
Mario Salvi¹

PATHOGENESIS OF GRAVES' ORBITOPATHY

Graves' ophthalmopathy (GO) is the most common extrathyroidal manifestation of Graves' disease (GD) and is characterized by inflammation of the orbital tissue, namely the eye muscle and orbital connective tissue, and tissue remodeling due to a skewed production of pre-adipocytic fibroblasts and increased adipogenesis. Immunological cross-reactivity between antigens expressed in the thyroid and the orbit is the putative mechanism of GO pathogenesis, of which co-expression of the TSH receptor (TSH-R) and the IGF-1 receptor (IGF1-R) on orbital fibroblasts has been shown to play a pivotal role. The main players involved in the process of the inflammatory phase of GO, also called "active phase", in which disease progresses to cause increasing orbital involvement with deterioration of visual function and of the patient's quality of life, are three: 1) the antigens expressed on the target organ of inflammation, namely the TSH-R and the IGF-1R receptor on the fibroblasts; 2) the cytokines and other humoral factors involved in the various stages of disease progression; and 3) the immune effector cells, B and T cells. All these antigens can now be targeted by novel immunomodulating agents which may be used with the purpose of modifying the natural course of disease and not just to control inflammation.

¹ Mario Salvi, Graves' Orbitopathy Center, Endocrinology, Fondazione Cà Granda IRCCS, University of Milan, Milan, Italy.