PKR and HMGB1 expression and function in rheumatoid arthritis

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ABSTRACT. The pathogenesis of rheumatoid arthritis (RA) is characterized by inflammation. We aimed to examine the roles of double-stranded RNA-activated protein kinase (PKR) and high-mobility group box chromosomal protein 1 (HMGB1) in a rat model of RA. Male SD rats were divided into three groups: control, RA model, and intervention (RA model plus treatment). The model of RA was made by injecting Freund’s adjuvant into the posterior right limb of the rat and the intervention group received a PKR-specific inhibitor C16 after RA modeling. The degree of limb swelling was measured following RA modeling and intervention. In addition, plasma levels of HMGB1 were determined using ELISA. The mRNA and protein levels of PKR and HMGB1 were detected in rat synovium using quantitative PCR and western blot, respectively. The degree of limb swelling in the RA model was increased compared to control, while it was decreased in the intervention model compared to the RA model. Plasma HMGB1 levels in the model group were significantly higher compared to the control group but were lower in the intervention group compared to the model group. PKR and HMGB1 protein and mRNA levels in the rat synovium were elevated in the model group and markedly reduced in the intervention group. Increased
levels of PKR and HMGB1 in synovium or blood appear to be involved in the occurrence and development of RA in a rat model. Selective inhibition of PKR improves the symptoms of RA, perhaps by inhibiting the release of HMGB1.

**Key words:** Rheumatoid arthritis; Inflammatory factor; Double-stranded RNA-activated protein kinase; High-mobility group box chromosomal protein 1