Conclusion: MHR was elevated in axSpA patients with a highest diagnostic value. PAR was elevated in active axSpA patients, showing a significant correlation to the disease activity.

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AB0154 WNT-BETA CATENIN PATHWAY MAY BE UPREGULATED IN ANKYLOSING SPONDYLITIS

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Background: The Wnt- β -catenin pathway may play a critical role in new bone formation in ankylosing spondylitis. Wnt- β -catenin signaling depends primarily on the activity of glycogen synthase kinase-3 β (GSK3 β) that plays a key role in controlling β -catenin stability/degradation. It has been clearly established that phosphorylation of serine 9 in GSK3 β correlates with the inhibition of its kinase activity and stabilization of β -catenin. Dickkopf-1 (DKK1) and sclerostin (SOST) are both upstream inhibitors of the Wnt/ β -catenin pathway. Given that AS is associated with new bone formation we are interested in the molecular pathways that lead to this clinical phenotype

Objectives: The objective of our studies was to test the hypothesis that "alterations in the Wnt- β -catenin activity may be a contributing factor in the pathogenesis of AS"

Methods: 5 healthy donors and 12 patients (mean age 48 y.o., HLA-B27+ 70%) with AS based on New York classification criteria were enrolled. RNA was extracted from whole blood collected in PAX tubes following PreAnalytix kit protocol. Total mRNA was reverse transcribed using the high capacity cDNA Reverse Transcription Kit (Thermo Scientific) according to the manufacturer's instructions. TaqMan® Gene Expression Assays (IDT) were used to quantify mRNA levels of DKK1, SOST, and β -catenin. LightCycler480, and $\Delta\Delta C_T$ method were used to quantify the data (normalized to RPLP0(60S acidic ribosomal protein P0)). Protein lysates were prepared using NucleoSpin RNA/Protein kit (Takara) from PBMCs isolated from blood collected from the same 12 patients. Equal amounts of protein were loaded on 4–12% SDS gels and transferred to PVDF membranes. Membranes were blocked with 5% milk in TBST and probed at 4°C overnight with primary antibodies [rabbit anti-phosphoGSK3 β (Ser9) (1:500; Cell Signaling, #9336), rabbit anti-GSK3 β (1:1000; Cell Signaling, #9315), and mouse anti- β -actin (1:1000; Santa Cruz Biotechnologies, sc-47778)]. Appropriate HRP-conjugated secondary antibody was applied at room temperature for 1 hour. Immunoreactive protein bands were visualized using ECL (Pierce) and imaged with VisionWorks Image Acquisition and Analysis Software (Analytik Jena US, Upland, CA). β -actin was used as a loading control.

Results: Compared to healthy controls the mRNA levels of DKK1 and SOST were significantly lower in AS patients ($p < 0.001$), while the mRNA level of β -catenin was significantly higher in AS patients than in healthy controls ($p < 0.05$) (Fig 1).

Compared to healthy controls, there was a several fold increase in the phosphorylation of GSK3 β (Ser9) protein in the AS patient's sample.

Conclusion: These data indicate that altered Wnt- β -Catenin activity may be contributing to the new bone formation in AS patients and thereby contributing to the disease pathogenesis and can be targeted for therapeutic development.

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AB0155 INTESTINAL MICROBIAL SIGNATURE IN ANKYLOSING SPONDYLITIS

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Background: Intestinal microbiota analysis is a current subject because of its important role in the pathogenesis of various autoimmune diseases such as intestinal inflammatory diseases or spondyloarthritis.

Objectives: The objective of this paper was to perform a quantitative determination of the intestinal microbiota in patients with ankylosing spondylitis (AS) and to highlight the main characteristics of intestinal dysbiosis in these cases.

Methods: We conducted a case-control prospective study that included 28 patients with AS and 32 control cases (healthy individuals). Intestinal microbiota analysis was performed by real-time PCR (polymerase chain reaction) in faeces. Intestinal microbiota analysis focused on the following bacterial species: *Bacteroides*, *Bifidobacterium*, *Clostridium coccoides* (XIVa) (*C. Coccoides*), *Clostridium leptum* (IV) (*C. Leptum*), *Faecalibacterium prausnitzii* (*F. prausnitzii*), *Lactobacillus*, *Escherichia coli* (*E. coli*).

Results: Intestinal dysbiosis in AS patients was characterized by a significant bacterial decrease compared to the control arm. Some bacterial species showed a numerical growth: *Bacteroides*, *C. coccoides* and *C. leptum*, *F. prausnitzii*. In other bacterial groups there was a significant decrease: *Bifidobacterium*, *Lactobacillus* and *E. coli*. Statistically significant correlations were observed only for *Bifidobacterium*, significantly increased in the axial form of AS compared to the peripheral form ($p = 0.035$). Other bacterial groups were numerically elevated in the axial form of AS (except *Bacteroides*), without statistically significant differences. In all AS cases, a moderate disease activity was evidenced (mean BASDAI = 4.83, mean BASFI = 9.11). BASDAI score inversely correlated with the total bacteria group ($p = 0.010$, $r = -0.606$) - intestinal dysbiosis worsens as disease activity increases. Also, direct proportional correlations were highlighted between BASDAI and *F. prausnitzii* ($p = 0.000$, $r = 0.764$), respectively *Lactobacillus* ($p = 0.047$, $r = 0.488$). An increase in AS activity is associated with an increase in proinflammatory bacteria. BASFI score statistically correlated with the total bacterial count ($p = 0.000$, $r = -0.764$), *F. prausnitzii* ($p = 0.010$, $r = 0.606$), *Bifidobacterium* ($p = 0.016$, $r = 0.843$) and *E. coli* ($p = 0.016$, $r = 0.575$). An important decrease in the functionality of these patients correlates with a decrease in total bacterial diversity. Improvement of intestinal dysbiosis has been observed in patients on synthetic and biological immunosuppressive therapy compared to the control arm.

Conclusion: The study highlights the characteristics of intestinal dysbiosis in AS patients. There is a direct relationship between the composition of intestinal microbiota and the AS activity scores. Specific treatment for AS leads to a decrease in proinflammatory bacteria, improving gut dysbiosis.

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