

Graves' disease is classified as an organ-specific autoimmune disorder associated with abnormal function of the thyroid, is the most common cause of hyperthyroidism (20-50/100 000 people). Major symptoms of that disease are weight loss, palpitation, tremor, anxiety, hyperactivity, and eye symptoms such as swelling, pain, redness, and/or double vision. Graves' orbitopathy (GO), a complication of Graves' disease, is recognized in 40-60 % of patients with that autoimmune disorder. It is predominantly associated with eye symptoms including orbital inflammation, ocular tissue expansion, remodeling, and even fibrosis of periorbital tissue. In the worst case, it can lead to dysfunction and vision impairment. Orbital tissue enlargement is mainly caused by an increased number of fibroblasts and adipose tissue volume.

Despite the established etiology of the phenomenon described, their exact pathomechanism is still unknown. Based on the current knowledge, GO onset was found to be associated with various factors including immunological, genetic, and environmental causes. In orbitopathy, we can distinguish two clinical stages of the disease: active and inactive, which are classified based on Clinical Activity Score (CAS) describing symptoms, signs, and changes within the orbital and periorbital tissue. The active phase is the initial and more severe stage which is characteristic by inflammation, tissue expansion, and orbital congestion. Over time, we can observe the transition from active to inactive (stable) phase via reducing inflammatory reactions and infiltration. Current therapies of orbitopathy are focused on symptomatic treatment strategies such as steroidal drugs and orbital decompression surgery but unfortunately, they have limited efficiency. Steroid application is one of the first-line therapeutic approaches for those patients aimed at reducing orbital tissue inflammatory infiltration and also preventing its enlargement. Unfortunately, prolong using high doses of steroids might cause many adverse complications and do not solve the cause of the orbitopathy. Moreover, chronic systemic therapy using steroids can be associated with a higher risk of serious side effects.

Following the complexity of immune processes in ongoing inflammation in Graves' orbitopathy and the lack of complete knowledge about pathogenesis, it is reasonable to supplement this information by thoroughly understanding the cellular interactions associated with these two different stages of the disease, especially in the context of the initial role of fibroblasts. An additional important aspect of this project is a detailed analysis of the mechanisms of tissue remodeling which is one of the main causes of ocular symptoms that can even lead to vision damage.

The aim of this project is an assessment of changes in immune, protein and molecular profile of orbital fibroblasts collected from active and inactive Graves' orbitopathy patients. That investigation will provide for the first detailed evaluation of the phenomenon associated with tissue remodeling and fibrotic processes in the course of Graves' orbitopathy.

The implementation of this project will provide extensive analysis of omics profiles within different orbital fibroblasts. Moreover, performed project allows us to establish the exact role of fibroblasts in the cellular interactions leading to remodeling processes in orbitopathy. Analysis of the described project will allow for a detailed description of phenomena occurring in the periorbital area and provide new insight into systemic response to the inflammatory process in Graves' orbitopathy. Furthermore, implementation of that project contributes to development of novel prognostic biomarkers and targets for the innovative therapeutic approach of the Graves' orbitopathy.