immune cell homing into targeted mucosae. We thus hypothesize that locally delivered IL-7 can act as an efficient adjuvant to trigger mucosal immune responses to vaccines.

This project aims to explore how locally administered IL-7 predisposes mucosae to elicit efficient and long-lasting specific T and B mucosal immune responses against locally delivered antigens. We will focus on pulmonary mucosae, a major portal of entry for pathogens. Indeed we already showed that mice intratracheally administrated with IL-7 before delivery of a model antigen (Diphtheria Toxoid –DT) by the same route triggers a stronger and a more prolonged specific mucosal immune response than mice administered with antigen alone. Moreover this procedure together with the administration of inactivated Influenza virus (IAV) protects mice against IAV pathology. We now want to understand at a cellular level the mechanism by which IL-7 acts on pulmonary parenchyma to trigger immune cell recruitment early after deposition.

This model will allow to better understand the mechanisms of the adjuvant property of IL-7 in the pulmonary mucosae and to better characterize the IL-7 triggered mucosal immune response able to protect against a virus infection.

Aims for the Master 2 :

1. Characterize pulmonary parenchymal cells producing chemokines in response to IL-7 (combining immunochemistry to RNAscope in situ hybridization on pulmonary tissue of mice sacrificed at early time points post-IL7 administration).
2. Better characterize T, B and other cell type that are organized in lymphoid aggregates as early as on day 2 post IL-7 within the pulmonary parenchyma (Immunocytochemistry and FACS analysis).

This work will establish the prerequisites of the use of IL-7 in pulmonary vaccine and will allow to go further in the macaque model, next step necessary to validate a mucosal vaccine against IAV or SARS-CoV2.

Dernières Publications en lien avec le projet :

1. Logerot S, Figueiredo-Morgado S, Charmeteau-de-Muylder B, Sandouk A, Drillet-Dangeard A-S, Bomsel M, Bourgault-Villada I, Couedel-Courteille A, Cheynier R, Rancez M. IL-7-adjuvanted vaginal vaccine elicits strong mucosal immune responses in non-human primates. **Front Immunol.** 2021 doi:10.3389/fimmu.2021.614115
2. Ponte R, Rancez M, Figueiredo-Morgado S, Dutrieux J, Fabre-Mersseman V, Charmeteau-de-Muylder B, Guilbert T, Routy JP, Cheynier R, Couedel-Courteille A. Acute Simian Immunodeficiency Virus Infection Triggers Early and Transient Interleukin-7 Production in the Gut, Leading to Enhanced Local Chemokine Expression and Intestinal Immune Cell Homing. **Front Immunol.** 2017. doi:10.3389/fimmu.2017.00588.
3. Rancez M, Couedel-Courteille A, Cheynier R. Chemokines at mucosal barriers and their impact on HIV infection. **Cytokine Growth Factor Rev.** 2012 Jun 22.
4. Beq S., Rozlan S., Gautier D., Parker R., Mersseman V., Schilte C., Assouline B., Rancé I., Lavedan P., Morre M. and Cheynier R. Injection of Glycosylated Recombinant Simian IL-7 Provokes Rapid and Massive T-cell Homing in Rhesus Macaques. **Blood** 2009, 114 :816-825.

Website : www.institutcochin.fr/la-recherche/3i/equipe-hosmalin/il7-comme-adjuvant

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