Introduction
Expanding the frontiers of therapy

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Treatment of rheumatoid arthritis (RA) has dramatically changed over the past decade, and much progress has been made in improving the prognosis of RA patients as a result of elaboration of novel treatment strategies and the development of biologic agents. Nevertheless, up to 50% of patients are either not controlled sufficiently or do not respond at all to current treatments, including biologicals. A better understanding of the background of these therapeutic limitations is required, but novel therapies that might help to reduce the residual and significant burden of the disease also represent future hopes.

RA is an autoimmune disease characterized by inflammation of the synovial membrane affecting cartilage and bone, which leads to joint destruction, disability and premature mortality. Given the therapeutic deficiencies that still exist, it is mandatory that we conduct further research to close the gap and find alternative therapies for RA patients. Currently, there exist several new molecules for the treatment of RA, aimed at different targets. They may soon become available to RA patients. These include a monoclonal antibody that targets inhibition of B cells and a fusion protein that is a T cell costimulation modulator (inhibiting the activity of T cells).

Another promising approach currently being developed is inhibition of IL-6 by blockade of both its membrane and soluble receptors. This approach is based on extensive research into the biology of and response to IL-6, and into the effects of IL-6 on target organs expressing the IL-6 receptor or organs that become sensitive to IL-6 when the concentration of either IL-6 or of its soluble receptor increase.

The well characterized joint and bone alterations that occur in RA appear to be partly linked to the effects of IL-6, as are many of the systemic signs of the disease. This observation has been confirmed in animal models of RA, and initial studies of IL-6 blockade have shown that blocking the effects of IL-6 improves adult RA and other autoimmune diseases in which IL-6 may be involved.

The papers included in this supplement describe in greater detail research into IL-6 activity as a potential target for therapeutic intervention in RA patients. They also describe the rationale for bringing IL-6 receptor inhibition from the bench to the bedside.

Competing interests

JSS has received financial compensation from and served on advisory boards for Roche and is an investigator in clinical trials of tocilizumab.