

Considering IL-6

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Targeting interleukin (IL)-6 or its receptor for the treatment of inflammatory disease is an attractive approach to the management of complex inflammatory diseases, especially those with a systemic component to their presentation and comorbidity. Biological drugs that target IL-6 receptor are already in clinical practice. Recently, more agents are emerging from clinical trials that block distinct parts of the IL-6/IL-6R pathway.

In this edition, Jones *et al* explore the rich diversity of biology mediated by IL-6. They address the diverse portfolio of functions that IL-6 has in both normal physiology and disease—delivering immune homeostasis in health, and yet driving pathology during infection, autoimmunity, and cancer. The authors share new insights into the workings of IL-6 addressing directly the three distinct forms of receptor signalling: classical receptor signalling, trans-signalling, and the recently reported trans-presentation. Thereafter, Takeuchi *et al* consider how drugs targeting IL-6 may be increasingly useful in the management of inflammatory arthritis. They provide an up-to-date summary of currently available agents and those in development. The IL-6 receptor blockers tocilizumab and sarilumab are discussed, alongside anti-IL-6 agents including olokizumab – a new

offering, which blocks engagement with the IL-6-receptor complex including gp130. Options for maximising the therapeutic potential of these agents are discussed including treatment timing and the use of combination therapy, as well as the individual pharmacokinetics and pharmacodynamics of each agent. In *Targeting IL-6: A Review of Data*, Smolen *et al* focus in more detail on the clinical data supporting the use of IL-6 targeting agents in rheumatoid arthritis, and in particular address the use of appropriate disease activity measures and endpoints for these agents, given the direct interaction of IL-6 with the acute phase response. Choy *et al* then take a closer look at the roles of IL-6 in other inflammatory and immune conditions beyond RA. In addition to the rheumatic diseases, IL-6 is implicated for example in systemic lupus erythematosus, scleroderma and giant cell arteritis, and some non-immune diseases such as endogenous depression. While the link with depression may be controversial, there is good evidence that this is biologically possible and intriguing in potentially transforming our views of the underlying aetiology of that condition. Thus, this edition of *Considerations in Medicine* explores the fascinating science of IL-6, and uncovers some of the extraordinary possibilities for anti-IL-6 therapies.

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