



# **Between the Lines of Genetic Code: Chapter Five. Gene-Gene and Gene-Environment Interaction in Rheumatoid Arthritis**

*Leonid Padyukov, Lars Alfredsson*

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Rheumatoid arthritis (RA) is a chronic autoimmune disease with poorly understood etiology. Over the years, many genetic risk factors and some environmental risk factors were discovered to be important for RA. Genetic variants from the HLA-DRB1 locus, the shared epitope alleles, in different populations show a relatively strong and consistent effect on risk of RA. Non-HLA genetic risk factors have only a moderate effect. Gene–gene and gene–environment interactions were suspected to be important with regard to the risk of RA. Indeed, some combinations were demonstrated to be extremely influential. An important feature of RA is the development of autoantibodies, e.g., RF and ACPA, that serve as biomarkers and are used in diagnosing the disease. Interestingly, most of the genetic predisposition for RA observed so far concerns risk of developing the autoantibody positive subset of the disease, that is, the form where antibodies are present. In this chapter, we will review the current knowledge on genetics in RA and introduce multiple examples of interaction.

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