Overexpression of P-glycoprotein on fibroblast-like synoviocytes in refractory rheumatoid arthritis patients: a potential mechanism for multidrug resistance in rheumatoid arthritis treatment

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ABSTRACT. This study aims to investigate the role of P-glycoprotein (P-gp) expression level in drug resistance to disease-modifying anti-rheumatic drugs in refractory rheumatoid arthritis (RRA). We evaluated and compared the expression levels of P-gp in fibroblast-like synoviocyte (FLS) cells in patients with rheumatoid arthritis (RA) and osteoarthritis (OA), and investigated the potential mechanism of P-gp-induced multidrug resistance in RRA. Ten patients were enrolled and divided into two groups: six in the RA group and four in the OA group. The expression level of P-gp in FLS cells was detected by western blotting following cell culture. A linear correlation algorithm was used to assess the association between the level of P-gp and disease activity

(using DAS28 scoring), as well as the duration of methotrexate (MTX) treatment in the RRA patients. The level of P-gp in the RRA patients was markedly higher than that in the OA patients ($P < 0.05$, $t = -4.179$). There was a positive linear correlation between the P-gp level in FLS cells and the duration of MTX treatment in the RRA group ($\Gamma = 0.733$, $P < 0.05$), whereas there was no significant correlation between the P-gp level and DAS28 scoring ($\Gamma = 0.206$, $P > 0.05$). P-gp might be upregulated during the progression of RRA, which possibly correlates with the development of resistance to MTX.

Key words: Multidrug resistance; P-glycoprotein; Refractory rheumatoid arthritis; Fibroblast-like synoviocytes