Molecular Portraits of Early Rheumatoid Arthritis Identify Clinical and Treatment Response Phenotypes.

Lewis MJ, Barnes MR, Blighe K, Goldmann K, Rana S, Hackney JA, Ramamoorthi N, John CR, Watson DS, Kummerfeld SK, Hands R, Riahi S, Rocher-Ros V, Rivellese F, Humby F, Kelly S, Bombardieri M, Ng N, DiCicco M, van der Heijde D, Landewé R, van der Helm-van Mil A, Cauli A, McInnes IB, Buckley CD, Choy E, Taylor PC, Townsend MJ, **Pitzalis C.**
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Lay Title:

Looking at Cells and Genes to Identify Types of Rheumatoid Arthritis Patients, in Order to Predict Disease Severity, and Tailor Drug Treatment

We are currently trying to identify which cells and genes are driving the transition from early, to established rheumatoid arthritis. We want to do this because it will make it easier to identify which people with early arthritis will develop more severe disease, and to inform the decisions made around which specific drug treatments we should give, based on these cells and genes from the individual patient.

To do this, we looked at the cells and genes from a large cohort of people recently diagnosed with rheumatoid arthritis, who were yet to start treatment. We took blood samples, and synovial (joint) tissue, which was taken by way of a minimally invasive, ultrasound guided biopsy, from an inflamed joint.

These people with early arthritis were recruited to the Pathobiology of Early Arthritis (PEAC) study, in which we took blood and tissue samples, and followed up those recruited regularly for one year, assessing their rheumatoid arthritis.

We wanted to put these people into groups, using the types of cells and genes in their blood and tissue as criteria.

Using the synovial tissue, we identified distinct groups as follows:

1. lympho-myeloid – contains predominantly B-cells and/or plasma cells. These types of immune cell produce antibodies.
2. diffuse-myeloid – the predominant cells are macrophages. They are the first line of defence in the immune system, ingesting foreign bodies like bacteria, viruses and abnormal cells and producing cytokines, molecules that further stimulate the immune system
3. pauci-immune – has very few immune cells. Cells that support the synovium (fibroblasts) are predominant, hence this pathotype is also referred as the fibroid type

This information from the joint tissue can help us anticipate the future severity of the disease for the individual, and give them more specific options for treatment, making treatment choices less ‘trial and error’.

We also found, from looking at RNA from the genes we sampled, that there were certain markers which correlated with a good response to initial drug treatment. This means that by

taking a blood sample, and looking at the RNA, we can make better predictions about which people will respond well to standard initial drug treatment for rheumatoid arthritis; and which may be more likely to experience a failure of initial treatment, and require more advanced ‘biologic’ drugs to control their disease.

A look at the blood plasma cell genes from the blood samples also revealed a group who have a poor prognosis, which means they are more likely to develop severe disease with progressive, permanent damage to their joints. Again, this information will help in predicting disease severity and informing specific individually tailored treatment from the beginning, helping to minimise the impact of rheumatoid arthritis for those who suffer from it.