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Thyroid Autoimmune Diseases and Graves' Ophthalmopathy: New therapeutics

The C-X-C chemokine receptor (CXCR)3 and its IFN-γ dependent chemokines (CXCL9, CXCL10, CXCL11) play an important role in the pathogenesis of autoimmune thyroiditis (AT), Graves' disease (GD) and Graves' Ophthalmopathy (GO). Thyrocytes, orbital fibroblasts and preadipocytes, under the influence of interferon (IFN)γ, secrete the aforementioned chemokines. Th1 lymphocytes recruitment in tissue increases IFNγ production, enhancing the IFNγ-inducible chemokine tissue secretion, and leading to the beginning and perpetuation of the autoimmune process. High levels of circulating IFNγ-inducible chemokines have been reported in patients with AT (especially in the presence of hypothyroidism), and in GD and GO patients particularly in the active phase. Peroxisome proliferator-activated receptor (PPAR)γ or -α agonists have a modulatory role on CXCR3 chemokines in AT, GD and GO. An immuno-modulatory effect on CXCR3 chemokines in GD is exerted by methimazole and corticosteroids, too. Further studies investigate the use of new molecules acting as antagonists of CXCR3, or blocking CXCL10, in HT, GD and GO. Recently novel agents targeting various agents involved in the pathogenesis of GO have been proposed as an alternative to corticosteroids. A randomized trial with Rituximab suggests good efficacy with a relative well tolerated profile in patients with active GO. Anyway, discordant results have been reported. Hoping results in GO have been given by small antagonists of thyroid stimulating hormone receptor molecules (interacting with the receptor on thyrocytes and fibroblasts), the anti-IGF-1 receptor antibody teprotumumab, and tocilizumab (an anti-soluble interleukin-6 receptor). Randomized and controlled studies are needed to generalize these intriguing results.

Biography

Alessandro Antonelli (Associate Professor, MD) has completed his degree in Medicine, *cum laude*, in 1982, Specialization in Endocrinology in 1985, Specialization in Occupational Health in 1987, and Specialization in Oncology in 1992, at the University of Pisa, Pisa, Italy. He is now working as Associate Professor in the Department of Clinical and Experimental Medicine at the University of Pisa. His researches have been published in more than 280 articles on International journals (Impact Factor > 920, H-I=54). He serves as an Editorial Board Member and is Referee and Reviewer of many scientific international journals.

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