

A fresh look at joint inflammation in rheumatoid arthritis patients

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Researchers at Trinity are providing fresh insights into joint inflammation in patients with rheumatoid arthritis (RA). The condition currently affects about 1 percent of the world's population and about

2,000 new cases are diagnosed annually in Ireland. Patients suffering from RA require lifelong treatment and can experience joint destruction, pain and disability, as well as depression, and social isolation. While treatments are improving, there is still a very real need to identify new treatment strategies, as unfortunately only one in every four patients will reach full remission.

The Molecular Rheumatology Group at the School of Medicine, led by Professor Ursula Fearon is working to better understand the complex cellular and molecular events that occur directly in the affected joints of patients. This urgent research will enable a more directed approach to treating this autoimmune disease. Two recently published papers from the group have presented unique insights into [joint inflammation](#) in RA.

Through the examination of cells and tissue from the site of inflammation in well-defined patient cohorts, the group aims to understand what drives disease and response and how cells interact with each other to orchestrate the inflammatory response.

Now, two of the groups research fellows, Dr. Mary Canavan and Dr. Achilleas Floudas are examining the cells in 'the synovium' which is the primary site of the inflammatory process, which if untreated leads to irreversible damage to the adjacent cartilage and bone. Two [cell types](#) involved in the inflammation process are 'dendritic cells' and 'T-cells' which interact with one another in the joint to drive inflammation.

Dr. Mary Canavan's findings were recently published in *Frontiers in Immunology*, and provide unique and previously unexplored insights into the complex role 'dendritic cells' may have in joint inflammation in patients with RA. Dendritic cells are a key immune cell in the body, and there are many different subtypes—each with its own unique role. This was the first study of its kind to examine these cells at the site of inflammation—that is, in the affected joints of the patients—and not

just in the peripheral blood.

Dr. Canavan said: "There is no doubt that the activities of these dendritic cells have consequences for neighboring cells in the synovium, such as T cells. Our findings also demonstrated that this CD1c+ dendritic cell population produces large amounts of 'matrix degrading enzymes' which can destroy cartilage and bone. Therefore, this study provides unique and previously unexplored insights into the complex role [dendritic cells](#) may have in joint inflammation in patients suffering from rheumatoid arthritis."

Dr. Achilleas Floudas's study, recently published in the journal *Annals of Rheumatic Diseases*, examines the previously unconsidered population of immune (T) cells found in synovial tissue become dysfunctional and exert many negative impacts associated with RA. Crucially, however—with regard to their potential as prognostic and therapeutic targets—these cells begin to malfunction before the clinical onset of RA. As a result, the scientists hope they may one day serve as "early-warning flares" that may allow medics to detect at-risk individuals and act before RA becomes established.

Dr. Floudas said: "The window for effective therapeutic intervention in rheumatoid arthritis (RA) is limited, and current T cell-specific therapies for treatment are broad and affect all T cells irrespective of their contribution to disease pathogenesis and progression, therefore not differentiating between protective and pathogenic T cell responses. Additionally, if we can spot the 'early-warning flares' set off by specific T cells in the synovial tissue of at-risk individuals, we should be able to extend the window for effective therapeutic intervention."

Professor Ursula Fearon, professor of molecular rheumatology, said: "We have found that the level of dysfunction observed in these immune cells varies between individual patients and is associated with level of

disease activity, thus may also allow the opportunity to monitor disease as well as develop more refined and targeted therapeutic strategies while limiting the side effects and toxicity. Understanding the role that these specific immune [cells](#) play in driving [inflammation](#) in the individual patient, has the potential for the development of precision treatments that prevent onset or impact early in disease, thus would have a significant impact for the patient's quality of life."

More information: Mary Canavan et al, Functionally Mature CD1c+ Dendritic Cells Preferentially Accumulate in the Inflammatory Arthritis Synovium, *Frontiers in Immunology* (2021). [DOI: 10.3389/fimmu.2021.745226](#)

Achilleas Floudas et al, Loss of balance between protective and pro-inflammatory synovial tissue T-cell polyfunctionality predates clinical onset of rheumatoid arthritis, *Annals of the Rheumatic Diseases* (2021). [DOI: 10.1136/annrheumdis-2021-220458](#)

Provided by Trinity College Dublin

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