Method for identifying individuals at high risk of developing arthritis

- Determining the risk of developing rheumatoid arthritis (RA)
- Monitoring the response to a preventive treatment of arthritis
- Prevention of RA by starting early treatment

rheumatoid arthritis | preRA | BCRclones | RA prevention | early treatment

Background

RA is a chronic autoimmune disease with unknown etiology. Clinically manifest arthritis due to synovial inflammation is the hallmark feature of RA. However, it is not the first sign of disease, as the development of synovial inflammation may be preceded by the presence of disease-specific autoantibodies. Since not all individuals that have RA-specific antibodies progress to full-blown RA, researchers have been searching for highly accurate biomarkers that predict which of these individuals will develop RA in the short term. This will enable development of treatment in a phase of the disease, the “window of opportunity”, where the disease shows better treatment response. Early intervention studies already showed substantial effects in this phase of the disease. Therefore, it is an object of the invention to provide a novel highly accurate biomarker for determining the risk of developing arthritis, or for monitoring the response to a preventive treatment of arthritis in a subject.

Invention

The invention is based on the finding that an increase in the number of dominant B-cell receptor (BCR) clones in peripheral blood is associated with arthritis development and outperforms clinical prediction markers. When individuals progressed to arthritis or RA, dominant BCR clones disappeared from peripheral blood and appeared in synovial tissue, suggesting a direct role of these clones in disease pathogenesis. This marker may be used in guiding institution of more aggressive treatment in a very early window of opportunity. Moreover, the present invention for the first time shows that during onset of the clinical manifestation of arthritis in patients, these BCR clones disappear from the blood, while they appear as dominant clones in the synovium, even in clinically non-inflamed joints. The invention therefore provides a method for determining the risk of developing arthritis or for monitoring the response to a preventive treatment.

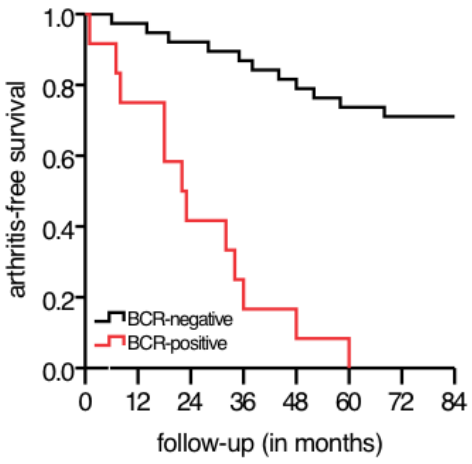

Figure 1: Kaplan Meier arthritis free survival in BCR+ and BCR- at risk pateints in replication cohort.

Applications

The method can be used to determine the stage of development of RA, prevent RA by starting early preventive treatment, and monitor response to treatment.

	test cohort (n=65)	validation cohort (n=50)
Sensitivity	78% (40-96%)	67% (39-87%)
Specificity	92% (60-100%)	94% (79-99%)
PPV	72% (33-94%)	83% (51-97%)
NPV	94% (64-100%)	87% (71-95%)

Figure 2: Test characteristics in test and validation cohort.

Intellectual property

European patent application has been filed

Inventor

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What are we looking for?

Licensing partner for this technique and also to collaborate on the evaluation of in vitro data and to extend the existing data set with in vivo data.

Key Publication

P.P. Tak, M.E. Doorenspleet, M.J.H. de Hair, P.L. Klarenbeek, M.H. van Beers-Ta, A.H.C. van Kampen, D. Van Schaardenburg, D.M. Gerlag, F. Baas, N. de Vries. Dominant B-Cell Receptor Clones in Peripheral Blood Predict Onset of Arthritis in Individuals at Risk for Rheumatoid Arthritis. Oral presentation & abstract ACR Annual Meeting 2016 Washington.