LABEX IGO – 2024 INTERNAL CALL FOR PROJECTS FOR YOUNG INVESTIGATORS

Comparing Natural Killer Cell Profile in Inflamed Salivary Glands of Systemic Sclerosis and Sjögren's Disease Patients

Marie FRUTOSO, LBAI – UMR1227

Sjögren's Disease (SjD) and Systemic scleroderma (SSc) are rare autoimmune diseases that currently have no curative treatment. Both diseases are distinct in terms of main target organs and prognosis. However, patients suffering from SjD or SSc display common sicca syndrome1 (*fai2r*). The term sicca syndrome describes severe dryness of the eyes and mouth, which can be highly debilitating and profoundly alters the quality of life. While, the salivary gland dryness in SSc remains poorly understood, due to a complete lack of knowledge regarding its pathophysiology, in SjD, salivary gland involvement is mainly explained by an intense lymphocytic infiltration. Whether the pathological processes leading to sicca syndrome in SjD and SSc are similar or different is currently unknown. Natural Killer (NK) cells, positioned at interface between the innate and adaptive immune systems, could be pivotal players in these processes. Renowned for their cytotoxicity and rapid response to pathogens, NK cells are also located in tissues under both physiological and pathological conditions where they exhibit diverse functions. In particular, they can induce inflammation, through the activation or recruitment of specific immune cell types, or, on the contrary, dampen inflammation, through the regulation of adaptive immune cells. The presence of NK cells in salivary glands has been associated with the severity of SjD, highlighting their potent pathogenic role. However, so far, no studies have evaluated the precise phenotype of these infiltrating NK cells nor their potential role in the exacerbation of the inflammation in the salivary glands. Importantly, NK cell activation relies upon inflammatory cytokines such as type I IFN which are key elements in the pathophysiology of both SSc and SjD, with an IFN signature found in the blood as well as in the target organs. This common signature highlights a very likely involvement of NK cells in both diseases. On the basis of these observations, I hypothesized that NK cells play a major pathophysiological role in salivary gland involvement in systemic SSc and SjD. The goal of this project is to obtain NK cell profile in SSc using state-of-the-art phenotypic and transcriptomics technologies with spatial resolution, for further comparison with NK cell profile in SjD tissues. This exploratory study will establish for the first time the immunological, glandular and vascular landscape of salivary glands in SSc with particular emphasis on the NK cell profile. A precise delineation of NK cell engagement in the salivary glands of SjD and SSc patients holds promise for groundbreaking medical insights, and the development of new therapeutic targets in both diseases.