general practitioner, 126 immunization campaign, 19 nurse, 9 rheumatologist, 4 pulmonologist, 1 infectious disease specialist, 1 family doctor and 1 internist. 260 (54%) reported having their immunization records. Only 37 had been vaccinated with influenza, 27 pneumococcus, 4 human papilloma virus and 2 Hepatitis B in the past. 372 (77%) accepted the invitation to be vaccinated on the day of their interview, but only 72 (19%) went to get the immunization; 41 of whom were given anti-influenza vaccines and 34 Pneumococcus (PPSV 23). The main causes for which the patient considers not to be vaccinated are: 85% "Because *my* treating doctor has not recommended me to go get vaccinated", 36% "They often do not have the vaccine to apply", 36% "I forget to get the vaccine on time", 31% "I think the application of the vaccine can make me sick", 14% "A vaccination center is not accessible", 7% "I think it is not useful to get vaccinated", and 5% "My doctor recommended me not to get vaccinated". These patients presented a total of 172 recurrent infections that included: upper airway infection 55, pneumonia 4 and others; 90 hospitalizations were required due to infection of which the main were due to: pneumonia 29, pulmonary tuberculosis 4, kidney 3, bone 1 and meningitis 1.

Conclusions: Immunization in this group of patients is low and rarely accepted mainly because their rheumatologist does not provide them with this information and due in general to a lack of information. This action is extremely important as it might reduce some serious infectious processes that lead to hospitalizations and increase the mortality in these immunosuppressed patients.

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OP0159 THE INITIATION, BUT NOT THE PERSISTENCE, OF EXPERIMENTAL SPONDYLOARTHRITIS IN HLA-B27/HUβ2M TRANSGENIC RATS IS CRUCIALLY DEPENDENT ON THE IL-23 AXIS

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Background: The pro-inflammatory cytokine IL-17A is a central driver of pathology in human spondyloarthritis (SpA). IL-17A production was originally proposed to be dependent on the upstream cytokine, IL-23. Emerging preclinical and clinical evidence from SpA-related diseases suggest, however, that IL-17A and IL-23 have a partially overlapping but distinct biology.

Objectives: Here, we aimed to assess to what extend pathogenic IL-17A is dependent on IL-23 in SpA by selectively targeting the IL-23R in the HLA-B27/Huβ2m transgenic rat model of SpA, which we showed previously to be IL-17A-dependent.

Methods: HLA-B27/Huβ2m tg rats were immunized with low dose heat-inactivated *M. tuberculosis*/IFA. Rats were treated with a depleting anti-mouse/rat chimeric IL-23R antibody or PBS in a prophylactic (treatment initiation after immunization, before disease onset) or therapeutic (treatment initiation after disease onset) experiment. Clinical measurements included spondylitis and arthritis scores and hind paw swelling (plethysmometry). At the end of the study spleen and lymph nodes were used to assess cytokine expression, serum samples were analyzed for exposure to anti-IL23R.

Results: In the prophylactic treatment strategy, 58% and 67% of the rats in the control group developed spondylitis and arthritis, respectively. The average arthritis score at the end of the study was 3.9±1.1 and the average hind paw swelling was 0.35±0.09 cm^3. Prophylactic treatment with anti-IL-23R completely protected the rats against the development of spondylitis as well as arthritis. In the therapeutic treatment strategy, however, anti-IL23R treatment failed to reduce the incidence or decrease the severity of experimental SpA (fig. 1). With an average increase in arthritis score after the start of treatment of 1.6±2.8 versus 2.1±2.5 and an increase in paw swelling of 0.6±0.7 versus 0.3±0.6 cm^3in anti-IL23R treated versus control animals. The differential effect of IL-23R targeting in the initiation phase versus established disease could not be explained by pharmacokinetic differences as serum analyses revealed similar exposure levels. Mechanistically, the expression of presumably downstream effector cytokines such as IL-17A ($p<0.05$) and IL-22 ($p<0.01$) was reduced in the popliteal lymph nodes of rats treated prophylactically with anti-IL23R versus controls, with a similar trend in spleen. Accordingly, IL-17A production upon ex vivo re-stimulation was reduced in samples from prophylactically treated rats. In contrast, similar popliteal lymph node expression data in samples from the therapeutic experiment indicate a twofold increase in IL-17A expression and no difference in IL-22 expression in the anti-IL23R treated rats compared to controls.

Conclusions: IL-17A expression and production is dependent on the IL-23 axis in the initiation phase of experimental SpA but not in established disease. Accordingly, targeting of this axis with an anti-IL23R antibody completely prevented the onset of arthritis and spondylitis in HLA-B27/Huβ2m transgenic rats, but failed to reduce axial and peripheral joint inflammation in established disease. The cellular origin of IL-23-independent IL-17A production in established disease and the relevance to human SpA remains to be further investigated.

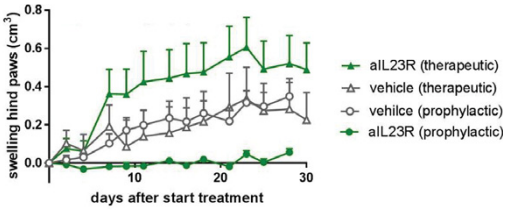

Figure 1: Swelling of the hind paws during follow up in prophylactic versus therapeutic treatment with anti-IL-23R or vehicle control (data are means +/- SEM)

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OP0160 GUT-DERIVED TNF AS RISK FACTOR FOR THE DEVELOPMENT OF SACROILIAC INFLAMMATION

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Background: An intruiging link exists between gut and joint inflammation in spondyloarthritis (SpA). About 50% of patients has subclinical (eg. microscopic) gut inflammation, which represents a risk factor for development of Crohn's disease, sacroiliac inflammation and evolution in to Ankylosing Spondylitis. However, the underlying mechanisms are still relatively poorly understood.

Objectives: Our goal was to examine the relationship between TNF, microscopic gut inflammation and axial inflammation using human samples and a novel mouse model. We speculated that TNF in the gut represents an important risk factor for disease severity and progression in SpA.

Methods: We examined in situ expression of TNF, TNFR1 and TNFR2 using triple in situ hybridisation in gut biopsies of human SpA patients. Furthermore, we generated intestinal specific human TNF transgenic mice, in which hTNF is under control of a rat iFABP (fatty acid binding protein) promoter, generating a mouse-model over-expressing human TNF in the ileum. These mice, together with wild type littermates, were evaluated for the development of arthritis up until the age of 13 weeks after which they were euthanized and ankle and sacroiliac joints as well as ileum were processed for histology.

Results: There was a marked upregulation of TNF in inflamed versus non-inflamed gut biopsies of human SpA patients. We also noted a predominant upregulation of TNFR1 on intestinal epithelium and TNFR2 in lamina propria respectively. Of interest, IL-17 and IL-23 were also markedly increased while IL-22 was most abundant in chronically inflamed samples. In line with this, we found that patients with gut inflammation had a higher need for anti-TNF therapy and their degree of clinical response after anti-TNF was also markedly higher.

Our transgenic mice exhibited a runt phenotype and hallmarks of inflammatory bowel disease, including increased intestinal permeability and inflammation compared to their wild-type littermates. While in peripheral joints no clear signs of arthritis were observed, the sacroiliac joints in transgenic mice, by contrast, showed marked signs of inflammation as well as bone erosion and destruction.

Conclusions: These data propose a new paradigm that gut-derived TNF is sufficient to trigger sacroiliitis and provide an alternate explanation on the relationship between gut inflammation, evolution to inflammatory bowel disease and axial inflammation in SpA.

Disclosure of Interest: None declared

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OP0161 THE JAK1 SELECTIVE INHIBITOR FILGOTINIB REGULATES BOTH ENTHESIS AND COLON INFLAMMATION IN A MOUSE MODEL OF PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is a heterogeneous chronic inflammatory disease characterized by the association of musculoskeletal involvement and extra-skeletal symptoms such as psoriasis and Inflammatory Bowel Disease