Response to: 'Synovial cellular and molecular signatures stratify clinical response to csDMARD therapy and predict radiographic progression in early rheumatoid arthritis patients' by Buch *et al*

We would like to thank Professor Buch and colleagues for their interest and thoughtful comments regarding our manuscript,[1] and we are grateful for the opportunity to provide further clarification on the clinical phenotype displayed by the rheumatoid arthritis (RA) patients with a pauci-immune pathotype analysed in our early arthritis cohort.[2] We have segregated this group into anti-citrullinated peptide antibodies (ACPA) +ve and -ve subsets and analysed age distribution, disease activity score (DAS28) components, ultrasound (US) scores, joint biopsied and modified Sharp van der Heijde score (SHSS) components, as indicated by Buch and colleagues to evaluate whether significant differences in clinical parameters could be identified (table 1).

In all parameters evaluated, we found no significant differences in clinical indices except for mean erosion score that, as expected, was significantly higher (S 0.812 vs 0, p=0.027) in ACPA +ve patients. Although the study did not capture specific radiological measurements of osteoarthritis (OA) through MRI or US the lack of difference in joint space narrowing between groups strongly suggests that OA was not a significant factor driving synovitis, although we acknowledge that a future prospective study integrating these parameters over time maybe of interest to further address this point.

This notion is also supported by the similar distribution in age between ACPA +ve and -ve groups. Although we agree that OA can manifest in the wrist joint, it more commonly presents in the knee, first metatarsal phalangeal or first carpometacarpal, none of which were biopsied in the pauci-immune cohort. Also, in the hand while distal interphalangeal (DIP) and proximal interphalangeal (PIP) joint involvement is frequent in OA, the involvement of the second and third metacarpal phalangeal (MCP) is rarer and more commonly associated with secondary OA such as in manual labour MCP arthropathy or in haemochromatosis or calcium pyrophosphate dihydrate crystal deposition disease, which present with typical radiological features absent in our patients.

Moreover, new onset synovitis of the wrist (which was found in 29/35 patients) would be an unusual presentation of OA and the comparable frequencies in wrist biopsy (which defines the joint presenting with most significant synovitis[3]) would again not support an underlying primary diagnosis of OA.

Finally, we would also like to highlight that, due to the strict application of the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for selection of the patients we analysed in our study, if the synovitis could be better explained by another disease, these patients were excluded from the study.

Nonetheless, we agree that long-term follow-up of these patients is critical to fully evaluate disease evolution, and in particular determine whether the pauci-immune subgroup does indeed represent postinflammatory change as postulated which may be hypothesised to associate with self-remitting RA; or in some cases it may represent disease in early evolution which could transform into a more inflammatory state over time. We look forward to presenting these data in due course.

Table 1 Demographics of pauci-immune group stratified by ACPA mean (SD) displayed unless otherwise indicated

	Pauci-immune fibroid ACPA -ve, n=17	Pauci-immune fibroid ACPA +ve, n=18	P value
Age (years)	53.6 (13.2)	48.4 (15.6)	0.35
Age by decade (n)			
20–30	0	3	
30–40	2	2	
40–50	6	6	
50–60	4	3	
60–70	3	2	
70–80	2	2	
DAS28-ESR	5.21 (1.60)	4.79 (1.50)	0.35
ESR	23.5 (24.1)	26.8 (26.1)	0.72
CRP	13.6 (40.7)	11.1 (37.8)	0.58
Tender	12.6 (8.38)	9.0 (7.98)	0.17
Swollen	6.35 (5.42)	4.83 (5.68)	0.27
VAS	62.4 (29.2)	56.1 (23.1)	0.33
US 12 max score			
ST	12.9 (7.66)	13.8 (8.87)	0.78
PD	2.64 (5.40)	3.92 (3.99)	0.49
US biopsy joint			
ST	1.79 (0.80)	1.94 (0.64)	0.55
PD	0.786 (1.12)	1.00 (0.91)	0.55
Biopsy joint, n (%)			
Wrist	15 (43)	14 (40)	0.66
MCP	2 (5.7)	4 (11)	
SHSS total	2.07 (3.89)	1.69 (4.05)	0.86
SHSS erosions	0 (0)	0.812 (1.80)	0.027
SHSS JSN	2.07 (3.89)	0.875 (2.33)	0.43

CRP, c-rective protein; ESR, erythrocyte sedimentation score; JSN, joint space narrowing; PD, power doppler; ST, synovial thickening; VAS, visual analogue score.

Frances Humby [1], **Myles Lewis** [2], **Michael J Townsend**,[3] **Costantino Pitzalis** [4]

[1]Centre for Experimental Medicine and Rheumatology, Barts and the London School of Medicine and Dentistry, London, UK
[2]William Harvey Research Institute, Queen Mary University of London - Charterhouse Square Campus, London, UK
[3]ITGR Biomarker Discovery Group, Genentech Inc, South San Francisco, California, USA
[4]Experimental Medicine and Rheumatology, William Harvey Research Institute, London, UK

Correspondence to Professor Costantino Pitzalis, Experimental Medicine and Rheumatology, William Harvey Research Institute, London EC1M 6BQ, UK; c.pitzalis@qmul.ac.uk

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ORCID iDs
Frances Humby http://orcid.org/0000-0003-1280-9133
Myles Lewis http://orcid.org/0000-0001-9365-5345
Costantino Pitzalis http://orcid.org/0000-0003-1326-5051

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