PROJECT 1

DoS: Dr. Alessandra Bragonzi

Title: The relevance of IL-17Rs-mediated host defence during chronic respiratory disease

Curriculum: Basic and Applied Immunology and Oncology

Link to OSR/UniSR personal page: N/A

**Project description (Number of characters, including spaces: 2.000 - 3.000):**

Chronic respiratory diseases are disorders targeting the lung and its structure. Some of the most common are chronic obstructive lung disease, asthma, occupational lung diseases and bronchiectasis (http://www.who.int/respiratory/en/). Recurrent or chronic infections by several opportunistic pathogens, including the gram-negative bacterium *Pseudomonas aeruginosa*, contribute to the severity and progression of chronic respiratory disease, such as chronic obstructive pulmonary disease or bronchiectasis (1,2). In this context, inflammatory processes, activated against pathogens, play a critical role in determining the graveness of the chronic respiratory diseases.

In the lung the IL-17-mediated host response is an emerging inflammatory determinant influencing pulmonary defence and immunopathology (1). With respect to immunity, IL-17 cytokines may modulate the outcomes of pathologic processes in particular during chronic lung disease. The IL-17 cytokine family represents a wide class of pleiotropic inflammatory molecules that are structurally related. Among factors involved in IL-17-mediated responses, IL-17receptor(R)A plays a pleiotropic role by interacting also with other IL-17 receptors (IL-17RC, IL-17RB, IL-17RE), thereby potentially activating pathways other than those triggered by IL-17A. Our previously publication demonstrated that the IL-17A/IL-17RA axis play a critical role in host defence and immunopathology during the development of chronic respiratory disease in mice (2). In particular these data highlighted the potential involvement of other IL-17 receptors (IL-17RC, IL-17RB, IL-17RE) during host response against *P. aeruginosa* infection. How and to which extent IL-17RA through the interaction with IL-17RC, IL-17RB or IL-17RE mediates host defence and immunopathology into the lung during chronic disease is still unknown.

Thus, the main objective of the project is to decipher, through a multidisciplinary approach, the dynamic expression and the specific relevance of IL-17Rs (IL-17RC, IL-17RB, IL-17RE) during the progression of chronic respiratory infection by *P. aeruginosa*. The novelty of our overall hypothesis guiding this proposal is that the IL-17Rs (IL-17RC, IL-17RB, IL-17RE) may modulate the double-edge sword activities of IL-17 in the lung by controlling host response during chronic respiratory disease. This project aims at defining in mice the dynamic expression of IL-17Rs (IL-17RC, IL-17RB, IL-17RE) and understanding how IL-17Rs modulate the balance between host defence and immunopathology during chronic airway infection by *P. aeruginosa*, as an experimental model of chronic respiratory disease (3). In conclusion, this research proposal will elucidate how IL-17 mediated response governs the balancing between host defence and immunopathology, and determines the graveness of the disease, with particular attention on illness mediated by the opportunistic pathogen *P. aeruginosa*. 
Skills to be acquired by the student:

- learning and generating scientific knowledge on immune response in the context of respiratory infection
- technical know-how on development of new transgenic mouse model
- methodological knowledge on immunological/molecular biology/microbiological techniques
- technical know-how on data analysis and how to work towards the result
- independence and initiative, critical thinking, problem solving

References (max. 3)


2) Lorè NI et al., 2016 “IL-17A impairs host tolerance during airway chronic infection by Pseudomonas aeruginosa.” Sci Rep. 2016 May 18;6:25937