Monocyte gene expression signatures predict how RA patients respond to anti-TNF therapy

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Distinct gene expression signatures in rheumatoid arthritis patients could help rheumatologists predict how these individuals will respond to tumor necrosis factor inhibitors, and may one day enable a more personalized approach to RA therapy, according to new research findings presented this week at the 2016 ACR/ARHP Annual Meeting in Washington.

Rheumatoid arthritis (RA) is a chronic disease that causes pain, stiffness, swelling, and limitation in the motion and function of multiple joints. Though joints are the principal body parts affected by RA, inflammation can develop in other organs as well. An estimated 1.3 million Americans have RA, and the disease typically affects women twice as often as men.

Early diagnosis and initiation of effective therapy is an important strategy in RA management. Researchers at the Mayo Clinic in Rochester, Minn., drew on their recent findings that showed that RA patients' pre-treatment serum type-1 interferon (IFN)-β/α ratio could predict their response to tumor necrosis factor-alpha inhibitors (TNFi). They conducted a new study to look for the cellular mechanisms involved in this response.

"The aim of this study was to better understand the impact of the type-I interferon ratio that predicts non-response to TNFi therapy on a major inflammatory cell type involved in RA," said Theresa L. Wampler Muskardin, MD, a rheumatologist in the Department of Pediatric and

Adolescent Medicine, and a lead author of the study. "Effects of type-I interferon on single cells and immune cell subtypes may be missed when we analyze whole blood or mixed cell populations. Using single cell gene expression technology, we hoped to find differences in expression of select genes between treatment responders and non-responders, which could ultimately lead to a blood test that we can use to guide treatment decisions in RA patients prior to starting biologic therapy."

The researchers used single cell expression analysis to study whether monocyte gene expression was significantly different among RA patients based on their pre-treatment blood serum IFN- β/α ratio. They isolated single classical (CL) and single non-classical (NC) blood-derived monocytes from 15 seropositive RA patients before TNFi therapy. The patients were divided into two groups according to their pre-TNFi serum ratio: six patients in IFN-β/α>1.3 and nine patients in IFN-β/α1.3 is predictive of non-response to anti-TNF therapy in RA patients. In this study, their findings show that gene expression in monocyte subsets differ in RA patients who have an IFN-β/α ratio>1.3, the ratio of type-I IFNs that predicts non-response to anti-TNF therapy.

"Difference between therapy response groups was strongest when the monocyte subsets were analyzed separately, rather than together, and distinct expression signatures were identified in the subsets," said Dr. Muskardin. "This suggests that investigating these biological pathways in monocyte subsets will provide further insight into the biology that determines TNFi treatment response in RA, and may identify other targets for therapy or other markers predictive of TNFi response that may be easier to measure."

Future studies should focus on monocyte subsets to identify possible molecular differences that could also determine treatment response to TNFi biologics. In the future, rheumatologists may be able to tailor therapy to an RA patient based on his or her underlying disease biology,

Dr. Muskardin concluded.

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