RHEUMATOID ARTHRITIS MIR-155 MEDIATES INFLAMMATION

Targeting microRNA 155 (miR-155) might be a route to blocking aberrant cytokine expression in rheumatoid arthritis (RA). After studying mouse models and synovial biopsies from patients with RA or osteoarthritis, Iain McInnes and colleagues report in *Proceedings of the National Academy of Sciences* that this post-transcriptional regulator has a critical role in antigen-dependent arthritis and cytokine-driven joint inflammation.

That microRNAs regulate physiological and disease processes is increasingly recognized, and miR-155 is aberrantly expressed in patients with RA. To find out how it contributes to the disease process, McInnes *et al.* studied its detailed expression in biopsied synovia, finding it to be upregulated in CD68⁺ macrophages in the membrane-lining layer, and CD14⁺ cells in synovial fluid, from patients with RA. This pattern correlated inversely with the expression of a target of miR-155, SH2 domain-containing inositol-5'-phosphatase 1 (SHIP-1). Overexpression of miR-155 in cultured CD14⁺ cells decreased SHIP-1 expression and boosted production of downstream cytokines implicated in synovitis, with the inverse effect produced by its inhibition. Indeed, transfection of a miR-155 antagomir blocked lipopolysaccharide-induced production of tumor necrosis factor.

Mice deficient in miR-155 were protected from collagen-induced arthritis, but not from the arthritis that follows passive transfer of anti-collagen antibodies. The mice were impaired in proinflammatory cytokine production, development of autoreactive type 17 T helper cells, and generation of IgGs specific for collagen-II.

These data support a role for miR-155 in B-cell differentiation and antibody class-switching, and suggest that blocking its action might be a way to prevent excessive inflammation in patients with RA.

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Original article Kurowska-Stolarska, M. *et al.*

MicroRNA-155 as a proinflammatory regulator in clinical and experimental arthritis. *Proc. Natl Acad. Sci. USA*
doi:10.1073/pnas.1019536108