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An Update on Connective Tissue Disease Diagnosis

Connective Tissue Disease (CTD) is a heterogeneous group of diseases characterised by antinuclear antibodies (ANA), as well as other distinctive autoantibodies. Ampath is pleased to announce a simplified approach to the diagnosis of connective tissue disease, with updated antibody profiles and terminology.

UPDATED TERMINOLOGY

- **CTD (Connective Tissue Disease)**

  The CTD screen was previously referred to as the ENA (extractable nuclear antigen) screen.

  The CTD screen consists of RNP, Sm, SSA (Ro), SSB (La), Scl-70 (Topoisomerase I), Jo-1, Centromere-B, PM-Scl, Mi-2, Fibrillarin, PCNA, Ribosomal P-protein, dsDNA antibodies, RNA Pol III and Ro-52.

  If the CTD screen is positive, the following test options are available:

  CTD Profile 1: (includes seven markers, only six billed)
  RNP, Sm, SSA (Ro), SSB (La), Scl-70 (Topoisomerase I), Jo-1 and Centromere-B.

  CTD Profile 2: (includes five markers, five billed)
  PM-Scl, Mi-2, Fibrillarin, PCNA and Ribosomal P-protein.

  * Please note that dsDNA, RNA Pol III and Ro-52 are not included in the abovementioned profiles, but are included in the CTD screen. It is of the utmost importance that the dsDNA is requested separately, if indicated. RNA Pol III antibodies can be assessed on Ampath's systemic sclerosis profile (LIA), while Ro-52 antibodies are available on all the autoimmune profiles (see below).
  * Individual CTD antigens can be requested.

- **Double-stranded DNA**

  Although the antibody is part of the CTD screen, it does not form part of the CTD profiles and should be requested separately. A second SLE-specific dsDNA ELISA (dsDNA complexed with nucleosome) is available to confirm the positive dsDNA result. This test must be specifically requested.

- **Cytoplasmic Antibodies**

  If cytoplasmic antibodies are identified on the ANA screen, this will be reported with an option to do a cytoplasmic autoimmune profile.

TABLE 1: UPDATED AUTOIMMUNE PROFILES

Profile	Components
Cytoplasmic profile	AMA-M2, 3E (BPO), Ribosomal P-protein, Jo-1, SRP, PL-7, PL-12, EJ, OJ and Ro-52
Myositis profile (previously Myositis Western Blot)	Mi -2a (Mi -alpha protein); Mi -2β (Mi – 2 beta protein), TIF1Y, MDA 5, NXP 2, SAE 1, KU, PM-Scl 100, PM-Scl 75, Jo-1, SRP, PL -7, PL-12, EJ, OJ and Ro-52
Systemic sclerosis profile (previously Systemic Sclerosis Western Blot)	Scl-70 (Topoisomerase), Centromere A, Centromere B, RNA Pol III (RP 11), RNA Pol III (RP 155), Fibrillarin, NOR-90, Th/To, PM-Scl 100, PM-Scl 75, Ku, PDGFR and Ro-5
Autoimmune liver profile (previously Liver Western Blot)	AMA-M2, 3E (BPO), Sp 100, PML, Gp210, LKM1, LC1, SLA/LP and Ro-5
ENA profile (previously ENA Western Blot)	The ENA profile is more comprehensive than the CTD profiles 1 and 2, and includes 16 antigens: Sm/RNP, Sm, SSA (Ro), Ro-52, SSB (La), Scl-70 (Topoisomerase), PM-Scl, Jo-1, Centromere B, PCNA, dsDNA, Nucleosome, Histone, Ribosomal P-protein, AMA-M2 and DFS-7

STREPTAVIDIN

The streptavidin biotin system is incorporated into many immunological assays, which enhances the detection of antibodies. Ampath's primary test platform (CTD screen, CTD1, CTD2, PR3 and MPO) exploits this naturally occurring protein-ligand interaction. Occasionally, patients with streptavidin antibodies are identified, which can lead to false positive results. A commercial reagent to identify streptavidin antibodies is not available. This phenomenon can be resolved by requesting an ENA profile (line immunoassay). Please note, the abovementioned autoimmune profiles are streptavidin free.

IMPLEMENTATION

The aforementioned changes will be implemented with effect from 23 May 2022. In the interim, result commentary will guide the clinician on available options. An updated comprehensive autoimmune request form is available. Personalised request forms can be ordered and tests can be requested electronically from the area marketer.

IN CONCLUSION

Ampath aims to not only simplify the process of requesting diagnostic tests for CTD, but more importantly, to contain costs to the patient. A positive CTD screen will incur a CTD 1 profile, only for clients where additional testing is allowed. Further testing will be available on request. In this rapidly developing field, rare and new autoantibodies can be requested as a send-away test to international centres. Ampath remains committed to implement novel and relevant autoimmune testing.