

New study shows genes can predict response to arthritis treatment, paves the way for future drug development

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New research from Queen Mary University of London, published in *Nature Medicine*, has shown that molecular profiling of the diseased joint tissue can significantly impact whether specific drug treatments will work to treat rheumatoid arthritis (RA) patients. The researchers also identified specific genes associated with resistance to most available

drugs therapies, commonly referred to as refractory disease, which could provide the key to developing new, successful drugs to help these people.

While there has been much progress made over the past decades in treating arthritis, a significant number of patients (approximately 40%) do not respond to specific [drug](#) therapies, and 5-20% of people with the disease are resistant to all current forms of medication.

The researchers carried out a biopsy-based clinical trial, involving 164 arthritis patients, in which their responses to either rituximab or tocilizumab—two drugs commonly used to treat RA—were tested. The results of the original trial published in [The Lancet](#) in 2021 demonstrated that in those patients with a low synovial B-cell [molecular signature](#) only 12% responded to a medication that targets B cells (rituximab), whereas 50% responded to an alternative medication (tocilizumab). When patients had high levels of this genetic signature, the two drugs were similarly effective.

As part of the first-of-its-kind study, funded by the Efficacy and Mechanism Evaluation (EME) Program, an MRC and NIHR partnership, the Queen Mary team also looked at the cases where patients did not respond to [treatment](#) via any of the drugs and found that there were 1,277 genes that were unique to them specifically.

Building on this, the researchers applied a data analyses technique called machine learning models to develop computer algorithms which could predict drug response in individual patients. The machine learning algorithms, which included gene profiling from biopsies, performed considerably better at predicting which treatment would work best compared to a model which used only tissue pathology or clinical factors.

The study strongly supports the case for performing gene profiling of

biopsies from arthritic joints before prescribing expensive so-called biologic targeted therapies. This could save the NHS and society considerable time and money and help avoid potential unwanted side-effects, joint damage, and worse outcomes which are common amongst patients. As well as influencing treatment prescription, such testing could also shed light on which people may not respond to any of the current drugs on the market, emphasizing the need for developing alternative medications.

Professor Costantino Pitzalis, Versus Arthritis Professor of Rheumatology at Queen Mary University of London, said:

"Incorporating molecular information prior to prescribing arthritis treatments to patients could forever change the way we treat the condition. Patients would benefit from a personalized approach that has a far greater chance of success, rather than the trial-and-error drug prescription that is currently the norm.

"These results are incredibly exciting in demonstrating the potential at our fingertips, however, the field is still in its infancy and additional confirmatory studies will be required to fully realize the promise of precision medicine in RA.

"The results are also important in finding solutions for those people who unfortunately don't have a treatment that helps them presently. Knowing which specific molecular profiles impact this, and which pathways continue to drive disease activity in these [patients](#), can help in developing new drugs to bring better results and much-needed relief from pain and suffering."

The incorporation of these signatures in future diagnostic tests will be a necessary step to translate these findings into routine clinical care.

More information: Myles Lewis, Rituximab versus tocilizumab in

rheumatoid arthritis: synovial biopsy-based biomarker analysis of the phase 4 R4RA randomized trial, *Nature Medicine* (2022). DOI: [10.1038/s41591-022-01789-0](https://doi.org/10.1038/s41591-022-01789-0).

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Provided by Queen Mary, University of London

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