Response to: 'IL-23 expression and activation of autophagy in synovium and PBMCs of HLA-B27 positive patients with ankylosing spondylitis' by Neerinckx *et al.*

We read with interest the study by Neerinckx *et al*[1] addressing the expression of interleukin (IL)-23p19 and of autophagy genes in the synovium and in the peripheral blood mononuclear cells of patients with ankylosing spondylitis (AS). Differently from our observation in the gut,[2] the authors failed to demonstrate any significant increase by RT-PCR in the expression of synovium autophagy-related genes (ATG16L1, IRGM, MAP1LC3A, ATG5, HSPA8 and HSP90AA1) together with no significant overexpression of IL-23p19 compared with disease and healthy controls.

We have previously demonstrated by immunohistochemistry that in the gut of AS, Paneth cells (PC), specialised epithelial cells located at the bottom of intestinal crypts, highly express IL-23p19.[3] Subsequent studies have demonstrated the role of the autophagy related ATG16L1 gene, a genetic risk factor for Crohn's disease, in causing PC dysfunction[4] and the important interconnection between PC and autophagy in determining the pathogenesis of murine Crohn's disease.[5] Starting from these findings, we studied the expression of autophagy in the gut of patients with AS. We demonstrated a significant upregulation of the genes involved in the autophagy pathway in the gut of patients with AS by RT-PCR and confirmed autophagy activation in infiltrating mononuclear cells and epithelial cells resembling PCs.[2] Interestingly, modulation of autophagy results in a significant modulation of the expression of IL-23p19 in isolated lamina propria mononuclear cells of patients and controls.[2 6] Autophagy has been demonstrated to play an important role in the innate immune response against intestinal bacteria and its expression seems to be potentially modulated by specific gut microbiota.[7–9] The presence of an active bacterial stimulation of the innate immune system in patients with AS is indirectly suggested by the activation of PC in producing their antimicrobial products (lysozyme, phospholipase A2 and defensin 5).[10] In this scenario, the activation of autophagy genes in the gut of patients with AS and its absence in the synovial samples and in the peripheral blood of patients with AS, is not surprising in our opinion.

Conversely, the absence of any significant increase of IL-23p19 expression in the synovial samples of patients with AS observed by Neerinckx *et al* appears to be surprising.[1] IL-23p19 has been, in fact, demonstrated by immunohistochemistry to be overexpressed in the inflamed tissues of patients with AS (gut and zygapophysial joints).[3 11] Since RT-PCR results need to be confirmed by protein demonstration, immunohistochemistry should also be performed in order to confirm this interesting observation. We, however, agree with Neerinckx *et al*[1] in thinking that IL-23p19 might play a tissue-specific role (in the gut and/or in the lymph node), specifically priming the subset of IL-23-responsive proinflammatory cells.

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