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EXPERIMENTAL ARTHRITIS

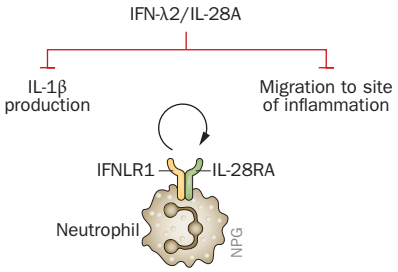
Antiviral IFN-λ2 has unexpected roles in inflammation

Type III interferons—IFN-λ1, IFN-λ2 and IFN-λ3—are best known for their antiviral activity but have broader roles in autoimmune and inflammatory disease than previously appreciated, according to new research published in *The Journal of Experimental Medicine*. Irina Udalova and colleagues found that IFN-λ2 (IL-28A) treatment resulted in abrogation of disease and reversal of joint damage in mice with collagen-induced arthritis (CIA) by inhibiting neutrophil IL-1β production and neutrophil migration.

"We have always hypothesized that being within the type II cytokine family, and being structurally related to both type I IFNs as proteins and IL-10 with regards to exon–intron structure, type III interferons may have anti-inflammatory activity," explains Udalova. To test this hypothesis, the researchers treated mice with CIA with IFN-λ2 (obtained from Zymogenetics) or phosphate-buffered saline (PBS) on day 1 of disease onset. "To our great surprise, the first experiment with IFN-λ2 treatment showed a complete reversal of the pathology," explains Udalova. "The arthritis was halted and the joints of treated mice remained intact while the controls developed severe inflammation, cartilage destruction and bone erosion."

Analysis of the cellular changes occurring in the mice showed that IFN-λ2 treatment resulted in reduced numbers of IL-17-producing type 17 T helper cells and γδ T cells in joints and draining lymph nodes compared with control mice, but had no effect on numbers of these cells or on T-cell proliferation or anti-collagen antibody levels in the periphery. Numbers of neutrophils were also reduced in the joints of IFN-λ2-treated mice compared with control mice. Further experiments using the air pouch model of acute inflammation showed that IFN-λ2 treatment resulted in reduced neutrophil IL-1β production and also inhibited the migratory capacity of these cells.

As Udalova concludes, "IFN-λ2 seems to impair neutrophil migration to the site of inflammation without significantly affecting their numbers in the blood, which indicates a lack of toxicity and adverse effects. We would like to validate these findings in human neutrophils and explore the possibility of repurposing IFN-λ2, which is now in clinical trials for hepatitis C, for inflammatory diseases such as rheumatoid arthritis."



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Original article Blazek, K. *et al.* IFN-λ resolves inflammation via suppression of neutrophil infiltration and IL-1β production. *J. Exp. Med.* doi:10.1084/jem.20140995