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The human anti-thyroid peroxidase autoantibody repertoire in Graves' and Hashimoto's autoimmune thyroid diseases.

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Abstract

Human anti-thyroid peroxidase (TPO) autoantibodies (aAb) are generated during autoimmune thyroid diseases (AITD). Within recent years, increasing knowledge of the TPO-specific aAb repertoire, gained mainly by the use of combinatorial library methodology, has led to the cloning and sequencing of around 180 human anti-TPO aAb. Analysis of the immunoglobulin (Ig) variable (V) genes encoding the TPO aAb in the ImMunoGeneTics database (IMGT) (http://imgt.cines.fr) reveals major features of the TPO-directed aAb repertoire during AITD. Heavy chain VH domains of TPO-specific aAb from Graves' disease patients preferentially use D proximal IGHV1 genes, whereas those from Hashimoto's thyroiditis are characterized more frequently by IGHV3 genes, mainly located in the middle of the IGH locus. A large proportion of the anti-TPO heavy chain VH domains is obtained following a VDJ recombination process that uses inverted D genes. J distal IGKV1 and IGLV1 genes are predominantly used in TPO aAb. In contrast to the numerous somatic hypermutations in the TPO-specific heavy chains, there is only limited amino acid replacement in most of the TPO-specific light chains, particularly in those encoded by J proximal IGLV or IGKV genes, suggesting that a defect in receptor editing can occur during aAb generation in AITD. Among the predominant IGHV1 or IGKV1 TPO aAb, conserved somatic mutations are the hallmark of the TPO aAb repertoire. The aim of this review is to provide new insights into aAb generation against TPO, a major autoantigen involved in AITD.

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