Abstract FRI0162 – Figure 1. Type H vessel association with ectopic bone formation in 6-week-old murine vertebra. Left panel: Confocal tile scan of tmTNF tg vertebrae showing endomucin* (red), which labels all vessels except arteries, and CD31* (green) endothelial cells. Osterix (white) labels osteoprogenitors and nuclei are labelled by Hoechst (blue). Right panel: Higher magnification of Osterix* osteoprogenitors at ectopic location. Osterix* cells are found around type H (CD31^{hi}endomucin^{hi}) vessels.

Conclusions: tmTNF overexpression in mice leads to development of type H vessels associated with ectopic osteogenesis. In addition, extensive lymphoid aggregates develop in the BM. Current studies are aimed at identification of signalling pathways in ECs that contribute to these processes.

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FRI0163 DEVELOPMENT OF A PRECLINICAL TESTING PIPELINE FOR A NOVEL TRANSMEMBRANE TNF-DRIVEN SPONDYLOARTHRITIS MODEL

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Background: Spondyloarthritis (SpA) is a complex disease characterised by chronic inflammation, bone erosion and pathological new bone formation. The TgA86 transmembrane TNF (tmTNF) transgenic mouse is a unique model of SpA, developing spontaneously and with 100% incidence early progressive SpA characterised by peripheral inflammatory arthritis and axial ankylosing spondylitis with cardiovascular involvement. This closely recapitulates the pathological findings and comorbid conditions described in human patients.

Objectives: To characterise in greater detail the development and progression of the TgA86 pathology and its similarities to human disease and to standardise reliable preclinical protocols and specific readouts for the assessment of the efficacy of human therapeutics.

Methods: TgA86 peripheral and axial pathology was assessed at different time points from 2.5 to 28 weeks of age. Disease severity was evaluated using clinical parameters and histopathological analysis of ankle and sacroiliac joints, lumbar and caudal vertebrae, as well as whole mount skeletal staining. Clinical and histopathological readouts were used to assess the therapeutic effect of Etanercept that was administered thrice weekly at 30 mg/Kg starting either from 2.5–5 weeks of age (prophylactic protocol) or from 9 weeks of age (therapeutic protocol).

Results: Clinical pathology in TgA86 mice appears already from 2.5 weeks of age, with signs of paw swelling, digit deformation and tail crinkling, while by 9 weeks of age pathology is fully established, with severe peripheral arthritis and tail and spine ankylosis. Pathology progression was also evident histopathologically, characterised by the originally described features of progressive inflammation, cartilage destruction and bone erosion observed in sacroiliac and ankle joints as well as in lumbar and caudal vertebra. Additionally, new pathology features were detected by identifying signs of enthesitis, new bone formation appearing as

cartilaginous structures at the edges of vertebrae endplates, presence of red bone marrow during all stages of disease progression as well as signs of intervertebral disc (IVD) degeneration. Prophylactic treatment with Etanercept ameliorated effectively all clinical and histopathological features of the peripheral and axial pathology. Therapeutic treatment while affecting only minimally the clinical signs of both peripheral and axial pathology, it was found to reduce the peripheral arthritis histopathological score by at least 50%. Finally, treatment with Etanercept was also efficient in ameliorating the comorbid heart valve pathology observed in these animals.

Conclusions: We have shown that TgA86 pathology includes features of sacroiliitis, enthesitis, new bone formation, persisting red bone marrow and intervertebral disk degeneration, further strengthening the similarities of this model to human pathology. Based on the assessment of all pathology features during prophylactic anti-TNF treatment we suggest that early on in disease there may be a therapeutic window during which optimal treatment of the pathology can be achieved.

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FRI0164 ANTI-PFDN5 ANTIBODY AS A BIOMARKER FOR UVEITIS IN ANKYLOSING SPONDYLITIS

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Background: Noninfectious uveitis is the most common extra-articular manifestation of ankylosing spondylitis (AS). However, molecules related to the disease pathogenesis have yet to be identified, and no biomarkers are available for uveitis in AS.

Objectives: We aimed to identify the biomarkers for uveitis in AS, and elucidate the possible pathogenesis of uveitis in AS associated with the identified biomarkers.

Methods: Protein microarray using ProtoArray was performed to profile autoantibodies present in sera from patients with various autoimmune diseases, including eight AS patients with uveitis. The autoantibodies with higher reactivity in AS patients with uveitis compared with other patients were selected, and the levels of autoantibodies were measured using ELISA in the sera from AS patients with (n=32) or without uveitis history (n=32), patients with rheumatoid arthritis (n=20) and from healthy individuals (n=12). To evaluate the involvement of target antigen in pathogenesis of spondyloarthritis-related uveitis, we conducted an *in vivo* study using curdlan-induced SKG mice, which spontaneously develops arthritis as well as uveitis, and an *in vitro* study using retinal pigment epithelium cell-line (RPE19).

Results: 4 antibodies (Abs) were selected as a candidate for biomarker (anti-PFDN5, area under curve [AUC]=1.00; anti-serine threonine protein kinase 24 Ab, AUC=0.906; anti-odontogenic ameloblast associated protein Ab, AUC=0.859; anti-protocadherin alpha C2 Ab, AUC=0.859). In ELISA, anti-PFDN5 Abs was significantly elevated in AS patients with uveitis compared to AS patients without uveitis. Ocular histology showed that compared to PBS-treated SKG mice, SKG mice with uveitis had strong expression of PFDN5 in iris, ciliary body, and retina. PERK and pelf2α, which are ER stress related proteins, were downregulated in PFDN5 siRNA-treated RPE19 cells in tunicamycin-induced condition, suggesting that PFDN5 enhances ER stress via PERK and pelf2α pathway.

Conclusions: We identified anti-PFDN5 antibody as a putative biomarker for uveitis in AS. PFDN5 was increased in ocular lesion, which may be associated with disease pathogenesis.

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