Methods: Sera were obtained from 101 patients satisfying the ILAR classification criteria for JIA and in 25 patients with two other dysimmune disorders (type 1 diabetes and juvenile inflammatory bowel disease). Level of IgG antibodies against *P. gingivalis* and *Prevotella Intermedia* were obtained by homemade ELISA already used previously (5).

Results: In the JIA group, major children were oligoarthritis (47.5%), polyarthritis represents 31.7% of JIAs, ERA and systemic forms of JIA are respectively 9 and 11%. For the control group, 10 (40%) children had diabetes and 15 (60%) had IBD.

Levels of anti-*P. gingivalis* anti-*Prevotella Intermedia* antibodies were higher in AJI group compared at control groups ($P < 0.01$, $P < 0.05$). These difference are mainly related to oligoarthritis and ERA subsets for both *P. gingivalis* and *Prevotella Intermedia*.

Figure 1. Relative titer of antibodies to *P. gingivalis* and anti *Prevotella intermedia*.*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$. *P. gingivalis* (control vs oligoarthritis $p = 0.0032$, control vs ERA $p = 0.0092$). *Prevotella intermedia* (control vs oligoarthritis $p = 0.0194$, control vs ERA $p = 0.0039$).

Conclusion: We confirmed high level of anti-*P. gingivalis* and anti-*Prevotella intermedia* antibodies in JIA compared to other inflammatory disorders. For the first time, we observed that this high level was mainly in oligoarthritis and ERA. Further investigations are required to investigate involvement of oral dysbiosis in AJI pathogenesis. As observed in RA, it could be a new way to integrate in JIA therapy management.

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POS0069

INCREASED T CELL RESPONSES, METABOLIC ACTIVITY AND FIBROBLAST INVASIVE CAPACITY IN CHILDREN WITH DOWN'S SYNDROME-ASSOCIATED ARTHRITIS COMPARED TO JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) was thought to be the most common inflammatory arthritis in children (Shih *et al.*, 2019). However an aggressive,

erosive arthritis of little-known immunologic mechanism occurs 20 times more frequently in children with Down's syndrome (Foley *et al.*, 2019).

Objectives: This study was undertaken to characterize immune cell responses and synovial fibroblast invasiveness in children with Down's syndrome-associated arthritis (DA).

Methods: Multiparametric flow cytometric analysis was used to examine peripheral blood T cell, B cell and monocyte populations. In addition, T cell cytokine responses and their metabolic profile in children with DA, JIA, Down's Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of DA primary synovial fibroblasts (FLS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF- α , IL-17a, IFN- γ , GM-CSF). The two major energy pathways glycolysis (ECAR) and oxidative phosphorylation (OCR) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified by wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, and ELISAs.

Results: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of CD4⁺ and CD8⁺ TNF- α , IFN- γ and GM-CSF producing T cells. The frequency of T peripheral helper (Tph) cells were elevated in children with DA compared to all other groups. In parallel, an increase in their metabolic profile evident by higher phosphorylation of mTOR pathway components AKT, mTOR and S6. Comparison of DA and JIA FLS demonstrated that DA FLS display a more invasive/migratory capacity and are more metabolically active. Based on the increased cytokine responses in DA T cells, we next examined the effect T cell derived cytokines TNF- α , IL-17a, IFN- γ and GM-CSF alone and in combination on DA FLS function. TNF- α , IL-17a and IFN- γ induced IL-6, RANTES and MCP-1 secretion, with no effect observed for GM-CSF. Furthermore, TNF- α and IL-17a induced DA FLS migration and PBMC adhesion to DA FLS. Finally IL17a and IFN- γ potentiated the effect of TNF- α on IL-6 and MCP-1 secretion compared to stimulations alone.

Conclusion: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLS phenotype compared to that of JIA, with T cell derived cytokine alone and in combination further inducing DA FLS pathogenic mechanisms. These effects mirror the increased erosive disease observed clinically.

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POS0070

POPULATION PHARMACOKINETICS OF INFLIXIMAB IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Higher dosage regimes for Infliximab (IFX) have been described to be effective in partial- or non-responding adults and children with rheumatic disease and appear to be safe (1,2). To optimize IFX treatment in juvenile idiopathic arthritis (JIA) patients, therapeutic drug monitoring (TDM) might be beneficial. To support routine TDM of IFX and dose regimen optimization in JIA patients, more in-depth knowledge of the pharmacokinetic (PK) variability of IFX is needed. Ultimately, as soon as the optimal therapeutic drug ranges will be known, PK model-based simulation can be used to individualize drug dosing recommendations. Individual dosages may be adjusted by taking specific patient characteristics into account that explain inter-patient variability in pharmacokinetics (PK). Inter-patient variability can be quantified and investigated by the population approach.

Objectives: Our hypothesis is that optimizing dosage and frequency of IFX administration for individual patients will improve treatment outcome. In this current study, the population PK for IFX are described for JIA patients.

Methods: Data including IFX trough concentrations and anti-IFX antibodies of 27 JIA patients on IFX maintenance treatment were retrieved from electronic charts. Three population pharmacokinetic models from literature were validated for our dataset using nonlinear-mixed effects modeling program NONMEM (3,4,5). A novel population pharmacokinetic model was developed based on our study data.