included the mitogen-activated protein kinase (MAPK) p38 and Akt. MXT did not inhibit TNFα-induced nuclear factor kappa B (NFκB) transcriptional activation, signaling or target gene expression. However, MXT induced pro-inflammatory markers such as vascular cell adhesion molecule (VCAM)-1 in an additive manner with TNFα. Functionally, MXT did not induce apoptosis but caused S-phase cell cycle arrest, which, along with p38 and Akt activation, could be abrogated by supplementing with folic acid. Findings to date in EC subjected to shear stress are somewhat different. MXT had no or a mild inhibitory effect on kinase signaling in EC under LSS and OSS respectively. MXT did not affect cell proliferation nor baseline or OSS-induced VCAM-1 expression in EC under shear stress.

Conclusion: In static EC, low-dose MXT 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 stimuli. This is the first report to study the effects of MXT on EC under shear stress, which will be crucial in understanding its molecular actions on the vasculature.

REFERENCES


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AB0132

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-difing 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, MRPI and inflammatory cytokines IL-1β, 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-severe, moderate groups, and the control group. Firstly, the mRNA expression of P-gp, BCRP, MRPI in spleen lymphocyte cells were measured by RT-PCR. The concentrations of IL-1β, 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 Spearman rank-order correlation.

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 = -14.383, P < 0.05, Z = 4.375, P < 0.05). Compared with 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 mRNA expression level of P-gp and BCRP among the groups, but the mRNA expression level of MRPI were significantly increased (P < 0.05).

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

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**References**


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**AB0134**

**HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS AMELIORATE COLLAGEN-INDUCED ARTHRITIS VIA IMMUNOMODULATORY EFFECT ON T LYMPHOCYTES**

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**Background:** Rheumatoid arthritis (RA) is an autoimmune disease that results in cartilage and bone destruction. Overactivation of T lymphocytes and imbalance of T lymphocyte subsets are closely related to the occurrence and development of RA. These have become important mechanisms of inflammation, immune activation, and bone destruction. RA treatment ideally involves regulation of immune abnormalities and maintenance of immune homeostasis. Mesenchymal stem cells (MSCs) are multipotent adult stem cells with high proliferation, multi-differentiation, and bone destruction. RA treatment ideally involves regulation of immune abnormalities and maintenance of immune homeostasis. MSCs have been shown to have anti-inflammatory effects on T lymphocytes to improve RA symptoms, inhibit synovial hyperplasia, and reduce cartilage and bone erosion. However, the specific molecular mechanisms have not been fully elucidated.

**Objectives:** This study investigated the effect of human umbilical cord mesenchymal stem cells (hUCMSCs) on collagen-induced arthritis (CIA) in rats in comparison with that of methotrexate (MTX), a classical drug for RA. It evaluated T lymphocyte proliferation, apoptosis, differentiation, and associated inflammatory factors, further explored the regulatory mechanism of T lymphocyte differentiation at the gene transcription level. This study elucidated that hUCMSCs play an immunomodulatory role in T lymphocytes of CIA rats through multiple pathways and explored the possible mechanism of hUCMSCs in RA treatment via the immunomodulated T lymphocyte pathway.

**Methods:** The effects of hUCMSCs on arthritis, radiological and synovial pathological changes in CIA rats were assessed. Flow cytometry was conducted to detect T lymphocyte proliferation, apoptosis, the ratio of Th17 and Treg cells in the spleen, and IL-17 and TGF-β levels in the sera from CIA rats. Further, Foxp3 and ROR-γT expression in the spleen were assessed by immunohistochemistry, Foxp3 mRNA and ROR-γT mRNA expression were assessed by reverse transcription-polymerase chain reaction (RT-PCR). Results: hUCMSCs inhibited proliferation and promoted apoptosis of T lymphocytes, up-regulated Foxp3 mRNA and protein expression, increased the proportion of Treg cells, down-regulated ROR-γT mRNA and protein expression, and decreased the proportion of Th17 cells in the spleens of CIA rats. Correction of the Foxp3/ROR-γT imbalance to regulate the Treg/Th17 ratio, promoted anti-inflammatory factor TGF-β expression and inhibited pro-inflammatory factor IL-17 expression, thereby improving arthritic CIA in rats, delaying radiological progression, and inhibiting synovial hyperplasia. This effect was similar to that of MTX.

**Conclusion:** hUCMSCs exert immunoregulatory effects on T lymphocytes in CIA rats through many pathways and are expected to become a new immunomodulatory therapy for RA.

**References**


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**AB0134**

**ANALYSIS OF INTESTINAL MICROBIOME PROFILE OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS**

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**Objectives:** Describe the intestinal microbiome profile in RA patients and analyze the mechanisms through which intervenes in the pathogenesis RA.

**Methods:** **Design:** Controlled, observational, cross-sectional study of established RA cohort. **Patients:** Forty consecutive RA patients (ACR/EULAR 2010 criteria) >16 years, selected from a prospective inclusion cohort (2007-2011) and 40 sex-age matched healthy controls. **Protocol:** Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity were collected during the follow-up and analytical values were determined. Fecal samples were frozen within 24 hours of collection. **Main outcome:** Fecal samples exam. Microbial DNA was extracted from fecal samples using QIAamp DNA stool Mini kit. The concentration and quality of DNA was determined by Nanodrop. Secondary technical assistance. **Statistical analysis:** Analysis of microbiota profile: UniFracPCoA (Principal Coordinate Analysis) was performed with the abundance data of operational taxonomic units (OTU) by means of the variancecovariance matrix implemented in Quantitative Insights Into Microbial Ecology (QIIME). The relative abundance of each OTU (taxa) was compared using a Wilcoxon test. The variations of abundance and diversity were compared by ANOSIM pathway. The calculation of α and β-diversity was carried out using QIIME.

**Results:** Most of subjects were women (75%) (table). In RA patients, the average DA528 was 3.6. β-diversity data showed that patients tend to die from healthy subjects according to their microbiota (p = 0.07). Patients with RA exhibited decreased gut microbiome diversity compared with controls, although was not statistically significant. Regarding in species richness, the analysis suggested an increase of the Collinsella aerofaciens species and enteroccocus genra in patients compared with controls. Likewise, an increase of arginine deaminate activity was observed, which belonged, in approximately 90%, to the RA genes of the genus Collinsella. The multivariate analysis identified ACPA positive (β [95% CI], 0.33 [27.4-39.0]), smoking (0.3 [8.8-256.4]) and age (-0.3 [27.4-39.0]) as factors associated with Collinsella.Also, we observed a decrease in other bacterial lin- eages. On the other hand, RA patients showed an altered metabolic capacity for the transport of zinc and copper.

**Conclusion:** These observations suggest a dysbiosis in RA patients, resulting from the abundance of certain bacterial (i.e Collinsella) and decrease of other bacterial lineages. These alterations could inuence in a significant way in the perpetua-

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