Letters to the Editors

Comment on: Standardisation of the term "anti-Ro/SSA" in patients with Sjögren's disease and other disorders

Sirs,

I read with interest the letter by Dr Lee concerning the terminology of the SSA antigens and their autoantibodies. I fully agree with him regarding the unmet need to standardise and harmonise the terms for better clarity.

The reasons for that are:

1. The SSA 60KD and the SSA 52KD proteins are two distinct antigens as already shown by the original study discovering the SSA 52KD peptide (1). The 52KD peptide is part of the tripartite motif-containing protein 21 (TRIM21) family, whereas the SSA 60KD is from the family of ribonucleoproteins (RNPs) (2, 3).
2. There is no cross-reactivity between their autoantibodies although their antigens display similar intracellular distribution and immunofluorescent patterns (1). Moreover, both antibodies precipitate in the same line in the gel double diffusion method (Ouchterlony) suggesting that both peptides are present together.
3. These antibodies appear in many autoimmune diseases other than Sjögren's syndrome (SS) so it is not justified to call them anti-SSA antibodies which stands for SS antigen A (in addition to the other SS antigen B (SSB) (4).
4. The occurrence of the different autoantibodies (anti SSA 60KD and anti SSA 52KD antibodies) correlates with various phenotypes of different rheumatic diseases (4, 5). Therefore, it is fully justified to treat and name both antigens-antibodies systems separately.

However, when one intends to name a peptide or an antigen it is preferred to avoid using eponyms and to try to define the protein by its composition, chemical characteristics, or by its role and function if known. Therefore, naming these antibodies: anti-Ro-52 or anti-Ro-60 is wrong at least for two reasons:

- Ro stands for Robert, the first patient with SLE in whom the anti-Ro antibody was detected. We do not want to use an eponym since it does not contribute anything to our understanding of the antigen's significance, composition, or function.
- We are not sure at all whether or not the serum of Robert also contained the anti-52 KD antibodies, since it was detected by immunodiffusion, a method that could not segregate between both antigens. Moreover, at that time (1969) the 52KD antibodies have not yet been identified (6). It should be mentioned that only in 1982 it was shown that anti-Ro antibodies are identical to anti-SSA antibodies and at that time SSA antigen was considered as a single peptide with a molecular weight of 60KD.

Thus, at first glance, it is preferred to use the terminology anti-SSA-60 or anti SSA-52 over anti Ro52 or anti Ro 60. However, since these antibodies are present in many autoimmune diseases in addition to SS (such as SLE, scleroderma, or myositis), the name "anti-SSA" antibodies which stands for anti-Sjögren's Syndrome antigen A antibodies is also inaccurate.

This leads to a possible better suggestion which should include only the chemical composition of the antigens with their sizes: anti TRIM21(52KD) and anti RNP (60KD) antibodies. These names do not connect these antibodies specifically to SS and offer some details and clues about the structure and potential function of the antigens. The first is a peptide consisting of a tripartite motif-containing protein 21 [TRIM21]) that functions as an E3 ubiquitin ligase and cytosolic Fc receptor whereas the other is a ribonucleoprotein (4). Similar way of naming has been employed in the case of anti-DNA, anti-U1RNP and anti-centromere where the names of the antigens are meaningful.

E. Ben-Chetrit, *MD*
Rheumatology Unit, Department of Medicine, Hadassah-Hebrew University Medical Center, Jerusalem, Israel.

Please address correspondence to:
Eldad Ben-Chetrit
Rheumatology Unit,
Hadassah-Hebrew University Medical Center,
91120 Jerusalem, Israel.
E-mail: eldad@hadassah.org.il

Competing interests: none declared.

References

1. BEN-CHETRIT E, CHAN EKL, SULLIVAN KF, TAN EM: A 52-kD protein is a novel component of the SS-A/Ro antigenic particle. *J Exp Med* 1988; 167(5): 1560-71. https://doi.org/10.1084/jem.167.5.1560
2. BEN-CHETRIT E, GANDY BJ, TAN EM, SULLIVAN F: Isolation and characterization of cDNA clone encoding the 60-kD component of the human SS-A/Ro ribonucleoprotein autoantigen. *J Clin Invest* 1989; 83: 1284-92. https://doi.org/10.1172/jci114013
3. CHAN EKL, HAMEL JC, BUYON JP *et al*.: Molecular definition and sequence motifs of the 52 kDa component of human SSA/Ro autoantigen. *J Clin Invest* 1991; 87: 68-76. https://doi.org/10.1172/jci115003
4. CHAN EKL: Anti-Ro52 autoantibody is common in systemic autoimmune rheumatic diseases and correlating with worse outcome when associated with interstitial lung disease in systemic sclerosis and autoimmune myositis. *Clin Rev Allergy Immunol* 2022; 63(2): 178-93. https://doi.org/10.1007/s12016-021-08911-z
5. BEN-CHETRIT E, FOX RI, TAN EM: Dissociation of immune responses to the SS-A (Ro) 52-kd and 60-kd polypeptides in systemic lupus erythematosus and Sjögren's syndrome. *Arthritis Rheum* 1990; 33(3): 349-55. https://doi.org/10.1002/art.1780330307
6. CLARK G, REICHLIN M, TOMASI TB JR: Characterization of a soluble cytoplasmic antigen reactive with sera from patients with systemic lupus erythematosus. *J Immunol* 1969; 102(1): 117-22.