associated with various inflammatory diseases. However, whether GDF11 interacts with TNF- α and plays a role in RA still remains unknown.

Objectives: To investigate the potential role of GDF11 in development of RA, and to testify the underlying mechanisms involved.

Methods: NF- κ B-luciferase transgenic mice (Balb/c strain), DBA-1 mice, micro-CT, *in vivo* imaging system (IVIS), mice bone marrow-derived macrophages (BMDM), cell immunostaining, collagen induced arthritis model (CIA), collagen antibody induced arthritis model (CAIA), GDF11 recombinant protein, co-immunoprecipitation Co-IP, Western blot, real time PCR, Histology, immunohistochemistry, unpaired t-tests (Mann-Whitney), paired t-tests, and ANOVA.

Results: The interaction between GDF11 and TNFR1/TNFR2 in BMDM was implied by co-immunoprecipitation (Co-IP) (figure 1A-B). BMDM cells were cultured with stimulation of 10 ng/ml TNF- α , in the presence or absence of 10 μ g/ml GDF11. Inflammation-associated cytokines, including IL-1 β , IL-6 and inducible nitric oxide synthase (iNOS) were assessed at 12 hour time point through real time PCR (figure 1C-1E), and expression level of IL-1 β was assayed through ELISA at 72 hour time point (figure 1F). As a result, GDF11 suppressed TNF- α -induced expression of inflammatory cytokines. Every experiment was repeated for three times. Collagen-induced arthritis (CIA) mice model was established in DBA-1 mice, and intraperitoneal injection of GDF11 attenuated clinical score (figure 2A), synovitis, pannus and bone erosion (figure 2B-2D) compared with PBS control group (n=7 for each group). Representative pictures of the paw (figure 2E), micro-CT (figure 2F) as well as HE staining (figure 2G) revealed that GDF11 greatly suppressed joint destruction in CIA model. In addition, GDF11 inhibited TNF- α -induced expression of biomarkers for activation of NF- κ B signalling pathway, including NF- κ B2 (figure 3A), phosphorylation of I κ B α (figure 3B) and nuclear translocation of p65 (figure 3C) in BMDM, which were tested through real time PCR, Western blot and cell immunostaining, respectively. To testify the function of GDF11 in activation of NF- κ B signalling pathway *in vivo*, p-I κ B α expression was detected through immunohistochemistry in CIA model, and GDF11 diminished phosphorylation of I κ B α (figure 4A) compared with PBS group (n=5). Moreover, CAIA arthritis model was established in BALB/C strain-based NF- κ B luciferase mice, and GDF11 markedly repressed intensity of bioluminescence signal in the paws of CAIA model (figure 4B-4C). The values are the mean $\pm$ SD. *p<0.05, **p<0.01 and ***p<0.005 vs control group.

Conclusions: These results reveal GDF11 as potential antagonist for inflammatory function of TNF- α . Besides, GDF11 displays promising protective function in inflammatory arthritis mice models. In conclusion, GDF11 may shed light on treatment of inflammatory arthritis and provide a potential therapeutic instrument for RA in the future.

REFERENCES:

- [1] Tang, et al. *Science* 2011.
- [2] Zhao, et al. *Ann Rheum Dis* 2015.
- [3] Lai, et al. *Ann Rheum Dis* 2014.

Acknowledgements: This work was supported by the National Natural Science Foundation of China (Grant No. 81501880).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2210

OP0008 MODELLING AN AUTOINFLAMMATORY IMMUNOPROTEASOME DISEASE NAKAJO-NISHIMURA SYNDROME WITH HUMAN PLURIPOTENT STEM CELL-DERIVED MYELOID CELL LINES

M. Saito. Center for PS Cell Research and Application, Kyoto University, Kyoto, Japan

Background: Nakajo-Nishimura syndrome (NNS) is an immunoproteasome-associated autoinflammatory disorder caused by a mutation of PSMB8 gene.¹ Although dysfunction of immunoproteasome causes various cellular stresses attributed to the overproduction of inflammatory cytokines and chemokine in NNS, precise underlying mechanisms of autoinflammation are still largely unknown.

Objectives: We aim to investigate and understand the detailed mechanisms and signal pathways in NNS and to seek potential therapeutic candidates.

Methods: We established a panel of isogenic pluripotent stem cell (PSC) lines with the homozygous G201V mutation in PSMB8 gene using CRISPR/Cas9-mediated genome editing system. Myeloid cell lines (MLs) were established from each clone and used for functional analysis.^{2,3}

Results: Immunoproteasome activity of PSMB8-mutant PSC-derived MLs (MTMLs) reduced even without stimulation, compared to that of the isogenic wild-type counterparts. When stimulated, MT-MLs showed overproduction of inflammatory cytokines and chemokines, with elevated reactive oxygen species (ROS). The levels of phosphorylated p38 MAPK and STAT1 also increased. Treatment with a p38 MAPK inhibitor, a JAK inhibitor and anti-oxidants dose-dependently decreased the abnormal production of cytokines and chemokines in MT-MLs. Both unstimulated and stimulated MT-MLs showed distinct transcriptional profiles, indicating the ML-MLs were already in a 'primed' state before stimulation.

Conclusions: The current PSC models revealed a specific ROS-mediated inflammatory pathway and provide a platform for studying the pathophysiology of NNS and searching for the alternative therapeutic options for NNS and related immunoproteasome disorders.

REFERENCES:

- [1] Arima K, et al. *PNAS* 2011;108(36):14914–9.
- [2] Kawasaki Y, et al. *Arthritis Rheum* 2017;69(2):447–459.
- [3] Takada S, et al. *J Allergy Clin Immunol* 2018;141(1):339–349.

Acknowledgements: We thank Dr. Fumiko Honda-Ozaki and Ms Madoka Tera-shima for conducting research. We also thank Drs. Nobuo Kanazawa, Akira Niwa, Masakatsu Yanagimachi, Akitsu Hotta and Tatsutoshi Nakahata, and Ms. Haruna Ito for participating. Funding was provided by Japan Agency for Medical Research and Development, Tokyo, Japan.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3422

WEDNESDAY, 13 JUNE 2018

Statistics made simple: a practical approach to complex concepts

OP0009 RISING PREVALENCE OF FUNCTIONAL DISABILITY IN PATIENTS WITH RHEUMATOID ARTHRITIS OVER 20 YEARS

E. Myasoedova¹, J.M. Davis, III¹, S.J. Achenbach², E.L. Matteson¹, C. S. Crowson². ¹Rheumatology; ²Health Sciences Research, Mayo Clinic College Of Medicine, Rochester, MN, USA

Background: Despite the advances in treatment of rheumatoid arthritis (RA) over the recent decades many patients with RA do not achieve remission or full physical functioning. The trends in prevalence of functional disability (FD) in patients with RA are not fully understood.

Objectives: To assess the prevalence of patient-reported FD in patients with RA compared to subjects without RA over the past two decades of calendar time, across different age categories and over the duration of RA disease.

Methods: This retrospective population-based cohort study included Olmsted County, MN residents who met 1987 ACR criteria for RA from 1/5/1999 to 12/31/2013 and a cohort of subjects without RA matched by age and sex from the same underlying population. Each non-RA subject was assigned an index date matching RA incidence date of a corresponding RA patient. Activities of Daily Living (ADL) were recorded annually over the past 20 years at patients' routine medical care visits based on patient provided information about performing six ADL without assistance including feeding oneself, dressing, using the toilet, bathing, walking, housekeeping. FD was defined as having difficulty with ≥ 1 of the six ADLs. Analyses were performed using age- and sex-adjusted logistic regression models with random subject effects to account for multiple measures per patient.

Results: Five hundred eighty-six patients with RA (mean age 55, 70% females) and 531 non-RA subjects (mean age 56, 70% females) have completed 7446 questionnaires (4,301 RA and 3145 non-RA) from 1/5/1999 to 1/5/2018 on or

following their RA incidence/index date. There has been a significant increase in the prevalence of FD among patients with RA compared to the non-RA cohort over the past two decades ($p=0.003$, figure 1). When analysing by age group, patients with RA compared to the non-RA subjects had at least a 15% excess in the proportion of FD at any given age up to the 8–9th decade of life while the proportions were similar in both cohorts. When analysing FD over the duration of RA disease, its prevalence was significantly higher in the RA compared to non-RA subjects, starting at RA incidence/index date (26% in RA vs 11% in non-RA subjects, $p<0.001$), with persistent excess in prevalence over the entire follow-up time. When FD was defined as having difficulty with ≥ 2 of the six ADLs the trends were similar for calendar year, age categories and RA disease duration, although the proportion of patients affected with functional disability was smaller.

Conclusions: Patients with RA have significantly higher prevalence of FD compared to their non-RA counterparts. The prevalence of FD in RA has increased in the recent decades with a persistent excess in the proportion of affected patients in the RA compared to the non-RA cohort across the age-range and over RA disease duration. This substantial and growing FD burden is despite the recent advances in controlling RA disease activity with modern antirheumatic therapies. More studies are needed to understand the underlying causes for these trends in FD and to improve outcomes in patients with RA.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3788

OP0010 USE OF CLAIMS AND ELECTRONIC MEDICAL RECORD DATA TO PREDICT RA DISEASE ACTIVITY

C.H. Feldman¹, K. Yoshida¹, B. Pan¹, M. Frits¹, N. Shadick¹, M.E. Weinblatt¹, S. E. Connolly², E. Alemao², D.H. Solomon¹. ¹Brigham and Women's Hospital, Boston; ²Bristol-Myers Squibb, Princeton, USA

Background: Prior studies have demonstrated challenges in developing and validating claims-based algorithms that accurately predict RA disease activity.^{1,2} The ability to adjust for and predict RA disease activity would be a powerful epidemiological tool for studies that lack direct disease activity measures such as the DAS28.

Objectives: We used machine-learning methods to incorporate claims and electronic medical record (EMR) data to develop models to predict DAS28 (CRP) as a continuous measure, and to distinguish moderate-to-high disease activity from low activity/remission.

Methods: We identified 300 adults (≥ 18 years of age) with RA enrolled in a single academic centre cohort with ≥ 1 year of linked Medicare insurance claims preceding a DAS28 (CRP) measurement between 2006 and 2010. Of these, 95 had Medicare Part D pharmacy data. From claims we included demographics, co-morbidities, joint replacement surgery, physical therapy visits, numbers of RA-related codes, laboratory values and imaging studies, and healthcare utilisation. For those with Part D pharmacy data we included medications (steroids, analgesics, DMARDs) and switches between drugs. From the EMRs we obtained smoking status, BMI, blood pressure, medication use, laboratory values for seropositivity (RF or anti-cyclic citrullinated peptide antibodies), haematocrit, ESR and CRP. We constructed models with claims only, claims with medications and claims with EMR data. We examined these models with DAS28 (CRP) as a continuous measure and as a binary outcome (moderate/high activity vs low activity/remission). We used adaptive least absolute shrinkage and selection operator (LASSO), which avoids model overfitting by penalising large coefficients and selects a subset of variables by shrinking some coefficients to zero. We used adjusted R^2 to compare continuous model fit and C-statistics to compare binary models.