Institut Pasteur de Lille - Lung Infection and Innate Immunity

Présentation de l'unité

Nom de l'unité :	
Nom de l'équipe (des équipes)	Lung Infection and Innate Immunity -Team 8
Nom du responsable de l'unité :	Dr François Trottein
Organisme(s) de rattachement :	INSERM U1019- CNRS UMR8204 - Institut Pasteur de Lille - Université Lille-Nord de France
Adresse :	1, rue Calmette - BP245 - Institut Pasteur -59019 - Lille Cedex
Mail :	Philippe.gosset pasteur-lille.fr
Tél. :	0320877965
Domaine scientifique :	Innate immunity, inflammation , respiratory infection
Nombre de scientifiques (par catégorie)	4 PH (0.1 ETP); 1 MCU (0.5 ETP); 4 CR, 2 DR ; 2 IE,1 TL3 (0.5 ETP), 1 TS (0.8 ETP), 1 TR4, 3 post docs, 7 doctorants.
Mots – clés (5 max)	Innate immunity, inflammation , respiratory infection , COPD, vaccine

L'Unité en bref (historique, objectifs... – 10 lignes max) :

We will investigate the role of **innate immune** cells in **host defences** and pulmonary **pathogenesis** during experimental **influenza A** virus and ***Streptococcus pneumoniae*** infection, which are both of clinical importance. We will particularly focus on Th17 cytokine-producing innate immune cells, including NKT cells, γδ T cells and ILCs. We will define the modes of action of IL-17 and IL-22 (mainly on the barrier functions) and identify novel effectors important in host defences and/or regulation of pathogenesis.
We will determine immune mechanisms of **increased susceptibility to respiratory bacterial infections** during acute (influenza) and chronic (COPD) pulmonary inflammation. We will test the hypothesis that the dysregulated Th17-type cytokines and IL-10 production impacts on dysbiosis and immune cell homeostasis, thus leading to bacterial infection and disease progression.
The third topic concerns the development of new interventional strategies to trigger **optimal mucosal immunity** and/or to attenuate **lung damage** during respiratory infections and COPD.

Axes de recherche de l'unité :

We have developed three main topics in our team:
1) Our objective is to investigate the role of innate immune cells in host defenses and pulmonary pathogenesis during respiratory infections. Two clinically relevant pathogens are studied: Influenza A virus and *Streptococcus pneumonia*e.
2) We also aim at determining immune mechanisms of increased susceptibility to respiratory bacterial infections during acute (viral infection) and chronic pulmonary inflammation (theme 2). For the latter, chronic obstructive pulmonary disease (COPD, the third cause of death in 2020) is being studied.
3) *In fine*, we seek to develop new strategies to trigger optimal mucosal immunity and/or to attenuate lung damage caused by respiratory pathogens (theme 3). For this, we want to identify new adjuvants aiming to prime innate immune response to lung infections.

Principaux projets en cours (5 max) :

Thèmes et objectifs scientifiques associés :

1. Our studies seek to understand the mode of activation and the role of innate immune cells in these processes with a major focus on non-conventional T lymphocytes and innate lymphoid cells (ILCs). Invariant Natural Killer T cells (NKT cells) recognize, through their TCR, lipid Ags presented by APCs, including dendritic cells (DCs).
2. We want to define the modes of action of IL-17 and IL-22 (mainly on the barrier functions) and identify

novel effectors important in host defences.
3. Identification of the factors responsible for the susceptibility to respiratory bacterial infections after flu disease.
4. Identification of the factors responsible for the susceptibility to respiratory bacterial infections during COPD and impact of these infections on the progression of the disease.
5. Modes of action and optimization of two different immuno-stimulatory molecules, namely flagellin (WO2009/156405; WO2011/161491) and α-GalCer.

Opérations et/ou projets liés à chaque axe (éventuellement préciser le responsable et les participants) :

1. Evaluation of the role of innate lymphocytes during respiratory infections (Dr F trottein, Dr JC Sirard)
2. To measure the role of IL-17, IL-22 and associated cytokines in the defense mechanisms against respiratory pathogens and in diseases (Dr F trottein, Dr JC Sirard, Dr P. Gosset)
3. To define the role of IL-10 and IL-17-type cytokines in the superinfection due to infection by influenza type A virus (Dr F. Trottein)
4. Identification of the factors responsible for the susceptibility to respiratory bacterial infections during COPD and impact of these infections on the progression of the disease (Dr P. Gosset).
5. Modes of action and optimization of two different immuno-stimulatory molecules, namely flagellin (WO2009/156405; WO2011/161491) and α-GalCer. Impact of vaccination during super-infection associated to flu and to COPD (Dr F trottein, Dr JC Sirard, Dr P. Gosset)

Liste de publications représentatives des activités de recherche sur les 5 dernières années (max. 4) **:**

Pichavant M, Rémy G, Bekaert S, Le Rouzic O, Kervoaze G, Vilain E, Just N, Tillie-Leblond I, Trottein F, Cataldo D, Gosset P. Oxidative stress-mediated iNKT-cell activation is involved in COPD pathogenesis. Mucosal Immunol. 2013 Oct 30.

Van Maele L, Fougeron D, Janot L, Didierlaurent A, Cayet D, Tabareau J, Rumbo M, Corvo-Chamaillard S, Boulenouar S, Jeffs S, Vande Walle L, Lamkanfi M, Lemoine Y, Erard F, Hot D, Hussell T, Ryffel B, Benecke AG, Sirard JC. Airway structural cells regulate TLR5-mediated mucosal adjuvant activity. Mucosal Immunol. 2013 Sep 25.

Renneson J, Guabiraba R, Ivanov S, Fontaine J, Paget C, Quesniaux V, Faveeuw C, Ryffel B, Teixeira M, Trottein F. 2011. A detrimental role for iNKT cells in the pathogenesis of dengue virus infection, *Am J Pathol.* 179,1872 (IF: 4.9).

Ivanov S, Fontaine J, Paget C, Macho Fernandez E, Van Maele L, Renneson J, Maillet I, Rial A, Leger H, Ryffel B, Frisch B, Chabalgoity JA, Sirard JC, Benecke A, Faveeuw C, Trottein F. 2012. Key role for respiratory CD103(+) DCs, IFN-γ and IL-17 in protection against *S. pneumoniae* infection in response to α-GalCer, *J Infect Dis*, 206,723 (IF: 6.4).

Ivanov S., Rennesson, J., Fontaine, J., Barthelemy, A., Paget, C., Macho Fernandez E., Blanc, F., De Trez, C., Van Maele, L., Si Tahar, M., Renauld, JC., Sirard, JC., Faveeuw, C and Trottein, F. 2013. IL-22 reduces lung inflammation during influenza A virus infection and protects against secondary bacterial infection. *J. Virol* 87:6911 (IF: 5.4).

Partenariats et réseaux :

Liste des partenariats actuels au sein de la Fondation Hippolia (concrétisés par des conventions et/ou publications en commun)

Investigation of the innate immunity in the lower respiratory tract in horses during training. Collaboration with Equine Sports Medicine, University of Liège, Boulevard de Colonster 20, Bâtiment B42, 4000 Liège.

Perspectives :

Projets liés à la santé équine que l'unité souhaiterait développer (moyennant identification du partenariat et du financement) (max. 4) **:**

Notre objectif est d'effectuer des recherches translationnelles (de la souris au cheval et de transférer cela à l'homme) sur la physiopathologie respiratoire en lien avec les modifications de l'immunité non-spécifique induites par l'environnement et l'effort permettant d'expliquer la susceptibilité aux affections respiratoires.