Macrophages, the IL23/IL17 pathway and dysregulation of IFN γ are strongly implicated in the pathogenesis of adult SpA but remain relatively unexplored in ERA.

Objectives: To compare levels of IL23 and IFN γ produced by monocyte-derived macrophages (MDMs) in the presence of lipopolysaccharide (LPS) from patients with ERA compared to healthy controls. The effect of clinical features such as enthesitis, peripheral and axial arthritis on IL23 and IFN γ expression was also studied.

Methods: Peripheral blood monocytes from 39 patients (68% HLA B27 positive, 84% male, median age 16 years 4 months, median disease duration 3 years 10 months) and 21 age and gender-matched healthy controls were differentiated *in vitro* with macrophage-colony stimulating factor in to macrophages. Differentiated cells were treated with IFN γ for 24 hours to upregulate HLA B after which the cells were washed and stimulated with LPS (50 ng/mL). IL23 and IFN γ expression from the cell culture supernatants were measured by ELISA and luminex assay respectively.

Results: IL23 expression was significantly higher in patients with ERA [median 53580 pg/mL (IQR 35735–83945 pg/mL) vs 32110 pg/mL (IQR 13745–48235 pg/mL), $p=0.01$], particularly in patients who were HLA B27 positive [median 64650 pg/mL (IQR 36400–99650 pg/mL), $p=0.0067$]. IL23 was not significantly different between patients with and without peripheral arthritis or axial arthritis. However, patients who had active enthesitis (assessed clinically or on scan within 6 months of the sample) had significantly higher IL23 expression compared to patients without enthesitis [median 75905 pg/mL (IQR 36728–99425 pg/mL) vs 38485 pg/mL (IQR 29923–63725 pg/mL), $p=0.014$] and healthy controls [$p=0.0017$]. Interestingly, patients who had both HLA B27 and active enthesitis had even higher levels of IL23 [median 79380 pg/mL (IQR 36540–103200 pg/mL), $p=0.0018$]. Conversely, levels of IFN γ were found to be lower from MDMs of patients with ERA compared to healthy controls, at baseline [median 3985 pg/mL (IQR 2820–6849 pg/mL) vs 6305 pg/mL (IQR 3938–8744 pg/mL), $p=0.0054$] and after LPS stimulation [median 9146 pg/mL (IQR 7438–11255 pg/mL) vs 11693 pg/mL (IQR 9481–13435 pg/mL), $p=0.013$]. No difference was found between patients who were HLA B27 positive and negative, although there was a trend towards lower levels of IFN γ in patients with enthesitis, this was not statistically significant.

Conclusions: IL23 expression is significantly higher from stimulated MDMs of patients with ERA compared to healthy controls, especially in HLA B27 positive patients with active enthesitis. This suggests a role for IL23 in the pathogenesis of ERA and supports the hypothesis that this sub-population of patients might benefit from IL23 blockade. Interestingly, IFN γ expression is lower in patients with ERA. Dysregulation of IFN γ has been shown to cause upregulation of the IL23/17 pathway in animal models¹ and thus may also contribute to the pathogenesis of ERA.

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OP0098 CLINICAL PICTURE AND SPECTRUM OF CONDITIONS ASSOCIATED WITH NLRP12 GENE MUTATIONS

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Background: NLRP12-related autoinflammatory disease (NLRP12-AID) is an exceptionally rare autosomal-dominant disorder caused by germ-line mutations in NLRP12 gene. Very few patients with NLRP12-AD have been identified worldwide, therefore there is a scarcity of data on phenotypic presentation of this syndrome.

Objectives: Here we provide evidence that NLRP12-AID may have clinical manifestations characteristic for primary immune deficiencies (PID).

Methods: 246 children with periodic fever (PF) of unknown origin were subjects to the next generation sequencing (NGS) analysis; 213 of these patients had signs of primary immunodeficiency (PID) manifested by recurrent infections, while 33 kids had isolated PF. The NGS panel was composed of 302 genes implicated in PID and/or AID.

Results: NLRP12 variants were detected in 20 cases (see the table 1). Median age of first AID-related fever episode was 12 months, ranging from 2 months to 13 years. Increased association with immune-mediated diseases ($n=15$, 75%) was observed. Nine patients demonstrated increased susceptibility to infection and two children suffered from Crohn's disease. Administration of short courses of

NSAID or corticosteroids resulted in resolution of the disease flare. In one severe case canakinumab (anti-interleukine-1 β antibody) was successfully used.

Abstract OP0098 – Table 1

NLRP12 mutation	ID, sex	NLRP12 related symptoms	Comorbid disease
p.H304Y	PK, f RI, m AA, f	PF, 1d/week Cyclic vomiting with hCRP since newborn Permanent aphthous stomatitis, PFAPA, AP	CVID, AIHA, pancytopenia, S, ILD Severe CD, food and drug allergy
Asn715>Ser	ZV, m KA, m VM, m	PF (infections?) PF 5–7d/month with LA, redness, eye pain	Congenital red-cell aplasia, AIHA, S, LA CVID, AIHA, S, LA, ILD, thrombocytopenia Chronic posterior scleritis Episodes of severe respiratory infection Severe CD, S
p.F402L	GA, f GE, m	PF PF	Meningitis, septic shock, otitis, Severe recurrent MAS, ILD
Thr861Ser	CA, m KS, m AR, m	PF (infections) Episodic AP, diarrhoea 1d PF	
Gln417Leu	SK, m	Persistent fever	
Arg352Cys	DE, f	PF, S, A, AP, urticaria, growth delay,	
p.Ala57Ser	AK, m	Respiratory and intestinal infections with PF	Bacterial meningitis
p.Ala5Glu	HT, m	PFAPA-like syndrome headaches +eye pain PF, A	
p.Arg723Gln	BA, f	PF (infections?)	Recurrent purulent sinusitis w/o fever
p.Val936Leu	GA, f		
p.Tyr246Cys	ES, f	FCAS, relapsed aseptic peritonitis	
p.Gly52Ser	KV, f	PF (infections?)	
p.R738fs	SD, m	1–4d of PF, cold-induced, 3–4/ year,	pneumonia, febrile seizures, brain oedema

Abbreviations: A-arthritis, ABA-abatacept, AIHA-autoimmune hemolytic anaemia, AP-abdominal pain, CD-Crohn's disease, CKB-canakinumab, CVID-common variable immunodeficiency, d-day, ILD-interstitial lung disease, LA-lymphadenopathy, PF-periodic fever, S-splenomegaly

Conclusions: Significant number of patients with genetically assigned diagnosis of NLRP12-AID have clinical features which close resemble PID. This phenotypic overlap may result in underdiagnosis of NLRP12-AID among patients with PID.

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OP0099 REMISSION IN JIA CAN BE PREDICTED FROM ONE YEAR FOLLOWING DIAGNOSIS IN A UK MULTICENTRE INCEPTION COHORT

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Background: One of the primary aims for children and young people with JIA is remission. Early improvement in disease likely predicts greater chance of remission in the longer-term.

Objectives: To assess the association between change in disease activity over the first year of disease and later occurrence of remission.

Methods: Children and young people with oligoarticular, RF-negative or RF-positive polyarticular JIA recruited to the Childhood Arthritis Prospective Study prior to January 2014 were selected for analysis.

Two definitions of remission based on clinically inactive disease at two consecutive study follow-ups were explored: 1) Wallace's preliminary criteria and 2) the clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS10). Association between changes in JIA core outcome variables and pain over the first year of disease and later occurrence of remission were analysed using logistic regression models, adjusting additionally for age, gender, symptom duration and predictor value at presentation. Oligoarticular and polyarticular JIA were modelled separately. Multiple imputation accounted for missing data.

Results: A total of 1045 children were included. Of these, 70% were female and the majority had oligoarticular JIA (67%). The median age at presentation was 7 years (IQR 3, 11). Within three years, 25% achieved remission according to Wallace's criteria and 39% according to cJADAS10. More children with oligoarticular JIA achieved remission than those with polyarticular JIA (table 1).