# Detection of myositis-specific antibodies: additional notes

With great interest, we read the letters that have commented on the recent European League Against Rheumatism/American College of Rheumatology classification criteria for idiopathic inflammatory myopathies[1] (IIMs) and ensuing discussions.[2 3] This highlights how harmonising myositis-specific antibodies (MSA) testing methodologies is currently a hot topic of debate among laboratory specialists, clinicians and manufacturers.

I would particularly like to share our own immunology laboratory experience by expanding on the letter entitled 'Detection of myositis-specific antibodies: additional notes' by M Mahler and M Fritzler[4] with which we wholly agree.

Newer technologies, such as line immunoassays (LIA) and dot blots (DB), which provide greater sensitivity and rapid serological diagnoses, have standardisation and specificity drawbacks, but the tight connection between autoantibodies and clinical phenotypes underline a great need for improving the test's accuracy. The UK NEQAS external quality assessment reports show clearly how these technologies are steadily increasing in the last years, compared with alternative methods. Though it may seem proficiency testing programmes have shown consistent inter-methods agreement results, the data results should be read carefully. Anti-Jo1 positive sera have been analysed very few times as this programme (UK NEQAS for antibodies to nuclear and related antigens) is not focused on anti-Jo1 detection but rather generalised to extractable nuclear antigen (ENA) specificities. Interestingly, there is a very new programme ('Pilot UK NEQAS for Myositis Associated Antibodies scheme') that will consider the anti-Jo1 antibodies in the ENA panel and the total MSA panel. Moreover, as sample selection was mostly limited to single donor serum from a patient with polymyositis, this provided a valid picture of diagnostic sensitivity rather than specificity.

In 2010, Ghirardello *et al* evaluated the accuracy of commercial LIAs limited to a restricted panel of MSAs showing good global agreement with in-house immunoprecipitation (IP) and immunoblot methods (sensitivity: 47% vs 51%; specificity 69% vs 77%).[5] On the other hand, recently, Cavazzana *et al* assessed the diagnostic accuracy of a new generation LIA by an enlarged panel including a wider spectrum of MSAs that thoroughly addressed the low specificity of LIA/DB methods compared with IP.[6]

Our own laboratory experience reflects how necessary the need to improve specificity performance is, mainly considering the advantages intrinsic to the method, that is, easy to use and inexpensive and its increasing widespread use even in non-specialised laboratories. The sizeable increase in MSA tests has also led to inappropriateness in the IIMs field, similarly to other antinuclear testing in connective tissue diseases (CTDs). As a consequence, a false positive for MSA detection may have a considerable clinical impact: patient anxiety, misdiagnoses, misguided therapies and an unnecessary cascade of insights. Furthermore, a suspected false positive for a cancer-associated MSA (ie, anti-TIF1Ɣ antibodies) may have ethical implications. The open question is: could an inappropriate request in these situations hide the predictive role of the MSAs? Only a strict patient follow-up and a better validation of the test will clarify this point, as there are few data on the predictive role of MSA in the literature.

Given the widespread new technologies and considering that today such a reliable test may allow us early diagnosis of aggressive diseases like those in the IIMs group, it is the manufacturers' and laboratory specialists' duty to strictly validate the LIA/DB tests, especially with regard to more critical antigens, such as anti-SRP and anti-NXP2. Similarly we would like to point out that all critical issues mentioned can be applied to other LIA/DB panels related to other diseases, like scleroderma or other CTDs. We thank the authors for opening the discussion and hope that harmonising the process will improve autoimmunology laboratory work globally.

**Maria Infantino,[1] Mariangela Manfredi,[1] Valentina Grossi,[1] Maurizio Benucci[2]**

[1]Laboratory of Immunology and Allergology, S. Giovanni di Dio Hospital, Florence, Italy
[2]Rheumatology Unit, S. Giovanni di Dio Hospital, Florence, Italy

**Correspondence to** Dr Maria Infantino, Laboratory of Immunology and Allergology, Ospedale San Giovanni di Dio, Florence 55100, Italy; maria2.infantino@uslcentro.toscana.it

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