Response to: 'Microbiome in Sjögren's syndrome: here we are' by van der Meulen *et al*

We would like to thank van der Meulen *et al* for their interest in our review and their comments regarding the role of the microbiome in Sjogren's syndrome (SS).[1 2] As they correctly point out, SS was not mentioned in our review primarily because we, along with the editors, have decided to include the most studied rheumatic and autoimmune conditions as they pertain to microbiome research. We agree that SS is a common disorder with an intriguing and yet to be fully elucidated etiopathogenesis, and that the characterisation of the microbiome in this context is indeed worth pursuing. We also note that the disease entities mentioned in our review were meant as examples of the types of studies currently being performed in the field. The purpose of the review is to outline techniques and strategies that can move microbiome research beyond correlative study designs and into the realm of mechanistic approaches that may have significantly more relevance to clinical practice irrespective of the disease process.

Although van der Meulen, *et al* reference valuable studies in SS, we underscore the fact that many of them draw conclusions based on relatively small sample sizes, rely solely on 16S rRNA sequencing, which is limited in scope, and more importantly, are correlative in nature, which restrict their application to clinical practice.[3–11] As we state in our review, in order for microbiome research to further the understanding of autoimmune disease pathogenesis, stratify patients and lead to the application of personalised therapies, the field must adopt state-of-the-art methods,[12] aim to study mechanisms rather than correlations, and allow for data validation and data sharing.

We further agree with van der Meulen *et al* that microbiome studies should not be restricted to the gut and that interventional studies may be clinically impactful. In fact, both of these points were discussed in our manuscript (see sections on 'Navigating and addressing challenges in microbiome research' and 'What the future holds'). The authors' suggestion that more than one rheumatic disease should be studied at a time is interesting, but would need to be pursued cautiously as there is established heterogeneity within even a single rheumatic disease (eg, systemic lupus erythematosus[13] or psoriatic arthritis[14]). Exploring multiple diseases at a time would introduce additional variables, making it potentially difficult to interpret outcomes. We appreciate the extra dos and don'ts put forward by van der Meulen, *et al*. There are certainly other caveats to microbiome research not covered within the scope of our review, though we have set up a framework for what future studies should strive for in the context of this fluid discipline.

Julia Manasson , Rebecca B Blank, Jose U Scher

Division of Rheumatology, Department of Medicine, New York University Grossman School of Medicine, New York, New York, USA

Correspondence to Dr Jose U Scher, Medicine, New York University School of Medicine, New York, NY 10016, USA; jose.scher@nyumc.org

Handling editor Josef S Smolen

Contributors All authors listed have contributed this work and have provided final approval of the version to be published.

Funding NIH/NIAMS R01AR074500, National Psoriasis Foundation, The Colton Center for Autoimmunity, The Riley Family Foundation and The Snyder Family Foundation (Scher).

Competing interests UCB, Janssen and Novartis (Scher)

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Provenance and peer review Commissioned; internally peer reviewed.

To cite Manasson J, Blank RB, Scher JU. *Ann Rheum Dis* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/annrheumdis-2020-218327

Received 25 June 2020
Accepted 25 June 2020

Linked

► http://dx.doi.org/10.1136/annrheumdis-2020-218213

Ann Rheum Dis 2020;**0**:1. doi:10.1136/annrheumdis-2020-218327

ORCID iDs
Julia Manasson http://orcid.org/0000-0003-3448-5520
Jose U Scher http://orcid.org/0000-0002-1072-6994

REFERENCES

1 van der Meulen T, Vissink A, Bootsma H, *et al*. Microbiome in Sjögren's syndrome: here we are. *Ann Rheum Dis* 2020. doi:10.1136/annrheumdis-2020-218213.
2 Manasson J, Blank RB, Scher JU. The microbiome in rheumatology: where are we and where should we go? *Ann Rheum Dis* 2020;79:727–33.
3 van der Meulen TA, Harmsen HJM, Vila AV, *et al*. Shared gut, but distinct oral microbiota composition in primary Sjögren's syndrome and systemic lupus erythematosus. *J Autoimmun* 2019;97:77–87.
4 Mandl T, Marsal J, Olsson P, *et al*. Severe intestinal dysbiosis is prevalent in primary Sjögren's syndrome and is associated with systemic disease activity. *Arthritis Res Ther* 2017;19:237.
5 Moon J, Choi SH, Yoon CH, *et al*. Gut dysbiosis is prevailing in Sjögren's syndrome and is related to dry eye severity. *PLoS One* 2020;15:e0229029.
6 Mendez R, Watane A, Farhangi M, *et al*. Gut microbial dysbiosis in individuals with Sjögren's syndrome. *Microb Cell Fact* 2020;19:90.
7 Li M, Zou Y, Jiang Q, *et al*. A preliminary study of the oral microbiota in Chinese patients with Sjögren's syndrome. *Arch Oral Biol* 2016;70:143–8.
8 Siddiqui H, Chen T, Aliko A, *et al*. Microbiological and bioinformatics analysis of primary Sjogren's syndrome patients with normal salivation. *J Oral Microbiol* 2016;8:31119.
9 Rusthen S, Kristoffersen AK, Young A, *et al*. Dysbiotic salivary microbiota in dry mouth and primary Sjögren's syndrome patients. *PLoS One* 2019;14:e0218319.
10 Sembler-Møller ML, Belstrøm D, Locht H, *et al*. Next-Generation sequencing of whole saliva from patients with primary Sjögren's syndrome and non-Sjögren's sicca reveals comparable salivary microbiota. *J Oral Microbiol* 2019;11:1660566.
11 Sharma D, Sandhya P, Vellarikkal SK, *et al*. Saliva microbiome in primary Sjögren's syndrome reveals distinct set of disease-associated microbes. *Oral Dis* 2020;26:295–301.
12 Kim D, Hofstaedter CE, Zhao C, *et al*. Optimizing methods and dodging pitfalls in microbiome research. *Microbiome* 2017;5:52.
13 Kaul A, Gordon C, Crow MK, *et al*. Systemic lupus erythematosus. *Nat Rev Dis Primers* 2016;2:16039.
14 Scher JU, Ogdie A, Merola JF, *et al*. Preventing psoriatic arthritis: focusing on patients with psoriasis at increased risk of transition. *Nat Rev Rheumatol* 2019;15:153–66.