Response to: 'ANA testing in "real life"' by Infantino *et al*

We thank Dr Infantino and colleagues for their comments[1] on our paper on assay variability in antinuclear antibody (ANA) testing by indirect immunofluorescence (IIF)[2] and subsequent communications that have been published in the journal.[3–7] We agree with their observations on assay variability as well as the potential role of computer-aided diagnosis in improving IIF determinations. The issue of titre is also important, although changing the threshold from 1:80 to 1:160, while reducing the frequency of false-positive results (ie, results from otherwise healthy subjects), will also likely decrease the frequency of positive results for patients with systemic lupus erythematosus (SLE), impacting on classification and diagnosis.

We think that the discussion of our paper has been important in highlighting the limitations of ANA testing in SLE, especially in the setting of clinical trials for 'active, autoantibody positive disease'. These limitations may also affect the utilisation of the newly proposed classification criteria for SLE; these criteria require a positive ANA by human epithelial type 2 cell IIF before a person can be further considered for classification.[8] In this regard, it is important to consider the experience of 'real life testing' by hospital or commercial laboratories as opposed to research studies in which experts make IIF determinations. Thus, while IIF testing has been considered the gold standard for ANA determinations, current approaches have notable variation that may relate to the performance characteristics of kits as well as the subjective nature of these determinations, especially with sera with low titre.

In view of the importance of ANA testing for both research and routine clinical care, we look forward to further dialogue on this subject as well as the development and validation of new analytic platforms for ANA determinations in SLE as well as related rheumatic diseases.

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REFERENCES

1 Infantino M, Manfredi M, Soda P. ANA testing in "real life". *Ann Rhem Dis* 2020;79:e3.
2 Pisetsky DS, Spencer DM, Lipsky PE, *et al*. Assay variation in the detection of antinuclear antibodies in the sera of patients with established SLE. *Ann Rheum Dis* 2018;77:911–3.
3 Mahler M. Lack of standardisation of ANA and implications for drug development and precision medicine. *Ann Rheum Dis* 2019;78:e33.
4 Meroni PL, Chan EK, Damoiseaux J, *et al*. Unending story of the indirect immunofluorescence assay on HEp-2 cells: old problems and new solutions? *Ann Rheum Dis* 2019;78:e46.
5 Pregnolato F, Borghi MO, Meroni PL, *et al*. Pitfalls of antinuclear antibody detection in systemic lupus erythematosus: the positive experience of a national multicentre study. *Ann Rheum Dis* 2019;78:e50.
6 Van Hoovels L, Schouwers S, Van den Bremt S, *et al*. Variation in antinuclear antibody detection by automated indirect immunofluorescence analysis. *Ann Rheum Dis* 2019;78:e48.
7 Willems P, De Langhe E, Westhovens R, *et al*. Antinuclear antibody as entry criterion for classification of systemic lupus erythematosus: pitfalls and opportunities. *Ann Rheum Dis* 2019;78:e76.
8 Tedeschi SK, Johnson SR, Boumpas D, *et al*. developing and refining new candidate criteria for systemic lupus erythematosus classification: an international collaboration. *Arthritis Care Res* 2018;70:571–81.