OP0327

CXCL4 DRIVES FIBROSIS BY PROMOTING SEVERAL KEY CELLULAR AND MOLECULAR PROCESSES

W. Marut¹, A. Affandi², T. Carvalho¹, A. Ottria¹, J. Haan³, M. Brandt³, R. Tieland¹, M. Brans³, B. Malvar-Fernandez¹, C. Bekker¹, M. van der Linden¹, B. Giovannone¹, D.-J. Heijnen⁴, A. Kowalska⁵, R. Lafyatis⁶, C. Cheng³, S. de Jager³, J. van Roon¹, T. Radstake¹. ¹Laboratory for translational immunology, University Medical Center Utrecht; ²Lundlaan, UMCU; ³Department of Experimental Cardiology; ⁴Department of Dermatology, University Medical Center Utrecht, Utrecht, Netherlands; ⁵Department of Hematology, Children's Hospital of Philadelphia, Philadelphia, USA; ⁶Rheumatology section, Boston University School of Medicine, Boston, Netherlands

Background: Fibrosis, characterised by excessive accumulation of extracellular matrix (ECM) through myofibroblasts, is a leading cause of mortality worldwide^{1,2}. Understanding the pathways involved in myofibroblasts activation is crucial to develop novel treatment strategies. Systemic sclerosis (SSc) is a prototypic fibrotic disease in which we previously identified CXCL4 to be strongly correlated with skin and lung fibrosis³.

Objectives: We aimed to elucidate the role of CXCL4 in fibrosis development using *in vitro* and *in vivo* assays.

Methods: Human primary dermal fibroblasts, endothelial cells, and pericytes, were (co-) cultured in the presence or absence of recombinant human CXCL4. CXCL4^{-/-} mice were used in bleomycin-induced skin and lung fibrosis model, and pressure-overload cardiac fibrosis model. Gene expression was assessed by qPCR, protein expression was determined by western blot or immunofluorescence, and collagen content was measured by trichrome staining or hydroxyproline assay.

Results: We found that CXCL4 induced the expression of myofibroblast markers α SMA and SM22 α , and collagen synthesis in human dermal fibroblasts, endothelial cells, and pericytes. CXCL4 also suppressed endothelial cell tubular formation in a co-culture with pericytes. In mice, CXCL4 expression was increased in a variety of mouse inflammatory and fibrotic models. Using CXCL4^{-/-} mice, we confirmed the essential role of CXCL4 in promoting fibrotic events in the skin, lung, and heart using two independent fibrosis models.

Conclusions: CXCL4 drives myofibroblast transformation from different precursors and it is required for fibrosis development across organs. Our findings implicate a pivotal role of CXCL4 in fibrosis further substantiating the potential role for neutralising CXCL4 as a novel therapeutic strategy.

REFERENCES:

- [1] Rockey, Bell, Hill, N. Engl. J. Med 2015.
- [2] Hinz B, et al. Am. J. Pathol 2007.
- [3] van Bon, Affandi, Broen, et al. N. Engl. J. Med 2015.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.6351

FRIDAY, 15 JUNE 2018

New approaches in measuring what matters to patients

OP0328-HPR

PATIENTS' VIEWS ON ROUTINE COLLECTION OF PATIENT-REPORTED OUTCOMES IN RHEUMATOLOGY CARE – A DANBIO FOCUS GROUP STUDY

J. Primdahl¹, D.V. Jensen², R.H. Meincke², K.V. Jensen³, C. Ziegler³, S. W. Nielsen³, L. Dalsgaard³, M. Kildemand⁴, M.L. Hetland⁵, B.A. Esbensen⁶. ¹King Christian X's Hospital for Rheumatic Diseases, University of Southern Denmark, Graasten; ²The Danbio registry, Rigshospitalet; ³Patient research partner, Copenhagen; ⁴Odense University hospital, Odense; ⁵The Danbio registry, Rigshospitalet, University of Copenhagen; ⁶Rigshospitalet, University of Copenhagen, Copenhagen, Denmark

Background: Patient Reported Outcomes (PROs) are important for shared decision-making regarding treatment. The DANBIO registry, which has included >60 000 patients (>5 000 000 visits), routinely collects PROs (health assessment questionnaire (HAQ), visual analogue scales for pain, fatigue and global health, patient acceptable symptom state (PASS) and an anchor) on touch-screens in the waiting room, as part of rheumatology standard care.¹ The aims of DANBIO are to 1) monitor the disease in individual patients, 2) improve treatment quality, 3) conduct research. Patients' experience with the collection of PROs in DANBIO has not been explored.

Objectives: To explore patients' views on the collection of PROs in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS)

Methods: We conducted a qualitative study based on one semi-structured focus group interview in each of the five geographical regions in Denmark. The analysis of the transcribed interviews was based on content analysis.² Four patient research partners were involved in all phases of the study.

Results: In total, 32 adult patients with RA (n=21), PsA (n=6) or AS (n=5) participated. 21 (66%) were female, mean age 60 years (range 32–80).

The analysis identified an overarching theme **Potential for improvement of communication** referring to patients' perception that PROs have the potential to inspire both patients and clinicians to prepare for and improve dialogue in the consultation. In addition, four subthemes emerged.¹ **Lack of information about why the data is collected** referring to patients' uncertainty as to whether the PROs aimed primarily at monitoring their own disease, to save money or for research purposes. Questions regarding who gets access to data (in addition to the rheumatologist or nurse), and if data were sold to external parties, were also expressed.² **Validity of the data** referring to patients' concerns about how to reply 'correctly'. The fluctuations in disease activity and timing in relation to pharmacological treatment affected the patients' answers. They were uncertain whether answers should reflect their present state or an average of disease manifestations since their last visit. Patients were also uncertain regarding the reference; should they compare to healthy individuals or to when the arthritis is as good as it can be. Some chose to answer as if they were doing worse or better than they actually felt, in order to enter into dialogue with the clinician or because they were worried that medical treatment would be withdrawn.³ **Inclusion of the PROs in the consultation** referring to patients' experiences varying from no use of the PROs at all to detailed review with the rheumatologist or nurse.

Conclusions: Systematic information and continuous dialogue regarding the purpose of the collection of PROs, how to answer the PROs and active use of the answers in the consultations are important for patients with arthritis

REFERENCES:

- [1] Ibelt E. et al. *Clin Epid* 2016;8.
- [2] Graneheim UH, Lundman B. *Nurse Educ Today* 2004;24.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3658