

Expression of certain transporter proteins may predict resistance to drug therapy

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The expression of a transporter protein called the Breast Cancer Resistance Protein (BCRP) in rheumatoid arthritis (RA) patients may indicate higher disease activity and could be a barrier to the effectiveness of disease-modifying antirheumatic drugs (DMARDs), according to the results of a study presented today at EULAR 2010, the Annual Congress of the European League Against Rheumatism in Rome, Italy.

In a Turkish study, researchers analysed specimens of synovium (the soft tissue that lines the surfaces within joints) from patients with RA who had undergone knee or [hip replacement](#) surgery. The presence of BCRP was reported in 41% of samples from RA patients, compared with 0% of samples in the healthy control group. The level of BCRP staining (a technique where a stain specific to a particular protein is used) was more prominent, indicating that the protein was being expressed at higher levels in cells actively involved in the immune response ([macrophages](#), [endothelial cells](#) and [fibroblasts](#)).

Furthermore, of the 40% of RA patients with cells that showed a presence of BCRP, some had a higher concurrent disease activity score (DAS28, an index that rates scores of 28 tender and swollen joints) despite receiving treatment for their condition, when compared with patients without BCRP. Researchers noted that this difference was not statistically significant (4.32 ± 0.32 vs 3.37 ± 1.16 , $p > 0.05$).

"The results of our study show that the presence of BCRP was only

detected in patients with RA and that arguably it is found more prominently in patients with high disease activity," said Dr. Umut Kalyoncu, Hacettepe University Rheumatology Department, Ankara, Turkey, and lead author of the study. "The BCRP protein is a pump involved in transporting substances across the cellular membrane. What we hypothesise is that, due to the location of the cells showing highest levels of BCRP, the presence of this protein may create a barrier for treatments entering the synovium of RA patients. Testing RA patients for the presence of BCRP may help us determine which patients will respond better to certain treatments."

Researchers screened samples using histochemical methods from seventeen patients (female n=14) with RA for the presence of p-glycoprotein (a protein involved in the transport of various molecules across cellular membranes), BCRP and multidrug resistance protein 1 and compared with samples taken from a control group of healthy controls and other inflammatory (ankylosing spondylitis, juvenile chronic arthritis) and non-inflammatory (osteoarthritis) rheumatic diseases. Prior to surgery, 53% of patients were taking methotrexate, 47% were taking sulphasalazine, 70% hydroxychloroquine, 18% leflunomide and 12% were taking anti-TNF drugs.

Provided by European League Against Rheumatism

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