Response to: 'Gut-derived CD8+ tissue-resident memory T cells are expanded in the peripheral blood and synovia of SpA patients' by Guggino *et al*

We were pleased to receive the correspondence of Guggino *et al*[1] commenting on our recent publication.[2] Their studies confirm our findings of an expansion of cells with an expression profile consistent with tissue-resident memory cells (TRMs) in synovial fluid of spondyloarthritis (SpA). They have added the valuable insight that these cells are also expanded in gut tissues of patients with SpA.

The CD8+ T cell in question reported by Guggino and colleagues, and the InEx cells in our paper, may well be TRMs. But at present, the field is wrestling with nomenclature. First, resident memory cells, by definition, do not leave the tissues in which they reside.[3] This tissue retention is best characterised by the expression of CD69, which blocks S1PR activity, hence limiting TRMs egress from tissue to the blood where S1P levels are high.[4] Second, as Guggino *et al* point out, many of the CD8+ T cells present in the gut are closely associated with the epithelia. CD8+ T cells in the gut epithelia are the prototypic intestinal epithelial lymphocyte (IEL), hence labelling the cells under discussion exclusively as TRMs should also acknowledge a large body of research on IEL. For example, CD8+ IEL were recently found to be depleted in gut biopsies from patients with HLA-B27+ axial SpA.[5]

The interplay of gut and joint inflammation has been supported by the clinical overlap between SpA and inflammatory bowel disease (IBD)[6] and between gut infection and reactive arthritis[7] as well as shared genetic susceptibility between IBD and ankylosing spondylitis.[6] Cells that posses a gut-resident phenotype that are expanded in the SpA joint include TRM and mucosa-associated invariant T cells,[8] the latter contributing to the interleukin 17-mediated inflammation in axial spondyloarthritis. Therapeutic modulation of gut–joint trafficking holds the potential for novel treatment approaches to SpA.

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