# The association between the repair of oxidative DNA lesions and Th17/Treg cell homeostasis in Patients with Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune disease that affects the joints and surrounding tissues. The etiology of RA is complex and still needs to be clarified. In RA patients, impaired functioning of regulatory T cells (Tregs) is observed, with a concurrent shift towards an immune response driven by Th17 cells. A key element in RA pathogenesis, that link the inflammatory process with regulatory immune disturbances, is DNA damage in cells caused by oxidative stress. This condition is associated with elevated levels of reactive oxygen species in RA patients compared to healthy individuals. Increased oxidative stress combined with impaired DNA damage response (DDR) can contribute to a worse disease course. Ineffective DNA damage detection and repair mechanisms in PBMCs RA are linked to premature aging of these cells and the accumulation of DNA damage, increasing susceptibility to mutations and epigenetic modifications.

**In this project, we will focus on investigating the efficiency of the Base Excision Repair (BER) pathway in Th17 and Treg lymphocytes in RA patients.**

The project objectives will be achieved through:

- assessment of the sensitivity of Th17 and Treg lymphocytes in RA individuals to a DNA-damaging agent (TBH)
- assessment of the efficiency of the DNA damage repair process via base excision repair in Th17 and Treg lymphocytes in RA individuals
- assessment of DNA damage level in Th17 and Treg cells in RA patients
- evaluation of aging markers in Th17 and Treg lymphocytes in RA patients
- assessment of BER gene expression changes in Th17 and Treg lymphocytes from individuals with RA
- evaluation of oxidative markers in Th17 and Treg lymphocytes in RA patients (8-oxoG, ROS)
- assessment of global DNA methylation levels (5-mC; 5-hmC)

We believe that such an approach will enable the achievement of both scientific and medical objectives. The proposed research has potential clinical implications. Enhancing the antioxidant capacity of individuals with reduced DNA repair efficiency could mitigate the effects of oxidative stress at the DNA level. This can be achieved through a diet rich in antioxidants and physical activity. The result of this work, leading to better understanding of the molecular basis of the disease, may contribute to the early diagnosis of clinical forms of RA and the implementation of more effective therapeutic strategies.