Results: An overall of 1788 studies was considered in the title/abstract screening. In the analysis, 51 articles were included, with an overall of 7488 participants. Twenty-two studies considered MVPA outcome alone, 16 studies number of steps alone and 13 studies reported information on both outcomes.
The results of this meta-analysis show that there is a high level of I^2 heterogeneity, 99%, according to diagnosis.
Recommended threshold for daily steps was reached for MVPA (36.35, 95% CI 29.39 - 43.31) but not for daily steps (-1092.60, 95% CI -1640.42 - -544.77), with fibromyalgia reporting a higher number (6290, 95% CI 5198.65 – 7381.62) of daily steps compared to other RMDs. Patients affected by chronic inflammatory arthropathies seem to fare better in terms of daily steps than the other categories. Patients with rheumatoid or other chronic arthritis reported a higher number of steps, respectively 6361 (95% CI 5382.51; 7340.35) and 6290.14 (95% CI 5198.65; 7381.62).
Non-elderly people show a higher overall level of physical activity compared to the elderly, 6796.11 (95% CI 5974.10; 7618.13) versus 5431.85 (95% CI 4633.76; 6229.95). Non-elderly group show higher level MVPA compared to the reference value 38.96 (95% CI 18.35; 59.68) vs 11.77 (95% CI 3.32; 20.21).
Conclusion: RMDs suffer of low level of physical activity and WDs are useful and affordable instruments to support the increase of it. WDs can be used in daily monitoring of physical activity in RMDs.
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Improving our care and understanding of paediatric RMDs

POS0164 GENETIC ANALYSIS OF WHOLE EXOME SEQUENCING IN A COHORT OF CHILDREN WITH REFRACTORY JIA REVEALS GENETIC RISK FACTORS FOR RARE JUVENILE DISEASES.

M. Tordoff[1], S. Smith[1], G. I. Rice[2], A. Morris[1], T. Briggs[2], W. Thomson[1,3], S. Eyre[1,3], J. Bowes[1,3]. [1]*The University of Manchester, Centre for Genetics and Genomics Versus Arthritis, Manchester, United Kingdom;* [2]*The University of Manchester, Division of Evolution, Infection and Genomics, Manchester, United Kingdom;* [3]*National Institute of Health Research Manchester Biomedical Research Centre, Manchester Academic Health Science Centre, Manchester, United Kingdom*

Background: Juvenile idiopathic arthritis (JIA) encompasses a group of heterogeneous rheumatic diseases of childhood onset. JIA can result in long term disability and remission is the main goal of treatment. However refractory disease can occur, which is defined as the absence of response to a standard disease therapy. A genetic basis for refractory disease has yet to be explored, where deleterious rare variants can complicate diagnosis or treatment outcome.
Objectives: To investigate, through genetic analysis, whether children with JIA that is refractory carry rare genetic risk factors in genes linked to monogenic diseases.
Methods: Whole exome sequencing of 99 children with JIA was performed with the Agilent SureSelect Human All ExonV6 kit. All quality control, variant filtering and annotation was performed in Varseq (version 2.2.1). Variants with a read depth <30 and genotype quality <80 were removed. Rarity and pathogenicity filters were then applied to remove variants with an allele frequency >1% (based on ExAC, gnomAD, gnomAD exome, NHLBI and 1KGp phase 3), classified as benign or likely benign on ClinVar, with a CADD PHRED score <15 and a REVEL score >0.7. Variants were annotated if they appeared in a gene from the primary immunodeficiency PanelApp (Martin et al., 2019), in a gene associated with an arthritis phenotype or in a gene that appeared on a paediatric monogenic gene list. The variants were then classified using ACMG guidelines (Richards et al., 2015) and benign, or likely benign, classified variants were removed.
Results: A total of 628 variants were identified and we found that 20 out of the 99 children screened were heterozygous for at least one recognised variant in a gene linked to a monogenic disease. Five of these children carried more than one recognised variant linked to monogenic genes. Here we provide a number of illustrative examples: three genes, *ADAR, ATP7B and MVK,* were prioritised based on prior evidence of associated disease. The variant p.Pro193Ala (gnomAD allele frequency (GAD) $2.2x10^{-3}$) of *ADAR* has previously been deemed pathogenic in a homozygous or compound heterozygous state for Aicardi-Goutières syndrome. Adenosine deaminases (ADARs) catalyse the hydrolytic deamination of adenosine to inosine in dsRNA and is suggested to act as a suppressor of type 1 interferon-stimulated genes. Within *ATP7B*, two distinct variants were detected; p.Gln1142His (GAD $1.6x10^{-5}$) and p.Ile1148Thr (GAD $4.0x10^{-5}$) have previously been reported as pathogenic, in combination with a third variant, for Wilson's disease and were carried by one individual in this cohort. *ATP7B* encodes copper-transporting ATPase 2, which supplies copper to ceruloplasmin. Variant p.Val377Ile (GAD $1.6x10^{-3}$) of *MVK* was detected in eight individuals in this cohort, interestingly five of these individuals also carried at least one *HLA-DRB1* stop-gained variant. This *MVK* mutation has been confirmed as pathogenic in a homozygous or compound heterozygous state for mevalonate kinase deficiency. MVK converts mevalonic acid into mevalonate-5-phosphate in the cholesterol synthesis pathway. Additionally, two stop-gained loss of function *HLA-DRB1* variants, p.Tyr107Ter and p.Gln125Ter, were detected in five and 20 individuals, respectively, in this cohort. *HLA-DRB1* is a recognised susceptibility locus for JIA.
Conclusion: Screening of a cohort of 99 children with JIA that have refractory disease has revealed that individuals carry deleterious variants in genes linked to monogenic forms of disease. These results highlight that the genetic basis for refractory disease needs to be further investigated. Carrying additional genetic risk factors to disease may complicate disease outcome and genetic screening of children with refractory JIA may improve treatment outcome in the future.
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POS0165 WHOLE EXOME SEQUENCING TO IDENTIFY RARE INFLAMMATORY VARIANTS IN AN IRISH COHORT WITH CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO)

D. O'Leary[1,2], O. Killeen[1,2], A. G. Wilson[1]. [1]*UCD, Centre for Arthritis Research, Dublin, Ireland;* [2]*Children's Health Ireland, National Centre for Paediatric Rheumatology, Dublin, Ireland*

Background: Chronic nonbacterial osteomyelitis (CNO) is a rare inflammatory disease affecting bone which predominantly occurs in the paediatric population. It is frequently associated with pustulosis, psoriasis, inflammatory bowel disease and arthritis, in particular enthesitis-related arthritis. Activation of the *NLRP3* inflammasome has been implicated in both human and mouse models of the disease.
Objectives: To identify a candidate list of rare, deleterious variants in known inflammatory genes in an Irish cohort with CNO.
Methods: 41 unrelated Irish children with CNO were recruited. Whole exome sequencing was performed on blood using Agilent SureSelect XT Human All Exon V6 kits and Illumina HiSeq 3000 with 150bp paired-end reads. Reads were aligned to the hg19 reference genome. After preprocessing, variants were hard filtered using quality by depth(QD) > 2.0, read depth (DP) >10 and genotype quality (GQ) >20. Synonymous variants and variants with MAF > 0.01 were excluded from further analysis. Remaining variants were filtered against existing databases of genes known to be associated with inborn errors of immunity, autoimmunity or autoinflammation. The Gene Damage Index (GDI) was used to identify genes which are least tolerant to variance and CADD phred-like scores to identify variants predicted to be deleterious. Genes with variants in >=2 CNO patients were included in the candidate list and variants manually checked using the Integrative Genomics Viewer (IGV).
Results: After filtering low-quality, synonymous and common variants, 17,293 variants were filtered against a database of 581 known inflammatory genes. 350 rare variants in 201 genes predicted to be intolerant to variance were identified. After excluding those present in one individual only, ranking by CADD phred-like scores and manual inspection on IGV, a candidate list of 25 genes remained. The same variant in *IL17RA, NLRP1* and *KMT2D* was present in 3 unrelated individuals (Table 1). *IL17RA* belongs to the Th17 pathway which is involved in psoriasis pathogenesis. *NLRP1* is implicated in several autoinflammatory diseases including psoriasis. None of the individuals carrying these variants in *IL17RA* or *NLRP1* have psoriasis. One individual with *IL17RA* variant has 1st-degree family history of psoriasis. Rare variants which are predicted to be deleterious were found in two individuals in each of the following genes in the IL-17 signalling/Th17 differentiation pathway: *IL17RB, IL17RE, IL25, HIF1A* (Table 1). This suggests that the Th17 pathway may play a role in disease pathogenesis in a proportion of children with CNO.
Conclusion: *IL17* +/- the IL-17 signalling/Th17 differentiation pathways, and *NLRP1* provide targets for further investigation in CNO. The role of these candidate genes may be further elucidated through gene-/pathway-based burden testing against a matched control population.
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