Abrogation of self-tolerance by misfolded self-antigens complexed with MHC class II molecules

Keywords: autoimmune diseases, autoantibody, Graves' disease, MHC

Graves' disease is an autoimmune disease in which autoantibodies against thyroid-stimulating hormone receptors (TSHRs) are produced. The research group of Hui Jin and Hisashi Arase (IFReC/RIMD, Osaka University) found that autoantibodies in patients with Graves' disease preferentially recognize TSHRs complexed with MHC class II molecules of Graves' disease risk alleles. This suggests that the aberrant TSHR transported by MHC class II molecules is the target of the autoantibodies produced in Graves' disease.

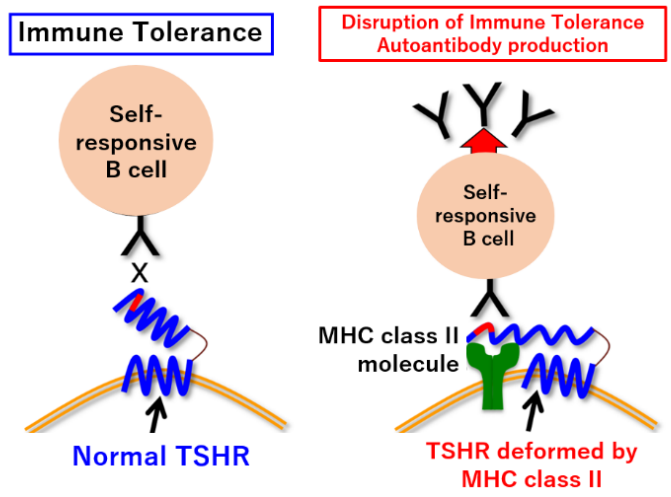

Figure: Autoimmune tolerance is maintained against normal TSHRs. However, if MHC class II molecules are abnormally expressed, TSHRs are deformed and their antigenicity changes. As a result, autoimmune tolerance is disrupted and thyroid-stimulating autoantibodies are produced.

Currently, the treatment of autoimmune diseases is limited to symptomatic treatment, which requires long-term medication. However, this study is expected to lead to the development of new therapeutic and preventive drugs that target the causes of autoimmune diseases.

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