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Innate immunity in rheumatic diseases

SAT0001 LACK OF OBESITY-RELATED FEATURES IN ADIPOCYTES AND INFLAMMATORY CELLS IN THE INFRAPATELLAR FAT PAD (IFP)

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Background: Obesity is associated with the development and progression of osteoarthritis (OA), both for weight-bearing and non-weight bearing joints. Several lines of research indicate that obesity-related systemic factors, such as adipose tissue-derived factors, could be involved in this association. The infrapatellar fat pad (IFP) is an adipose tissue depot localized in the knee joint. and could mediate obesity-associated effects. However, it is currently unknown whether and how obesity affects IFP.
Objectives: To investigate the presence of obesity-related features in adipocytes and infiltrating immune cells in the IFP of OA patients.
Methods: Knee OA patients (N=155: 68% women, mean age 65 years, mean (SD) BMI 29.9 kg/m^2 (5.7)) were recruited: IFP volume was determined by MRI in 79 knee OA patients, while IFP and subcutaneous adipose tissue (SCAT) were obtained from 106 patients undergoing arthroplasty. Crown-like structures (CLS) were determined using immunohistochemistry. Adipocyte size was determined by light microscopy and histology. Stromal vascular fraction (SVF) cells were characterized by flow cytometry.
Results: IFP volume (mean (SD) 23.6 (5.4) mm^3) was associated with height, but not with BMI or other obesity-related features such as waist circumference, fat percentage and waist to hip ratio. The volume of IFP adipocytes did not correlate with BMI, in contrast to SCAT adipocytes. Few CLS were observed in IFP and their number did not differ between individuals with high and low BMI. Moreover, high BMI was not associated with higher infiltrating immune cell numbers in IFP, nor with changes in immune cell populations. Likewise, no molecular differences were observed in FCM-secreted factors between high and low BMI, except for an increased TNFa secretion in obesity. Since obesity is usually associated with a shift towards pro-inflammatory macrophages in conventional adipose tissue, we have extensively characterized IFP macrophages. Surprisingly, CD206 and CD163, usually associated with an anti-inflammatory phenotype were the most abundantly expressed surface markers on macrophages (81% and 41% respectively). In contrast, cytokine profiles revealed a pro-inflammatory phenotype of the total macrophage population, with cells producing predominantly IL-6 and TNFα, but little IL-10. Interestingly, the CD163+ macrophages were bigger and had a more activated and pro-inflammatory phenotype than their CD163- counterparts. However, no association with BMI could be observed for different macrophage populations or their cytokines.
Conclusions: BMI-related features usually observed in SCAT and visceral adipose tissue could not be detected in IFP of OA patients, a fat depot implicated in OA pathogenesis.
Disclosure of Interest: None declared
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SAT0002 INNATE LYMPHOID CELLS (ILCS) ARE DIFFERENTIALLY DISTRIBUTED IN INFLAMMATORY AND NON-INFLAMMATORY JOINT DISEASES

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Background: Innate lymphoid cells (ILC) are immune cells of the lymphoid lineage not expressing specific antigen receptors.They are classified into three subsets: *ILC1* (including Natural Killer (NK) cells and ILC1) secrete IFN-γ and TNF-α; *ILC2* secrete IL-4, IL-5, IL-9, IL-13, and amphiregulin; *ILC3* (including Lymphoid Tissue Inducer (LTi) and NK cell activating receptor (NCR+ ILC3) secrete IL-17A and IL-22.
Objectives: To enumerate the different subsets of ILCs in peripheral blood and synovial fluids of patients with inflammatory and non-inflammatory joint effusions.
Methods: Patients with confirmed synovial effusion presenting at the Centre hospitalier universitaire de Sherbrooke (CHUS) signed an informed consent form. Cells from joint effusions were separated by Ficoll-density gradient centrifugation, stained for ILC, and analysed using a BD FACS Aria III flow cytometer. For cytokine detection, cells were stimulated for 6h with PMA/ionomycin prior to cell staining. The distribution of ILC subtypes according to various diagnoses is presented in cells/ml and ratios of ILC subtypes per ml of synovial fluid relative to peripheral blood. The protocol was approved by the CRC-CHUS ethics committee.
Results: Synovial fluids and blood from 57 patients with various diagnoses were analyzed. The highest concentrations (cells/mL) of ILC cell subtypes found in the synovial fluids/peripheral blood were: ILC1: 7/4; ILC2: 70/3; LTi: 4x10^4 (in RA)/8x10^4 (in OA); NCR+ ILC3: 1.3x10^5 (in JIA)/5.8x10^4; NK: 5/1.
Synovial fluids relative to peripheral blood frequently presented ratios of ILC cell subtypes $\leq$1, suggesting little preferential homing in the joints. However, synovial fluids (relative to blood) were enriched 45 and 7 times for NCR+ ILC3 in Juvenile Idiopathic Arthritis (JIA) and spondylarthropathy patients, respectively, and 8 and 6 times for LTi in Psoriatic Arthritis and Rheumatoid Arthritis (RA) patients, respectively. We observed marked heterogeneity in ILC numbers within patients with the same inflammatory joint diseases. Part of this heterogeneity was associated with the presence of concomitant joint degenerative disease and low cell numbers in the synovial fluids.
Conclusions: 1. LTi and NCR+ ILC3 subtypes are the ILC most abundant in synovial fluids.
ILC1 and NK cells are rare in synovial fluids and unlikely to be involved in pathogenesis; ILC2 remain infrequent, even when enriched in synovial fluid relative to peripheral blood (e.g. in JIA, RA and gout).
2. Relative to their concentrations in peripheral blood, LTi and NCR+ ILC3 subtypes are markedly enriched in synovial fluids of patients with autoimmune-mediated diseases, notably LTi in RA and Psoriatic Arthritis, and NCR+ ILC3 in spondylarthropathy and JIA. The abundance of these IL-17 secreting cells in synovial fluids from these diseases is especially intriguing.
3. We observed significant heterogeneity within patients with the same clinical diagnosis.
4. The pathophysiological implications of the differential distribution of subtypes of ILC cells across diseases and within clinical diagnoses remain unclear.
Disclosure of Interest: None declared
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SAT0003 SINGLE-NUCLEOTIDE POLYMORPHISMS ASSOCIATED WITH P2X7R FUNCTION REGULATE THE ONSET OF GOUTY ARTHRITIS

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Background: Gout is an inflammatory disease, considered to be caused by the increased production of IL-1β stimulated by monosodium urate (MSU) crystals. However, some hyperuricemia patients, even gouty patients with tophi in the joints, never have gout attack, indicating some other pathogenic pathways participating in the secretion of IL-1β rather than MSU in the pathogenesis of acute gouty arthritis. ATP-P2X7R-IL-1β axis may be one of them.
Objectives: The purpose of this study is to explore the role of ATP in the pathogenesis of gout, and the association between ATP receptor (P2X7R) function associated single nucleotide polymorphisms and gout arthritis.
Methods: The non-synonymous SNPs loci of P2X7R in Chinese people were screened, to compare the frequencies of different alleles and genotype distribution of selective SNPs in 117 gouty patients and 95 hyperuricemia patients. Then peripheral white blood cells were purified from the peripheral blood of randomly selected 43 gout patients and 36 hyperuricemia patients from the total. After culturing the cells with MSU or MSU+ATP, supernatants were collected and the concentrations of IL-1β were detected by enzyme linked immunosorbent assay (ELISA).
Results: 1. Eight SNPs loci including rs1653624, rs10160951, rs1718119, rs7958316, rs1621388, rs16950860, rs208294, rs17525809 and rs2230912 were screened and detected, and rs1653624, rs7958316 and rs17525809 were demonstrated associated with gout arthritis. 2. After the stimulation with MSU+ATP, the concentrations of IL-1β in supernatants of gouty patients were significantly higher than that in hyperuricemia groups [(131.08±176.11)pg/ml vs (50.84±86.10)pg/ml]. Furthermore, gouty patients carrying susceptibility genotype AA or AT of rs1653624 had significant higher concentration than that carrying non-susceptibility genotype TT [(104.20±164.25)pg/ml vs (21.90±12.14)pg/ml]. However, no differences were found while stimulated with MSU alone.
Conclusions: ATP promotes the pathogenesis of gouty arthritis by increasing the secretion of IL-1 β, and its receptor (2X7R) function associated single nucleotide polymorphisms may be related to gouty arthritis, which indicates that ATP-P2X7R signaling pathway plays a significant regulatory role in the pathogenesis of gout.
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SAT0004 NEW AUTOANTIGEN (JKTBP) PART OF STRESS GRANULES CLOSES THE SENSITIVITY GAP IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis triggers the formation of prion-like stress granules. To investigate which members of the heterogeneous nuclear ribonucleoprotein (hnRNP)-family, components of functionally important subcellular