

A Systems Approach to Rheumatoid Arthritis

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Arthritis is a chronic disease that causes inflammation of joints. Between two common forms of arthritis, Rheumatoid Arthritis (RA) is caused by autoimmune disorder while osteoarthritis (OA) is caused by joint degeneration. Although diagnosis and treatment has improved for RA, therapeutic options are limited due to its toxicity, patients' resistance and relapse. Therefore, novel molecular targets that may improve accuracy of diagnosis and treatment are needed. Therefore, we used systems method to identify potential targets. This approach may 1) identify core RA-related genes (RAG), 2) reconstruct RA-perturbed network, and 3) select potential targets for RA.

By integrating multiple gene expression datasets, 983 core RAGs with RA dominant differential expression when compared with OA expression were identified. From the RAGs, RA-perturbed network that describes key RA associated processes and transcriptional regulation was constructed.

The network revealed that 1) synoviocytes play major role in identification of RA-perturbed processes, 2) anti-TNF- α therapy restores many of these RA-perturbed processes and 3) 19 TFs deregulate RAGs in the network. The enriched TFs included well-known potential targets to prove validity of the model as well as new potential target that may serve as potential novel target. Overall, this approach provided a new opportunity to understand disease network and identify main targets for RA. This method may be used in understanding and treating other complicate autoimmune disease.