through upregulating cellular activities involving iNOS-presenting macrophages and B cell receptor signaling, which may be associated with the pathogenesis of P.g.-triggered RA.

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Figure 1. Expression level of the mechanosensitive gene Sclerostin (Sost). It dropped in response to exercise in entheseal tissues, but not in long bones, revealing a tissue-specific response to mechanical stimulation.

mRNAs were extracted from the long bones (flushed tibia and femur) and the ankles’ enthesis for real-time PCR analysis. μCT was performed on the femurs. Alkaline phosphatase activity was detected by histology on the anchorage of the Achilles tendon to the calcaneum, and by enzymatic assay in serum samples. Luminex analysis was also conducted on serum samples for II-6 and II-BK detection.

Results: Free access to the activity wheel resulted in a running exercise of 5.5±0.8 km/day (approximately 80 km in total) at 14.5±0.5 m/min. No effect was detected on the femur architecture by μCT. Sclerostin (Sost) gene expression was monitored as a mechanosensitive marker. Its expression was expectedly reduced by half in entheseal tissues, but no modulation was observed in long bones (Figure 1). Similarly, exercise-induced regulation of Osterix and Runx2 expressions was observed only in enthesis samples. This tissue-specific pattern was also verified for key genes of the sphingosine-1 phosphate metabolic pathway, which we recently implicated in spondyloarthritis pathophysiology [2]. The in situ staining of alkaline phosphatase activity suggested the presence of more positive cells in the anchorage of Achilles tendon of running mice, compared to control ones. However, alkaline phosphatase activity in serum samples and its gene expression in rough tissue extracts were unchanged. No inflammatory response was detected as II-B/K serum levels were similar in the control and the exercising group (59±14 vs 57±14 pg/mL). In addition, II-6 was not detected in the serum and its expression was very faint and constant in the tissue extracts.

Conclusion: This work is still in progress for a more complete characterization of the model. We believe that this experimental design will be useful to study the role of mechanical stimulation specifically in the enthesis and that it can help to better understand the spondyloarthritidis pathophysiology.

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Spondyloarthritis - aetiology, pathogenesis and animal models

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GENETIC VARIANTS WITHIN PSORIATIC ARTHRITIS (PsA)-WEIGHTED GENES FBXL19 AND HLA-B*39 MAY SERVE AS A POTENTIAL LINK BETWEEN PsA AND OBESITY

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Background: PsA patients have been observed to have a higher body mass index (BMI) compared to individuals with a similar disease (e.g., rheumatoid arthritis) or healthy controls1. Approximately 45% of PsA patients are considered obese with BMI’s exceeding 30 kg/m², and these patients have more severe arthritic disease and lower response to therapy2. A recent mendelian randomization study noted that higher BMI leads to higher risk of psoriasis when using genetic variants as instrumental variables for BMI2.

Objectives: To determine if known PsA-weighted genetic variants are overrepresented in an obese population.