physiologic circumstances. Enhancers do not always regulate the nearest gene, and may regulate more than one gene. Enhancers typically regulate genes within the same chromatin loop, or topologically associated domain (TAD).

Objectives: To gain a better understanding of the genetics of JIA by examining the broader chromatin architecture that encompasses the known risk haplotypes.

Methods: We used publically available chromatin conformation HiC data and the online JuiceBox software suite to query known JIA risk haplotypes for evidence of physical interactions between putative enhancers within the haplotypes and immunologically relevant genes. We specifically queried 20 haplotypes in which H3K4me1/H3K27ac marks were prominent within both lymphoid and myeloid cells. We queried data from GM12787 (B cell), K562 (lymphoblast), and THP-1 (monocyte/macrophage) cells, as well as human cord blood T cells. To identify TADs associated with specific enhancers, we used a 5KB resolution (which allowed us to visualize chromatin loops as peaks), setting the cursor at the center of each putative enhancer. We also identified the genes within the identified chromatin loop domains and used gene ontology (GO) analyses to identify functional associations among genes within the TADs incorporating the JIA risk loci.

Results: We identified at least one chromatin loop structure in all 20 of the JIA risk haplotypes for each of the 4 cell lines we queried. These loops were not cell type specific. That is, almost identical loops structures could be seen in each of the cell lines at each of the loci, suggesting that these enhancers regulate a broad range of common leukocyte functions. The TADs incorporating the JIA haplotypes invariably included genes of immunologic interest. For example, the TAD incorporating the *IL2RA* haplotype including *IL15R* (the alpha chain of the IL15 receptor) and *PKCQ*, a protein kinase C-family enzyme important in both T and B cell activation. The most complex locus was *C5orf56* which encompassed 23 genes (including *IL3*, *IL4*, and *IL13*) and 3 miRNA within 4 loops and sub-loops. Genes within the TADs were highly enriched for multiple GO terms for processes involved in leukocyte activation (e.g., MAP kinase signaling cascade), JAK-STAT responses, chemotaxis, and cytokine-mediated signaling pathways.

Conclusion: These 20 JIA-associated risk loci are situated within complex chromatin regions that show similar features in both lymphoid and myeloid cells. HiC data demonstrate direct physical contacts between putative enhancers within the risk loci and multiple genes of immunologic interest. We hypothesize that at least some of the genes within the haplotype-associated TADs are the long sought "target genes" of JIA-associated genetic variants. This work emphasizes the importance of broadening our focus beyond the "nearest gene" to the GWAS-identified tag SNPs.

Disclosure of Interests: None declared

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OP0154

A NOVEL RELA TRUNCATION IN A 3-GENERATION FAMILY WITH BEHCET'S DISEASE ALTERS THE APOPTOTIC RESPONSE TO INFLAMMATORY STIMULANTS

Emma Dorris¹, Fahd Adeebe², Dylan Lawless³, Wan Lin Ng⁴, Aqeel Anjum⁴, Niamh Morgan¹, Eoin Cummins⁵, Sinisa Savic³, Alexander Fraser⁴, Gerry Wilson¹.

¹University College Dublin, Centre for Arthritis Research, Dublin 4, Ireland;

²University Hospital Kerry, Rheumatology, Tralee, Ireland; ³University of Leeds,

Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; ⁴University Hospital Limerick, Rheumatology, Limerick, Ireland;

⁵University College Dublin, School of Medicine, Dublin, Ireland

Background: Behcet's disease (BD) is a heterogeneous multifactorial auto-inflammatory condition characterised by recurrent episodes of oral and genital ulceration, uveitis and skin lesions, with less frequent involvement of the gastrointestinal tract, large blood vessels and central nervous system. The NF- κ B pathway is a 'master-regulator' of immune and inflammatory signaling, with the ability to control the expression of key inflammatory genes and genes associated with apoptosis and proliferation.

Objectives: To identify the pathobiology associated with a novel genetic mutation identified in a 3-generation family with Behçet's-like mucocutaneous ulceration syndrome, primarily involving childhood-onset chronic oral and genital ulcers.

Methods: The novel RELA mutation was identified using whole exome sequencing. Immunoblot of peripheral blood mononuclear cell (PBMCs) lysates from affected family members was used to determine if the predicted truncated protein was expressed. PBMCs were stimulated with TNF; NF κ B phosphorylation was measured relative to unstimulated cells from affected and unaffected family members. HEK293T cells transfected with plasmids encoding either wild-type or the novel RELA-mutant and overexpression confirmed via immunoblot. An in vitro model of the RELA truncation was used to observe the effect of the RELA truncation on response to TNF stimulation. Apoptosis protein arrays, western blots, and ELISA assays were used to investigate the effect of TNF on wild-type RELA compared to the mutant protein. Mouse Embryonic Fibroblasts (MEFs) isolated from RELA^{-/-} mice, which do not express endogenous RELA, were transfected with plasmids encoding either wild-type or the novel RELA-mutant. Wild Type MEF cells (with endogenous RELA) were used as a control. Cells were stimulated with LPS (2.5ug/ml) or no treatment control for 12 hours.

Results: A heterozygous cysteine deletion at position 1459 in RELA was detected in all affected individuals as previously reported. This mutation results in a frame-shift His487ThrfsTer7, producing a truncated protein of 492 amino acids. RELA-His487ThrfsTer7 heterozygotes have different phosphorylation kinetics of key NF κ B pathway proteins in response to TNF compared to wild-type controls. Cells overexpressing RELAHis487ThrfsTer7, had increased pro-apoptotic proteins (BAD, cleaved caspase 3 and SMAC) whereas anti-apoptotic proteins (BCL2, CLASPIN) were decreased compared to cells transfected with wildtype RELA. Cells transfected with RELAHis487ThrfsTer7 were less sensitive to TNF stimulation compared to wild-type controls, as measured by induction of TNF-sensitive proteins.

Conclusion: This study gives novel information on both the genetic basis and biological mechanisms of BD in individual families. Familial mutations that induce haploinsufficiency of RELA have recently been associated with BD. However, the His487ThrfsTer7 results in protein truncation rather than haploinsufficiency. Our study supports several recently published studies that loss-of-function mutations in the NF- κ B pathway are linked with the development of familial early-onset BD-like syndromes. We propose that RELAHis487ThrfsTer7 causes altered NF κ B signaling resulting in reduced mucosal cell recovery and the observed Behçet's-like mucocutaneous ulceration syndrome.

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Transformative care – the future

OP0155-HPR

TARGETS FOR REDUCING PREMATURE MORTALITY IN OLDER ADULTS WITH OSTEOARTRITIS: RESULTS FROM A NOVEL PATH ANALYSIS WITHIN A COX PROPORTIONAL HAZARDS MODEL

Ross Wilkie, Simran Parmar, Milica Bucknall. Keele University, Keele, United Kingdom

Background: There is increasing evidence that it is the impact of osteoarthritis rather than the osteoarthritis itself that explains an excess risk of mortality. This indicates that potentially modifiable targets may reduce mortality for those with osteoarthritis. Mediation analysis can be used to investigate pathways, although this has rarely been undertaken using survival analysis due to the challenge of accounting for time. The study uses a novel approach to examine mediation using path analysis with Cox proportional hazard modelling (survival analysis).

Objectives: The objectives of this study were to identify potential mechanisms of the impact of osteoarthritis on mortality and examine the role of modifiable targets (anxiety, depression, insomnia and walking frequency) for health professionals in rheumatology (HPRs).

Methods: A population-based prospective cohort study was conducted using data from the North Staffordshire Osteoarthritis Project (NorStOP), in which primary care medical record data was linked to self-report information collected by questionnaire in adults aged 50 years and over (n=8066). Individuals were defined as having osteoarthritis if they had consulted general practice for osteoarthritis, identified by Read codes in the primary care medical record, and indicated moderate to severe pain interference in daily life in the Medical Outcomes Short Form 36 at baseline (2002). A Cox proportional hazards analysis was performed to determine the total effect (TE) of osteoarthritis on mortality, both with adjustment for confounding variables (age, sex, education, occupation, smoking status, ischaemic heart disease, chronic obstructive pulmonary disease, non-steroidal anti-inflammatories, obesity, cognitive impairment). Within the Cox model, path analysis was used to decompose the TE to assess the indirect (IE) and direct effects (DE) for each of four potential mediators (anxiety, depression, insomnia, walking frequency; all measured by questionnaire) with adjustment for confounders. Results are expressed as adjusted hazard ratios (aHR); bootstrap resampling was used to generate 95% confidence intervals (95% CIs).

Results: Mean age of participants was 65.2 (SD 9.8) years and 51.6% were female. 2396 (29.7%) had osteoarthritis. Participants were followed up over 10 years during which time 1188 (14.7%) died. The rate of mortality was greater in those with osteoarthritis (52 deaths per 1000 person years) compared to those without (38 deaths per 1000 person years). Osteoarthritis was significantly associated with mortality (aHR 1.14; 1.00, 1.28). The relationship between osteoarthritis and mortality was mediated by walking frequency, depression and insomnia (anxiety did not mediate the relationship (IE HR 1.00; 0.98, 1.02)). The strongest mediator was walking frequency (TE 1.14; 1.00, 1.29; DE 1.04; 0.91, 1.18; IE 1.08; 1.06, 1.11), followed by depression (IE 1.06; 1.03, 1.08) and insomnia (IE 1.01; 1.00, 1.03).

Conclusion: This is the first study to examine mediation and highlights the importance of potentially modifiable targets for HPRs to reduce mortality in older adults with osteoarthritis. Encouraging people to maintain levels of physical activity at a population level and targeting a reduction in physical limitation in clinical practice to allow this, is important.

Disclosure of Interests: None declared

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OP0156-HPR THE FEASIBILITY AND EFFECTIVENESS OF TELEMEDICINE FOR KNEE OSTEOARTHRITIS IN DISEASE MANAGEMENT: A RANDOMISED CONTROL TRIAL

Zhengping Huang¹, Xiaoyan Zhong², Zhimin Xie², Li. Tianwang¹. ¹Guangdong Second Provincial General Hospital, Guangzhou, China; ²Guangdong Online Hospital, Guangzhou, China

Background: Osteoarthritis (OA) is a serious health concern worldwide, and patients with OA are in urgent need of proper long-term disease management to prevent disability and improve the quality of life. Research has started to investigate the feasibility and effectiveness of telemedicine in providing disease management for patients with chronic diseases. Guangdong Online Hospital (GOH) is the first officially recognized web-based hospital that widely provides telemedicine services in southern China.

Objectives: This study aimed to establish the feasibility and effectiveness of GOH in providing long-term disease management for patients with knee OA via a 6-month, randomised control trial (RCT).

Methods: 40 patients with knee OA were randomly assigned to receive conventional therapy (CT) in the clinic or conventional therapy plus a brief GOH-based intervention (CT-GOHT). GOH-based intervention included educational lectures, medical suggestions and psychotherapy. The primary outcome was the drop-out rates and the secondary outcomes included the mean change of the self-reported total score of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), the Multidimensional Fatigue Inventory (MFI), the Hospital Anxiety and Depression Scale (HADS) and the Pittsburgh Sleep Quality Index (PSQI) from baseline to endpoint.

Figure 1. Flow chat of trial participation

Figure 2. A telemedicine intervention to patients with knee OA

Results: The baseline characteristics were comparable between the two groups. 3 patients in CT group and 1 patient in CT-GOHT group lost to follow-up during the study ($P = 0.598$). A statistically significant difference was observed in the mean change of WOMAC recommended index of joint pain (8.82 ± 5.02 vs. 13.90 ± 7.63 , $P = 0.026$), morning stiffness (3.12 ± 1.50 vs. 4.42 ± 2.06 , $P = 0.039$), functional limitation (27.65 ± 9.91 vs. 38.84 ± 17.28 , $P = 0.025$), HADS-Anxiety (3.24 ± 2.41 vs. 5.32 ± 3.23 , $P = 0.037$), and PSQI global score (2.35 ± 1.54 vs. 4.21 ± 3.34 , $P = 0.043$) from baseline to endpoint when comparing the CT group to the CT-GOHT group. In addition, Guangdong Online Hospital was widely accepted by the including OA patients for their disease management.

Conclusion: Delivering a telemedicine intervention to patients with knee OA via GOH is a feasible and potentially effective method in long-term disease management, especially for patients living in remote areas. The results provide preliminary experiences and guidance for an upcoming full-scale RCT in disease management via telemedicine.

Trial registration: ChiCTR1800014465.

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- [1] Huang Z, et al. Implementation of telemedicine for knee osteoarthritis: study protocol for a randomized controlled trial. *Trials*, 2018, 19(1):232.

Table 1. Baseline characteristics of the two study groups

Variable	CT group (n = 20)	CT-GOHT group (n = 20)
Age	72.25 ± 8.84	67.25 ± 10.97
Female, n	15	15
Education, n	12	14
Primary school	8	6
High school		
Han Chinese, n	20	20
Income, n	8	5
<¥2000	10	13
¥2000 - ¥5000	2	2
>¥5000		
BMI, kg/m ²	25.85 ± 3.87	26.29 ± 2.96
Distance to hospital, kilometre	105.83 ± 100.35	111.33 ± 92.54
Kellgren-Lawrence grade, n	8	6
Grade I	10	13
Grade II	2	1
Grade III		
WOMAC pain, 0-10	18.90 ± 10.08	21.00 ± 8.38
WOMAC morning stiffness, 0-10	8.45 ± 4.89	9.25 ± 4.68
WOMAC function, 0-10	58.05 ± 20.55	63.30 ± 25.31
MIF	43.55 ± 19.77	45.70 ± 20.43
HADS-A	8.90 ± 5.55	8.30 ± 4.64
HADS-D	7.10 ± 5.28	6.85 ± 4.55
PSQI global score	7.35 ± 4.56	7.70 ± 5.13

Table 2. Mean change of outcome measures from baseline to endpoint

Results	CT group (n = 17)	CT-GOHT group, (n = 19)	P value
WOMAC pain	8.82 ± 5.02	13.90 ± 7.63	0.026
WOMAC morning stiffness	3.12 ± 1.50	4.42 ± 2.06	0.039
WOMAC function	27.65 ± 9.91	38.84 ± 17.28	0.025
MIF	17.53 ± 7.73	20.95 ± 8.75	0.225
HADS-A	3.24 ± 2.41	5.32 ± 3.23	0.037
HADS-D	2.12 ± 2.06	2.36 ± 2.01	0.714
PSQI global score	2.35 ± 1.54	4.21 ± 3.34	0.043

Disclosure of Interests: None declared

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OP0157-HPR EUROPEAN PATIENT VOICE IN GOUT SURVEY – SUBJECTIVE SATISFACTION IN GOUT PATIENTS VERSUS OBJECTIVE SUBOPTIMAL GOUT CARE

Marc De Meulemeester¹, Tim Jansen², Gudula Petersen³, Fernando Perez-Ruiz⁴.

¹MEDIF sprl, Gozée, Belgium; ²VieCuri Medisch Centrum, Venlo, Netherlands;

³Grünenthal GmbH, Aachen, Germany; ⁴Hospital de Cruces, Barakaldo, Spain

Background: Gout is the most common form of inflammatory arthritis with an increasing prevalence and incidence in many countries (1). Few information is available about current management of gout and satisfaction of patients living with gout.

Objectives: To evaluate diagnosis and treatment of gout from patient perspective to improve treatment outcomes for gout patients in Europe.

Methods: A 15 minute online survey with gout patients from 14 European countries (Austria, Belgium, France, Denmark, Germany, Italy, Ireland, Malta, Netherlands, Norway, Portugal, Spain, Sweden, Switzerland) was conducted in 2018. The design and content of the survey has been developed together with several patient and clinical experts

Results: 1,100 gout patients (78% males, mean age 55 years) with a mean number of 2.9 flares in the past 12 months completed the survey. 77% percentage of patients are suffering from co-morbidities (hypertension 52%, dyslipidemia 41%, overweight 40%, type 2 diabetes 23%, long-term illness of kidney/renal insufficiency 17%). It was reported that mainly general practitioners are involved in the diagnosis of the disease (73%), discussion of gout (68%) and treatment of last gout flare (59%), whereas rheumatologists are less involved in diagnosis (8%), discussion (15%) and treatment (11%) of last gout flare. 22% of patients were not diagnosed until they have had 4 or more flares. 71% of patients had flares in the past 12 months (thereof 33% ≥3 flares) which seemed to be particularly an issue for younger patients. 58% of patients receive uric acid lowering therapies, 43% pain killers, 25% colchicine, 13% non-medical pain relief and 12% corticosteroids. 59% of patients do not have regular follow up appointments for their gout and 53%