### OP0333 DISCOVERY AND VALIDATION OF NOVEL AUTOANTIGENS IN SJÖGREN'S SYNDROME WITH POTENTIAL FOR SUBGROUPING OF DISEASE

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**Background:** Primary Sjögren's syndrome (pSS) is a common autoimmune disease with exocrine gland dysfunction and multi-organ involvement. With the growing interest in conducting clinical trials in pSS, there is a need for new biomarkers that can be used to diagnose pSS, identify clinical subsets of pSS, predict treatment outcome and assessment of disease activity. Activation of B-cells and dysregulation of the cytokine network plays a critical role in the pathophysiology of pSS. In the exocrine glands, elevated levels of cytokines, such as type I interferon (IFN), tumor necrosis factor alpha (TNF), interleukin 12 (IL-12) and B cell activating factor (BAFF) can be found. Dysregulated pathways of the innate and adaptive immune system lead to loss of tolerance and the production of organ-specific and non-specific autoantibodies. Current diagnostic criteria for pSS utilize autoantibodies directed to nuclear antigens (ANA), especially to SS-A/Ro (TRIM21, TROVE2) and La (SSB), but those are not specific, and can be identified as well in SLE and even in healthy volunteers. Several studies have shown that not all patients with pSS are tested positive for Ro and La autoantibodies, but suggested the existence of additional autoantibodies in pSS. This autoantibody burden is not well understood for the importance of disease progression, for its role in patient segmentation, or for response to treatments.
**Objectives:** The discovery of novel autoantigens may provide a deeper understanding of mechanisms of actions for pSS drugs, and may be useful to stratify patients.
**Methods:** The autoantibody reactivity pattern of pSS serum patients was analyzed using a Luminex bead-based antigen array (SeroTag) and 1,600 selected human protein antigens from our hPEX protein library of 8,000 recombinant proteins (1). We screened over 2,000 serum samples from patients with autoimmune diseases as active controls targeting Sjögren's Syndrome (n=70), SLE (n=>500), SSc (n=>250), RA (n=>500), and over 1,000 healthy individuals to confirm known and to discover novel autoantibodies. In a validation study, novel biomarker candidate antigens were evaluated using a cohort of 350 Patients with Sjögren's Syndrome.
**Results:** Apart from clear confirmation the known benchmark autoantigens known for many years we have discovered a small set of additional, novel autoantibodies, which were detected in frequencies of 8 to >20% in pSS. Accumulation of autoantibody reactivities allows for a first subgroup definition of Sjögren's, and for clear segregation of SjS/SLE overlap syndrome patients.
**Conclusions:** A set of novel autoantigens for diagnosis and subgroup definition in Sjögren's syndrome was discovered by high content screening using a Luminex bead-based array platform. Validation in additional, large patient cohorts is ongoing.
**References:**
[1] Budde P et al. (2016). Lupus. (8):812–22.
**Disclosure of Interest:** P. Schulz-Knappe Shareholder of: Protagen AG, P. Budde Employee of: Protagen AG, H.-D. Zucht: None declared, D. Wirtz Employee of: Protagen AG, K. Marquardt Employee of: Protagen AG, R. Thomas: None declared, T. Witte: None declared, M. Schneider Consultant for: Protagen AG, K. Sivils: None declared, A. Rasmussen: None declared
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## Optimizing treatment for osteoarthritis: take the phenotype in account "one size does not fit all"

### OP0334 PREDICTORS AND MRI-DETECTED STRUCTURAL PATHOLOGY WITH TRAJECTORIES OF KNEE PAIN SEVERITY: A 10.7-YEAR PROSPECTIVE STUDY

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**Background:** Knee pain is the most common manifestation of knee osteoarthritis (OA) and is generally thought to get worse with time. Risk factors for knee pain have been extensively investigated; however, whether the risk factors are associated with a specific pain trajectory has not yet been comprehensively explored. Furthermore, knee structural pathology on MRI, such as bone marrow lesions (BMLs), effusion-synovitis and cartilage defects, are thought to be the origin of knee pain. However, its underlying mechanisms remain to be elucidated and hampered by a large individual variation of pain course.
**Objectives:** To identify distinct trajectories of knee pain over 10.7 years in an older population, to describe risk factors with identified trajectories, and to explore MRI-detected structural pathology with the trajectories.
**Methods:** 1,099 participants (mean age 63 years) from a population-based cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological, lifestyle and comorbidities data were obtained at baseline. Knee pain was assessed using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) at each time-point. T1-weighted or T2-weighted MRI of the right knee was performed to measure knee structural pathology. Knee radiographic OA was assessed by X-ray at baseline. Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses with adjustment for potential confounders.
**Results:** 1,099 participants were included for the identification of pain trajectories and three distinct pain trajectories were defined. Participants in Group 1 ("Mild pain" n=568, 51.7%) had relatively stable mild pain over time. Participants in Group 2 ("Moderate pain", n=366, 33.2%) had moderate pain over time. Participants in Group 3 ("Severe pain", n=165, 15.1%) developed or displayed fluctuating severe pain over time. Compared with the "Mild pain", higher BMI, emotional problems, and musculoskeletal diseases were significantly associated with both "Moderate pain" and "Severe pain" trajectories. Also, younger age, lower education level and unemployment status were associated with "Severe pain" trajectory. The presence of cartilage defects and BMLs were associated with increased risk of "Moderate pain" and "Severe pain" trajectories before or after adjustment for potential confounders. Effusion-synovitis was not statistically associated with "Moderate pain" (P=0.082), but associated with "Severe pain" trajectory. Furthermore, a dose-response relationship was observed between number of knee structural abnormalities, and "Moderate pain" and "Severe pain" trajectories (both P for trend<0.001).
**Conclusions:** This is the first long-term study to identify pain trajectories and their risk factors, and explore the associations between structural pathology and pain trajectories. Three distinct pain trajectory groups were identified, suggesting that homogeneous subgroups exist and follow a specific trajectory over time despite large individual variation of pain course. Significant associations between structural pathology and pain trajectories suggest that peripheral stimuli may play a role in the development and maintenance of pain severity.
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### OP0335 EXPLORING ASSOCIATIONS BETWEEN HISTOLOGICALLY ASSESSED INFLAMMATION AND PAIN AND FATIGUE IN KNEE OSTEOARTHRITIS

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**Background:** Pain and fatigue are frequent symptoms of osteoarthritis (OA). However, the exact mechanism causing these symptoms remains unclear. Inflammation is important in OA pathophysiology. Associations between inflammatory aspects and clinical outcomes have been found. However, mainly (contrast-enhanced) MRI was used to assess synovial inflammation in these studies. Using this method, inflammation is assessed in an indirect way (e.g. infrapatellar fat pad signal enhancement, synovial fluid effusion and thickening of synovial tissue). Conversely, histological assessment of synovial inflammation is regarded as the gold standard. Using this method, specific aspects of inflammation can be distinguished and rated for severity.
**Objectives:** To evaluate the associations of inflammation-related histological parameters of the synovium with pain and fatigue in knee OA patients.
**Methods:** Fifty-nine patients fulfilling ACR criteria for knee OA were recruited from two prospective studies[1,2] and gave consent for synovial biopsy using a mini knee arthroscopy. Biopsies were taken from visually inflamed areas of the synovium. Tissue sections were histologically assessed for 1) number of synovial lining cells (absolute); 2) sub-synovial infiltration; 3) fibrin deposition; 4) vascularization; 5) fibrosis; and 6) perivascular edema (scores 0–3).[3] Average scores across sections were calculated for each parameter and for all parameters together. These data were combined with longitudinal clinical data from the prospective studies (WOMAC pain, SF36 vitality; 0=worst – 100=best). Associations between individual inflammatory features and clinical outcomes over time were assessed with mixed model analyses.
**Results:** Patient characteristics are shown in Table 1. Relatively mild levels of inflammation were found, in line with previous research (median 1.1 [95% CI 0.9–1.6]).[3,4] Longitudinal data was available for 56 patients. Age, gender, BMI and time since symptom onset were no confounders. No significant associations were found between any histological parameter and pain or fatigue over time (Table 2).

Table 1. Patient characteristics

| | Mean (Sd) |
|---|---|
| Male/Female | 28/31 |
| Age (years) | 56.4 (9.8) |
| Symptom duration (years) | 10.1 (10.3) |
| BMI (kg/m$^2$) | 29.7 (5.9) |
| Follow-up (years) | 1.2 (0.8) |

**Conclusions:** This is the first study to examine different parameters of histologi-