AB0123

CCL17 IN SYNOVIAL FLUID AND PLASMA OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Despite the advancements in management of rheumatoid arthritis (RA) in the last two decades, there are still a significant number of patients who cannot achieve low disease states or remission with the current available therapy. Granulocyte macrophage-colony stimulating factor (GM-CSF) is a key mediator in inflammation and autoimmunity, and has emerged as a novel therapeutic target in RA. However, potential adverse side effects warrant further investigation of a more specific target.

Objectives: Chemokine (C-C motif) ligand 17 (CCL17) is a downstream mediator of GM-CSF and has recently been shown to be regulated by GM-CSF in human monocytes. Significantly, CCL17 has a non-redundant role in inflammatory arthritis and pain. We investigated the expression levels of CCL17 in synovial fluid and plasma from RA patients.

Methods: We recruited RA patients with symptomatic swollen joints, who require joint aspiration for diagnostic and/or therapeutic purposes. Synovial fluid and plasma were collected and CCL17 protein levels were determined by ELISA.

Results: CCL17 protein was measured in synovial fluid and plasma samples from our cohort of RA patients. Levels of secreted CCL17 were higher in plasma [median 240 (40-580) pg/ml] compared to synovial fluid [median 100 (30-300) pg/ml] $p < 0.05$.

Conclusion: Significant levels of CCL17 were detected in RA synovial fluid and plasma. This is a novel study which demonstrates and compares the presence of CCL17 in synovial fluid and plasma from matching RA patients. The expression of CCL17 in plasma can make it a useful potential biomarker for RA, while its expression in synovial fluid suggests that CCL17 may be a therapeutic target for treating RA.

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AB0124

IMPACT OF INFLAMMATORY CYTOKINE IL-1B ON THE EXPRESSION OF MULTIPLE DRUG RESISTANCE PROTEIN BCRP/ABCG2 IN SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by synovitis and vasospasm^[1]. So far, The biggest challenge in the current field of RA treatment is the production of DMARDs multidrug resistance (MDR) and the most critical mechanism for the production of MDR is the ABC transporter family-mediated increase in target cell drug excretion, while inflammatory cytokines play an important role in its expression regulation. Our previous research have confirmed that IL-1 β , IL-6 and IL-17 are involved in the regulation of P-glycoprotein (P-gp) expression in lymphocytes of RA patients. The breast cancer resistance protein (BCRP/ABCG2) is also a highly efficient efflux pump, which absorbs, distributes, and excretes drugs or exogenous substances in the body^[2]. IL-1 β is a cytokine involved in the whole process of RA, which can aggravate the inflammatory response. However, there is no research on the effect of IL-1 β on the expression of BCRP in RA Fibroblast-like synoviocytes (FLS).

Objectives: To explore the effects of different concentrations of IL-1 β on the expression of drug resistance proteins in FLS of RA patients at different time points.

Methods: Synovial tissues of untreated RA patients (n=3) were extracted by Joint surgery, FLS culture system in vitro was established and passed to the fifth generation or so to do the experiments. FLS cells were divided into A, B, C, D four groups randomly with different treatments: Group A was the cell control group. Group B, C, D were respectively co-cultured with low (20ng/ml), middle (50ng/ml), high (100ng/ml) concentrations of IL-1 β . They were cultured respectively for 24 hours, 48 hours, and 72 hours. The effect of IL-1 β on the expression level of BCRP mRNA was observed at different concentrations and at different time points.

Results:

1. With the prolongation of IL-1 β culture, the expression of BCRP mRNA increased. Under the same concentration of IL-1 β (20ng/ml or 50ng/ml), the expression of BCRP mRNA in the 72h group was higher than that in the 24h group or 48h group ($P < 0.05$). At the concentration of IL-1 β of 20 ng/ml, the 48h group showed higher levels of BCRP mRNA expression than the 24h group ($P < 0.05$).
2. The expression of BCRP mRNA increased with the increase of IL-1 β concentration. After 48h of IL-1 β culture, the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 0 ng/ml group ($P < 0.05$). After 72h of IL-1 β culture, compared with the 0 ng/ml group, the expression of BCRP mRNA was significantly increased in the 20 ng/ml or 50 ng/ml or 100 ng/ml group ($P < 0.01$); and the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 20 ng/ml group ($P < 0.05$).

Conclusion: The expression of BCRP mRNA in FLS of RA patients has a certain concentration and time dependence of IL-1 β , suggesting that IL-1 β is involved in BCRP-mediated multidrug resistance, which lays a foundation for exploring its specific mechanism.

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Figure1: At the concentration of IL-1 β of 20 ng/ml, the 48h group showed higher levels of BCRP mRNA expression than the 24h group; the difference was statistically significant ($P < 0.05$); and the expression of BCRP mRNA in the 72h group was significantly higher than that in the 24h group or the 48h group; the differences were statistically significant ($P < 0.01$). At the concentration of IL-1 β of 50 ng/ml, the expression of BCRP mRNA in the 72h group was higher than that in the 24h group or 48h group; the difference was statistically significant ($P < 0.05$).

Figure2: After 48h of IL-1 β culture, the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 0 ng/ml group; the difference was statistically significant ($P < 0.05$). After 72h of IL-1 β culture, compared with the 0 ng/ml group, the expression of BCRP mRNA was significantly increased in the 20 ng/ml or 50 ng/ml or 100 ng/ml group; the differences were statistically significant ($P < 0.01$); and the 100ng/ml group showed high levels of BCRP mRNA expression compared with the 20 ng/ml group; the difference was statistically significant ($P < 0.05$).

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