

Correspondence

Reply

To the Editor:

We read with interest the correspondence by van Straalen¹ about our article reporting an association between anti-*Saccharomyces cerevisiae* antibodies (ASCAs) and hidradenitis suppurativa (HS), mainly in its severe and inflammatory forms, in comparison with healthy controls and severe psoriasis vulgaris.²

In this comment, van Straalen raises the possible association between ASCAs and specific clinical phenotypes of HS, which is supported by published works in Crohn disease and spondylarthritis, showing that ASCAs are associated with specific diseases endotypes in these 2 inflammatory disorders.^{3,4} In our study, we did not stratify patients according to already published clinical subclassification, and incorporated instead some criteria such as involved anatomical areas, and the inflammatory burden reflected by Hurley stage, associated inflammatory diseases, and the C-reactive protein serum level. Although we agree these criteria are likely to lack discriminating power, we were able to show that the most inflammatory forms are preferentially associated with the presence of ASCAs, and at this stage we may claim that HS-related autoinflammatory syndromes are one of the endotypes associated with this biomarker. However, we agree with van Straalen that prospective studies stratifying patients with HS at the clinical level with more granularity is of major interest when considering disease heterogeneity.

Whether such biological heterogeneity is underlined by a specific genetic background is at the center of the other van Straalen's major comment. We are aware that a study in patients with Crohn disease unraveled some correlation between the presence of a specific variant of *NOD2* (3020insC) and the presence of ASCA, with an impact of allelic dosing on ASCA IgA titers.⁵ In line with van Straalen, we tend to believe that specific genotypes are likely to influence the likelihood to develop ASCA as a surrogate biomarker of gut dysbiosis. However, although we did not investigate the genetic status of *NOD2* in our patients with HS, we did sequence all exons from this gene by the Sanger method in patients with HS-related autoinflammatory syndromes, and could not detect a mutation in any of the analyzed patients, as reported in Gottlieb et al.⁶ This limited set of data is in line with previous publications showing no evidence for mutations of *NOD2* in patients with HS.⁷ That said, we agree that it remains possible that some genotypes of *NOD2* or other innate immune genes predisposing to CD may overlap between

inflammatory bowel diseases and HS subpopulations, influencing the diseases patterns through common dysbiotic features.

In conclusion and referring to van Straalen's last remark on the diagnostic value of ASCA across different ethnic backgrounds, we can just agree that this parameter will have to be part of future studies investigating clinical and biological phenotypes/genotypes/microbiome correlations in HS.

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