

## **The role of phosphodiesterases in regulating the function of innate and adaptive immune cells in chronic respiratory diseases**

The human lung is continuously exposed to inhaled agents and pathogens from the external environment. The lung immune system has evolved to perceive and respond to these danger signals. The first barrier of the defense system is the respiratory epithelium, which responds rapidly to the different insults through the production of multiple mediators that promote the protection by directly killing microbes, activating resident immune cells in the tissue and recruiting leucocytes from the blood. Chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD), represent the third leading cause of death worldwide. These diseases result in multiple pathological processes involving cells of the innate and adaptive immune system. In the last few years, innate lymphoid cells (ILCs) and regulatory T cells (Treg) have received intense attention for their role in immune homeostasis. Several studies have shown that ILCs and Tregs actively participate in the development and progression of several chronic diseases including asthma and COPD. In fact, it was recently reported that ILC are increased in blood and sputum of patients with severe asthma in term of frequency and activity and have been correlated to drug resistance. Conversely, the frequency and function of Treg appear to be impaired in patients with asthma. Several mediators (such as hormones, vitamins, and cytokines), are able to control both the innate and adaptive immune responses. Among these, phosphodiesterases (PDEs), the enzymes responsible for cAMP hydrolysis, have been identified as key mediators in controlling immune cell functions. However, nothing is known the expression of PDE enzyme isoforms in ILCs and Tregs and their contribution in ILC and Treg regulation and function. Thus, the aim of this project is to decipher the role of PDE in ILC and Treg biology in the context of chronic respiratory diseases, in order to identify potential new therapeutic approaches for patients.