CCP levels. No patients had IgA anti-CCP detectable in both saliva and sputum samples.

Abstract OP0270 – Table 1

	Anti-CCP positive results (%)					
	Saliva IgA	Sputum IgA	Serum IgA	Saliva IgG	Sputum IgG	Serum IgG
HC	1/31 ⁽¹⁾	1/22 ⁽¹⁾	1/32 ⁽¹⁾	1/31 ⁽¹⁾	0/22 (0)	0/32 (0)
CCP+at-risk	8/55 ⁽¹³⁾	1/24 ⁽¹⁾	23/54 ⁽¹³⁾	23/54 ⁽¹³⁾	10/24 ⁽¹²⁾	50/54(93)
RA	10/40 ⁽¹⁵⁾	1/14 ⁽¹⁾	21/48 ⁽¹⁴⁾	23/42(55)	9/14(64)	47/48(98)

Conclusions: We found an increased prevalence of saliva but not sputum IgA anti-CCP antibodies in seropositive at-risk individuals. These findings support the concept that localised RA-related autoimmunity in at risk individuals can be site specific. IgA anti-CCP antibodies at the oral mucosa precede arthritis and may represent an important step in the initiation and propagation of disease.

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OP0271

GASTROINTESTINAL DAMAGE AND MICROBIAL TRANSLOCATION ARE INVOLVED IN THE DEVELOPMENT OF IMMUNE SYSTEM ACTIVATION IN INFLAMMATORY BOWEL DISEASE-ASSOCIATED SPONDYLOARTHRITIS

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Background: The altered composition of the gastrointestinal (GI) microbiota, known as dysbiosis, can induce and modulate the systemic inflammation, through microbial translocation and T-cell activation, in several immuno-mediated diseases, such as inflammatory bowel disease (IBD), HIV infection, and ankylosing spondylitis.

Objectives: In a cohort of 85 patients with inflammatory bowel disease-associated spondyloarthritis (SpA/IBD), we assessed gut bacterial infiltration and intestinal damage. In systemic circulation, GI epithelial damage, microbial translocation and immune system activation were assessed with intestinal-fatty acid binding protein (I-FABP), lipopolysaccharide (LPS), soluble CD14 (sCD14), respectively. Moreover, the *in vitro* activity of the latter two was evaluated on osteoblast cells.

Methods: I-FABP, LPS, sCD14, sclerostin (SOST) and anti-SOST antibodies (anti-SOST-IgG) were assayed with ELISAs. LPS and sCD14 were used *in vitro* to stimulate the MG63 human osteoblast-like cell line. Occludin, claudin-1, claudin-4, and the presence of bacteria were assessed, respectively, by real-time-PCR analysis and immunohistochemical staining of the ileum.

Results: Bacteria were detectable in the ileal epithelium of IBD patients, but only in SpA/IBD they were associated with epithelial damage and downregulation of occludin, claudin-1 and claudin-4 (figure 1A-B).

The serum levels of I-FABP, LPS and sCD14 resulted significantly higher in axial (187.9, 14.03, and 26.97, respectively) and peripheral SpA/IBD (130.3, 11.55, and 18, respectively) than in IBD patients (IFABP 43.65, $p<0.0001$ for both patients' groups; LPS 9.625, $p<0.0001$ vs Ax-SpA/IBD and $=0.007$ vs Per-SpA/IBD; sCD14 12.34, $p<0.0001$ for both patients' groups) (figure 1C).

In the SpA/IBD cohort, SOST was weakly correlated with I-FABP ($r=0.2683$), LPS ($r=0.3063$) and sCD14 ($r=0.3075$), and anti-SOST-IgG with LPS ($r=0.3959$) and sCD14 ($r=0.3414$). Moreover, sCD14 showed significant correlation with I-FABP ($r=0.3316$) and LPS ($r=0.5649$).

In vitro, LPS, but not sCD14, significantly induced SOST expression through the upregulation of both Wnt3a and Wnt5a and the downregulation of the b-catenin proteins (figure 1D). On the opposite, the combination of LPS and sCD14 downregulated SOST expression through the upregulation of ERK1/2 and b-catenin protein (figure 1D).

Abstract OP0271 – Figure 1 A. immunohistochemical staining of ileal bacteria. Ten ileal samples of patients affected by SpA/IBD or IBD were stained for bacteria infiltration (upper panel). Lower (from left to right): Gram and LPS staining of the same samples. B. Analysis of ileal tight-junctions proteins expression. From the left to the right: Ten ileal samples of patients affected by SpA/IBD or IBD were stained for occludin (and claudin-1 and -4, data not shown); count of occludin positive cells and quantitative real-time-PCR of occludin (and claudin-1 and -4, data not shown) expression in the same ileal samples. C. analysis of I-FABP, LPS and sCD14 serum levels in SpA/IBD and IBD patients. ELISAs assays were carried out in 45 patients with axial and 40 patients with peripheral SpA/IBD, and compared with IBD or HC. D. Western-blot analysis of MG-63 osteoblast-cells. The MG-63 osteoblast-like cell line was stimulated with LPS $\pm$ sCD14 *in vitro* and then cells were harvested for western blot analysis. Semi-quantitative densitometric analysis of the protein bands was carried out on the blot (data not shown). Statistical analysis: Kruskal-Wallis analysis. ** $p<0.01$; **** $p<0.0001$; if not reported: p not significant. Abbreviations. SpA/IBD: inflammatory bowel disease-associated spondyloarthritis; ax-SpA/IBD: axial SpA/IBD; peripheral SpA/IBD; IBD: Inflammatory bowel disease; HC: healthy controls; I-FABP: intestinal fatty acid binding protein; LPS: bacterial lipopolysaccharide; sCD14: soluble CD14; ERK 1/2: extracellular Signal-regulated Kinase-1/2. Wnt: wingless protein family; SOST: sclerostin.

Conclusions: The role of gut inflammation and microbial translocation in the onset of arthritis in IBD patients are still under investigation. We have demonstrated that in SpA/IBD there is a significant bacterial infiltration of the ileal tract, associated with the downregulation of tight-junctions' proteins (occludin, claudin-1 and claudin-4) and epithelial damage, that cause microbial translocation and higher plasma levels of I-FABP, LPS, and sCD14. LPS and sCD14, thus, could trigger a complex systemic inflammatory response acting on several biochemical pathways, linking the immune system (anti-SOST-IgG) and the bone (SOST).

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OP0272

INFLAMMATION AT BARRIER TISSUES SUCH AS SKIN AND GUT TRIGGERS MILD JOINT INFLAMMATION AND IS INFLUENCED BY BIOMECHANICAL STRESS INDUCED BY FORCED-RUNNING

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Background: The factors triggering the onset of psoriatic arthritis (PsA) and other forms of spondyloarthritis (SpA) are mostly unknown. These joint diseases are clinically associated with psoriasis (PsO) and inflammatory bowel disease (IBD). The three pathologies share the common leitmotiv of chronic inflammation and all of them have an at least partially shared genetic susceptibility. Entheses, the attachment sites of tendons and ligaments into the bones, are considered as a primary disease localization and a site of biomechanical stress. Increasing evidence supports the hypothesis that biomechanical stress, together with inflammatory triggers such as antigens and changes in the microbiome, can contribute to the onset of PsA and SpA by inducing local microdamage in the entheses.

Objectives: Here, we aim to understand early events leading to PsA and SpA by combining a protocol of forced exercise in mice with simultaneous locally-induced cutaneous or intestinal inflammation.

Methods: Forty 8 weeks old C57/Bl6 male mice were used to induce the PsO- or IBD-like disease, respectively by serial applications of imiquimod cream (IMQ) on a shaved area of the back skin, and administration to the intestine of dextran sodium sulphate (DSS) dissolved in drinking water. Forty control mice were left