



## Synovial fluid proteome expression patterns segregate juvenile idiopathic arthritis patients

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**Results:** Proliferation of T cells when co-cultured with adenoviral-infected DC was inhibited both in healthy volunteers (allogeneic response) and samples from PB from children with JIA. However only minimal or no significant reduction in T cell proliferation was seen when T cells were from the synovial fluid compartment. The effect was not due to direct rAd infection of T cells.

**Conclusions:** We have shown that tolerogenic DC from synovial cells of children with arthritis can be generated in vitro. These DC were able to inhibit T cell proliferation when T cells were obtained from peripheral blood. Our data suggest that T cells from the joint were resistant to this suppression. The mechanisms of this resistance will be important to elucidate since this may provide new therapeutic targets for childhood arthritis.

**Disclosure:** The authors have declared no conflicts of interest.

#### 87. THE USE OF AN AGE SPECIFIC NORMAL RANGE TO INCREASE DETECTION OF ANTI-CYCLIC CITRULLINATED PEPTIDE (ANTI-CCP) ANTIBODIES AND RHEUMATOID FACTOR (RF) IN JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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**Background:** The presence of anti-CCP antibodies has been well established in adult Rheumatoid Arthritis patients and children with JIA. Current commercial ELISA kits use a reference 'normal range' derived from the adult population. Anti-CCP antibody testing is not currently used for diagnosis of JIA given the low sensitivity (reported detection rates of 4-10% in recent studies).

The aim of this study is to demonstrate whether using a paediatric normal range for CCP and RF testing results in higher detection rates, which may increase the value of these tests in a clinical setting.

**Methods:** Serum samples were collected from 43 patients with JIA and 26 juvenile controls. Anti-CCP antibodies were detected using a combination of anti-CCP2 (Axis-Shield), anti-CCP3 (Inova) and an in-house peptide (cfc-1-cyc Invitrogen). IgM RF and IgA RF were also measured in these samples by ELISA. The manufacturer's normal range was compared with a normal range calculated from the 26 non-JIA controls (within 2 standard deviations from the mean).

**Results:** Measurement of anti-CCP2 antibodies in JIA identified 16% being positive using the manufacturer's normal range. Sensitivity was increased to 23% in this assay using a normal range calculated from serum of juvenile controls. Using a combination of all 3 assays, the detection rate of anti-CCP antibodies was also 23% when an adult normal range was applied. However, this increased to 33% if the juvenile normal range was applied. 2 of the 26 juvenile controls tested positive using the combined kits. Screening for RF isotypes IgM or IgA identified 11 out of 42 (26%) JIA patients. 20 out of 43 (47%) JIA patients had autoantibodies to either anti-CCP or RF.

**Conclusions:** We have found that using a juvenile rather than an adult normal range from age-matched controls increased the detection rate of anti-CCP antibodies in JIA. This suggests that levels of anti-CCP antibody may change with age. However, in order to prove this, a large scale study using appropriate age-matched controls is needed.

At present, there is no single auto-antibody which is useful in diagnosing JIA. We have demonstrated that combining RF with anti-CCP increased the serological positivity to 47%. Therefore, screening for a combination of auto-antibodies may be useful in diagnosing JIA.

**Disclosure:** The authors have declared no conflicts of interest.

#### 88. SYNOVIAL FLUID PROTEOME EXPRESSION PATTERNS SEGREGATE JUVENILE IDIOPATHIC ARTHRITIS PATIENTS

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**Background:** Synovial fluid (SF) is a potential source of novel biomarkers for many arthritic disorders involving joint inflammation, including Juvenile Idiopathic Arthritis (JIA). We first compared the distinctive protein expression patterns of local joint inflammation in SF with systemic profiles within matched plasma samples. Preliminary investigations were performed into whether local or systemic proteome 'fingerprints' could distinguish between oligoarticular, extended oligoarticular and polyarticular forms of this chronic juvenile disease.

**Methods:** In this study we analysed matched SF and plasma samples obtained from 10 newly diagnosed JIA patients (<6 months disease duration): 3 with oligoarticular arthritis, 3 extended oligoarticular and 4 polyarticular disease. Matched samples were taken at the initial inflammatory episode. We profiled the SF and plasma proteomes using a two-dimensional difference gel electrophoresis (DIGE) approach. Progenesis PG240 software analysis of plasma and SF gel scans was used to highlight joint-specific and plasma proteins differentially expressed across the study group. Protein spots of interest were identified by matrix-assisted laser desorption ionization (MALDI-TOF) and confirmed by nanoelectrospray-ionisation mass spectrometry.

**Results:** 2D DIGE reveals 899 spots per gel within the pH 4–7 range for synovial fluid and plasma. Comparison of plasma and synovial gel scans, revealed a sub-population of 143 spots which predominate in synovial fluid or plasma. Hierarchical clustering based on the expression levels of a set of 54 proteins with at least two fold expression differences between the two body fluids segregates the synovial

fluid from the plasma samples. Proteolytic fragments of anti-inflammatory proteins inter-alpha trypsin inhibitor, alpha-1 antitrypsin, transthyretin and apolipoprotein A-1 were identified. Principle component analysis of five different protein features could be used to segregate patients into clinical subgroups.

**Conclusions:** Synovial fluid and plasma proteomes can be used to segregate a heterogeneous group of JIA patients into clinical subgroups. Such an approach could allow us to identify biomarkers useful in the prediction of disease progression, and therefore enable earlier and more appropriate therapeutic intervention. Definition of protein profiles which discriminate clinical subgroups of arthritic disease may assist in the diagnosis of juvenile arthritis at an earlier stage than is currently possible.

**Disclosure:** The authors have declared no conflicts of interest.

#### 89. STEROID USE IN THE MANAGEMENT OF ACUTE JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS - A NATIONAL SURVEY

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**Background:** Corticosteroid treatments, along with cytotoxic and disease modifying agents, form the crux of the every day management of JSLE (Juvenile Systemic Lupus Erythematosus). However this is not without significant side effects, particularly in children. There are no randomised controlled trials investigating the optimal steroid regime in JSLE and there is a paucity of evidence to draw upon, even in adult studies.

**Methods:** On behalf of the UK JSLE Study Group we issued a standardised questionnaire, designed to elucidate current practise in the prescription of steroids during induction of remission and treatment of flare of JSLE, defined as a typical child presenting with BILAG (British Isles Lupus Assessment Group) A disease. This was sent to the lead paediatric rheumatologist & nephrologist in each UK tertiary centre involved the UK JSLE Study Group.

**Results:** 18/26 (69%) questionnaires were returned (8 nephrology; 10 rheumatology units) representing 13 centres.

Management of BILAG A at presentation:

All participants reported using pulsed intravenous methylprednisolone (IVMP) as the steroid treatment of choice for induction of remission at presentation. The most widely used dosing was 30 mg/kg (n = 11) or 600 mg/m<sup>2</sup> (n = 4) for 3 doses. The majority of clinicians (n = 14) gave repeated IVMP (variable intervals/duration). 17/18 reported using oral prednisolone in addition to the IVMP, the most widely used doses being 60 mg/m<sup>2</sup> (n = 5) or 1–2 mg/kg (n = 5). Weaning regime was determined by time in 4 units while 13 units used clinical parameters including reduction in BILAG, biomarkers, & physician's clinical assessment. Weaning regimes varied between all units. Ten units reported routine use of maintenance steroids; the dose range was usually 5–10 mg. Personal experience was the main rationale for treatment decisions.

Management of Disease Flare (to BILAG A):

In the treatment of flare of JSLE, 15 units reported using pulsed IVMP; 10 units also increased oral prednisolone doses; 3 reported increasing oral prednisolone dose alone. IVMP doses for flare were similar to those for induction of remission at diagnosis, as was the weaning regime of oral prednisolone (wide variance noted between clinicians) and use of maintenance steroids.

**Conclusions:** Steroid prescribing for acute JSLE varied widely between and within units. As part of the UK JSLE Study Group, with an emerging clinical trials agenda, it is vital to accrue an evidence base to direct steroid prescribing in the management of JSLE acute presentation and flare. With paucity of evidence from the literature, expert opinion (category D evidence) forms the main basis for current treatment. We aim to carry this research forward and clinical trials to guide steroid use in this setting are in development.

**Disclosure:** The authors have declared no conflicts of interest.

#### 90. PAIN AND QUALITY OF LIFE PERCEPTION IN CHILDREN WITH HYPERMOBILITY SYNDROME

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**Background:** Hypermobility syndrome (HMS) is a major source of morbidity in children. Due to pain, activities of daily living, physical and sports activities may be limited in children with HMS (Murray and Woo 2001). However, this has not been well documented. Ruperto et al (2004) reported that functional ability and physical and psychosocial well-being of children with generalised joint laxity were not affected when compared with healthy controls. Their study was conducted on children with generalised joint laxity, however, and not those with HMS. Therefore, it is currently unclear whether quality of life (QoL) in children with HMS is affected. This study compared pain and QoL in children diagnosed with HMS with healthy controls.

**Methods:** Sixty-six children (29 diagnosed with HMS and 37 healthy children) aged 8–15 years participated in this study. Ethical approval was obtained for the study. Informed written consent was obtained from the participants and their parents/guardians. A diagnosis of HMS was established using the Beighton criteria (Beighton et al 1973). The test knee was determined in healthy children using