

SUMMARY

BACKGROUND:

Rheumatoid arthritis (RA) is an autoimmune disease affecting about 1% of global population, and mainly leads to the joints destruction. Coexistence of the genetic and environmental risk factors increase the probability of disease development. A genetics risk involves mainly HLA risk alleles carriers. Despite of the great knowledge about risk factors the molecular mechanism of disease still remains unclear.

The interferon regulatory factor V (IRF5) is the transcription factor responsible for chronic and acute inflammation, and was involved in Toll-like receptor pathway which plays an important role in RA development. The suppressor of cytokine signaling 3 (SOCS3) and interleukin 6 receptor (IL6R) are involved in interleukin 6 signaling pathway, which plays a significant function in pathogenesis of RA.

AIMS:

The main aim of this study was to evaluate the molecular markers of RA and relationship between them and disease severity. Markers analysis involved DNA methylation of selected genes as well as micro-RNA (miR) expression. Secondary challenge was to evaluate the frequency of the single nucleotide polymorphisms (SNPs) between rheumatoid factor (RF) positive and RF-negative RA patients.

MATERIALS AND METHODS:

A total of 122 RA patients, 82 RF-positive and 40 RF-negative as well as 24 healthy controls were enrolled to the study. From RA patients, 32 in high disease activity and 22 in remission were selected. These patients and controls were included in DNA methylation and miR expression assessments. DNA methylation was evaluated by methylation-specific polymerase chain reaction (MSP), real-time polymerase chain reactions were used for SNPs genotyping and miRs expression analysis.

RESULTS:

In *IRF5* gene the methylation level was 43.6% lower in RA patients than in the healthy controls and methylation level was not associated with the disease activity. In *SOCS3* and *IL6R* no differences in methylation states were found. RF-negative patients have had a higher *IRF5* rs4728142 and *SOCS3* rs4969168 SNPs frequency, but it was associated with the used

genetic model. MiR-22 expression was higher about 62% in RA patients than in healthy controls and was associated with disease activity.

CONCLUSIONS:

DNA methylation changes in *IRF5* may be used as a new potential marker of RA in a whole blood which is independent of disease activity. MiR-22 expression may be considered as plasma marker of RA which expression is associated with disease activity.