included the mitogen-activated protein kinase (MAPK) p38 and Akt. MTX did not inhibit TNF α -induced nuclear factor kappa B (NF κ B) transcriptional activation, signaling or target gene expression. However, MTX induced pro-inflammatory markers such as vascular cell adhesion molecule (VCAM)-1 in an additive manner with TNF α . Functionally, MTX did not induce apoptosis but caused S-phase cell cycle arrest, which, along with p38 and Akt activation, could be abrogated by supplementation with folic acid.

Findings to date in EC subjected to shear stress are somewhat different. MTX had no or a mild inhibitory effect on kinase signaling in EC under LSS and OSS respectively. MTX did not affect cell proliferation nor baseline or OSS-induced VCAM-1 expression in EC under shear stress.

Conclusion: In static EC, low-dose MTX caused cell cycle arrest through folate depletion, which is a known mechanism of action in other cell types. Of note, this response was not seen in EC pre-conditioned by shear stress and emphasizes the impact of biomechanical forces on endothelial phenotype and response to exogenous stimulation. This is the first report to study the effects of MTX on EC under shear stress, which will be crucial in understanding its molecular actions on the vasculature.

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AB0131

THE CORRELATION OF EXPRESSION OF DIFFERENTIAL DRUG-RESISTANT PROTEINS AND INFLAMMATORY CYTOKINES IN COLLAGEN INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease. The most characteristic patho-logical changes are chronic synovitis. At present, the combination of traditional disease-difying anti-rheumatic drugs (DMARDs) and biological agents DMARDs has improved the therapeutic effect of RA, but some RA patients still have poor response due to Multidrug resistance (MDR) phenomenon. The main mechanism of MDR is related to the ATP-binding cassette (ABC) transporter superfamily members, which increases drug efflux and reduces intracellular drug concentration. We will study how cytokines regulate the expression of ABC transporters.

Objectives: By comparing the differential expression of ABC transporter family resistance-related proteins P-gp, BCRP, MRP1 and inflammatory cytokines IL-1 β , IL-2, IL-6, IL-10, TNF- α and IL-17 in CIA model mice, to investigate the correlation between Inflammatory cytokines and drug-resistant proteins.

Methods: Fourteen DBA1 mice were successfully induced by collagen and Freund's Adjuvant. According to the scores of synovial pathology, the CIA group was divided into mild, moderate-to-severe groups, another four mice were selected as control. The mRNA expressions of P-gp, BCRP, MRP1 in splenic lymphocyte cells were measured by RT-PCR. The concentrations of IL-1 β , IL-2, IL-6, IL-10, TNF- α , IL-17 in serum were detected by Cytometric Bead Array(CBA). Further analyze the correlation between different inflammatory cytokines and these proteins, then study one of the proteins which is most related with cytokines by immunohistochemical (IHC) in synovium. Two independent samples were analyzed by the Mann-Whitney U test. Non-parametric Kruskal-Wallis H test was performed on multiple independent samples. The correlation between variables was used by Spearman correlation analysis.

Results:

1. Compared with the normal controls, The level of IL-6 and TNF- α in the serum of mild CIA group, moderate-severe CIA group were significantly increased ($Z_1=14.383$, $P_1<0.05$, $Z_2=8.375$, $P_2<0.05$). Compared with the mild CIA group, the level of IL-6 in serum were significantly increased in the moderate-to-severe CIA group ($P<0.05$), but there was no distinct difference in the TNF- α level ($P>0.05$).

2. In the spleen lymphocytes, there was no significant difference in the the mRNA expression level of P-gp and BCRP among the groups, but the mRNA expression level of MRP1 were significantly increased ($P<0.05$). Compared with the mild CIA group, the MRP1 mRNA in the moderate-to-severe CIA group was higher, there was significant difference ($Z=12.634$, $P<0.05$). There was a correlation between mRNA expression of MRP1 and P-gp ($r=0.635$, $P=0.015$).
3. The mRNA expression of MRP1 was positively correlated with IL-6 level ($r=0.711$, $P=0.004$).
4. The expression of MRP1 in normal group, low-level IL-6 group and high-level IL-6 group were respectively as follows: 1.08(0.65,1.30), 1.40(1.13,2.07), 1.90(1.68,2.17).
5. Compared with the controls, the cytoplasm/membrane of the knee and ankle joint synovial tissue in the CIA group was yellowish-brown, which proved that MRP1 expression was positive.

Conclusion: In the CIA arthritis model, synovial tissue lesion is not only related to inflammatory cytokines, but also related to MRP1 expression in the ABC transport resistance protein family, and it is proved that IL-6 is highly correlated to MRP1.

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AB0132

A NOVEL TARGET FOR TREATMENT OF INFLAMMATORY JOINT DISEASES

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Background: The bile salt-stimulated lipase (BSSL) is a hitherto unrecognized player in inflammation. Animals devoid of BSSL (knockout mice) are protected from developing collagen induced arthritis (CIA) and collagen antibody induced arthritis (CAIA), and antibodies directed towards BSSL has been proven to prevent or mitigate arthritis in mouse and rat arthritis models¹. In humans, BSSL is present in blood² and accumulate at sites of inflammation. Patients with acute pancreatitis have significantly increased plasma BSSL levels compared to healthy controls. Whether BSSL in blood originates from pancreas, inflammatory cells, or both remains to be elucidated.

Objectives: To determine BSSL concentration in blood samples from patients with inflammatory joint disorders and to evaluate possible relationships between circulating BSSL levels and disease-activity variables.

Methods: BSSL concentrations in plasma or serum were determined in patients with rheumatoid arthritis (RA), psoriasis arthritis (PsA), and juvenile idiopathic arthritis (JIA) by a sandwich enzyme-linked immunosorbent assay (ELISA). Correlations between BSSL concentrations and disease activity score, erythrocyte sedimentation rate (ESR), blood levels of C-reactive protein (CRP), S100A8/9, leukocyte- and neutrophil counts, proinflammatory cytokines and chemokines were analyzed using Spearman rank-order correlation.

Results: Significant correlations between BSSL concentration in plasma and disease activity score (DAS28, $r_s=0.31$, $p=0.007$), ESR ($r_s=0.58$, $p<0.000$), CRP ($r_s=0.42$, $p=0.012$), leukocytes ($r_s=0.66$, $p<0.000$), and neutrophils ($r_s=0.71$, $p<0.000$) were found in RA. The BSSL plasma concentration decreased with duration of treatment with the TNF α inhibitor infliximab, in parallel with decreasing DAS28 score.

BSSL concentration was significantly higher in sera from PsA patients with both oligo- and polyarthritis compared with healthy controls. Moreover, BSSL concentration in serum correlated significantly with S100A8/9 and CRP concentrations ($r_s=0.54$, $p<0.001$ and $r_s=0.49$, $p<0.001$, respectively). No correlation between levels of BSSL and cytokines or chemokines were found in RA or PsA plasma or serum, respectively.

In JIA, levels of BSSL in serum correlated significantly with JIA disease activity score (JADAS27) ($r_s=0.26$, $p=0.007$), ESR ($r_s=0.47$, $p<0.000$), and leukocytes ($r_s=0.32$, $p<0.000$).

Conclusion: BSSL concentration in serum and plasma correlated with disease activity in patients with inflammatory joint disorders, i.e. RA, PsA and JIA. These data in humans support the relevance of our previous studies in rodents and