Tofacitinib, an oral janus kinase inhibitor, induces CD86^{-}MHC II^{+}macrophages

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Tofacitinib (TOF) is an oral janus kinase (JAK) inhibitor for the treatment of rheumatoid arthritis, and has similar efficacy compared to biologic disease-modifying antirheumatic drugs. By inhibiting JAKs, TOF may modulate leukocyte development and activation at inflammatory sites. Major histocompatibility complex class II (MHC II) and B7 (CD80/CD86) co-stimulatory molecules expressed on macrophages play a crucial role in T cell activation. Although macrophages are critically involved in the pathogenesis of rheumatoid arthritis, the influence of TOF on macrophage functions remains to be investigated. In this study, to clarify the effect of TOF on macrophage activation, we focus on the expression of MHC II and CD86.

RAW264.7 macrophages were pretreated with TOF, and then stimulated with IFN-γ. The treatment of IFN-γ with low-concentration of TOF induced CD86^{-}MHC II^{+}cells. In addition, low-concentration of TOF suppressed IFN-γ-induced CD86 mRNA levels. By contrast, IFN-γ-induced MHC II expression was enhanced by low-concentration of TOF in transcriptional levels. On the other hand, the STAT1 phosphorylation, a downstream effector of IFN-γ-JAK signaling, was inhibited by low-concentration of TOF. Receiving only MHC IIwithout co-stimulation via CD80/86 seems to lead to anergy of T cells, a process known as peripheral tolerance. Accordingly, TOF may has antirheumatic action through the induction of CD86^{-}MHC II^{+}macrophages.