Anti-topoisomerase antibodies (ATA) are autoantibodies directed against topoisomerase and found in several diseases, most importantly scleroderma. Diseases with ATA are autoimmune disease because they react with self-proteins. They are also referred to as anti-DNA topoisomerase I antibody (anti-topo I).

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### Epitopes and subtypes

Anti Scl-70 antibodies (also called anti-topoisomerase I after the type I topoisomerase target\(^\text{[1]}\)) is a type of anti-nuclear autoantibody seen mainly in diffuse systemic scleroderma, but is also seen the more limited form of systemic scleroderma called CREST syndrome.\(^\text{[2]}\) However, CREST syndrome is more closely associated with Anti-centromere antibodies.\(^\text{[3]}\) Scl-70 antibodies are associated with more severe scleroderma disease.\(^\text{[4]}\)

Anti-topoisomerase antibodies can be classified according to their immunoglobulin class (IgM, IgG or IgA). IgG-ATA is found most frequently in scleroderma, with IgA being quite common but IgM very infrequent.\(^\text{[5]}\)

### Pathology

Topoisomerase I is an enzyme that relaxes the strain on DNA by nicking and ligating the DNA. ATA inhibits the activity of this enzyme.\(^\text{[6]}\) Since this activity occurs in the nucleus of the cell ATA is a form of anti-nuclear antibody. Scleroderma results from the overproduction of collagen in affected tissues, one study claims that there is an increased density of Topoisomerase I sites in the collagen genes, and that the antibodies may be altering transcription at these loci.\(^\text{[7]}\) ATA correlates with rapid progression of disease.\(^\text{[8]}\)

In systemic lupus erythematosus ATA are associated with nephritis.\(^\text{[9]}\)

Increases in ATA+ in scleroderma and SLE are associated with increases in serum CTLA4.\(^\text{[10]}\)[11]
Genetics

HLA-DR2 (DR15 and DR16) are associated with Scleroderma and systemic sclerosis. It has been found that patients with ATA that recognize the ET4 domain of topoisomerase were frequently HLA-DR2,[12] and in another population study it was found that DR-15 is associated with ATA in systemic sclerosis.[13] In addition to HLA-DR, the protein tyrosine phosphatase, non-receptor type 22 (lymphoid) (1p13.2 - PTPN22 (http://www.genenames.org/data/hgnc_data.php?match=PTPN22)), "CT/TT" genotype showed significant association with anti-topo I.[14] The TAP1 (http://www.genenames.org/data/hgnc_data.php?match=TAP1)gene(6p21.3, HLA complex) has also been found in association with ATA+ sclerosis.[15]

References


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