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REVIEW SERIES: INFLAMMATION AND IMMUNE RESOLUTION
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Inflammation and immune resolution

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Summary

Inspired by the advances presented at the Inflammation and Immune Resolution Plenary Session at the British Society for Immunology Congress, December 2017, in this issue of *Clinical & Experimental Immunology* we present a Review Series on Inflammation and Immune Resolution. Our selection ranges from an overview of current genetic understanding of the similarities and differences between immune-mediated inflammatory diseases (IMIDs); discussion of several biological mechanisms underlying the aberrant activation of myeloid cells in RA, and how myeloid cell relevant anti-inflammatory mediators may contribute to immune resolution; presentation of fascinating evidence for the existence of innate immune memory in stromal cells and how this may exacerbate or restrain inflammatory disease; and a review of how the interleukin (IL)-6 family members IL-6 and IL-27 may drive or regulate inflammation. Inflammation and immune resolution are two sides of the same coin: the reviews presented in this series aim to equip readers with greater insight into the delicate balance between the two.

Inflammation is an essential and complex biological process that protects the body from potential harm caused by infection, injury or damage. An effective inflammatory response relies upon intricate cellular and molecular interactions between the immune system, the vascular system and the tissue. It is equally important that inflammation is resolved; when inflammation is not properly controlled, it can eventually result in immune-mediated inflammatory diseases (e.g. rheumatoid arthritis, inflammatory bowel disease, psoriasis, asthma, vasculitis), transplant rejection or impaired wound healing. Inflammation is also recognized increasingly as a contributor to cancer, neurodegeneration, long-term pain and certain psychiatric and mental health disorders. It is therefore paramount to understand the cellular and molecular biology of inflammation and immune resolution.

Barton and co-workers [1] discuss how genetics can improve our understanding of the similarities and differences between immune-mediated inflammatory diseases (IMIDs), with a focus on musculoskeletal disease. Indeed, several disease-associated genes have been found to be associated with different IMIDs, for example *CD25*, protein tyrosine phosphatase, non-receptor type 22 (*PTPN22*), tumour necrosis factor α-induced protein 3 (*TNFAIP3*), interleukin-23 receptor (*IL23R*) and cytotoxic T lymphocyte antigen-4 (*CTLA4*). The authors describe how detailed knowledge of disease-associated genes might have a clinical impact by informing drug efficacy and drug repurposing.

Myeloid cells are pivotal contributors to inflammation, as well as to immune resolution. McInnes and colleagues [2] present an overview of several biological mechanisms underlying the aberrant activation of myeloid cells, which may result in perpetuation of inflammation in rheumatoid arthritis (RA). They also discuss emerging data on myeloid cell relevant anti-inflammatory mediators that can contribute to immune resolution; these may inform a novel category of therapeutic targets to achieve disease remission.

In recent years, the concept of innate immune memory, particularly in myeloid cells, has been catapulted into the limelight by the elegant work of Mihai Netea and co-workers. In their review, Crowley *et al.* [3] present compelling evidence for the existence of innate immune memory in stromal cells. The authors discuss how stromal memory may exacerbate or restrain inflammatory disease. They also

pose important questions regarding the acquisition of stromal memory, its anatomical nature and whether it is cause or consequence of inflammatory disease.

Finally, Jones *et al.* [4] review the role of the IL-6 family members IL-6 and IL-27 in inflammation. IL-6 is generally regarded as a proinflammatory cytokine. IL-27 was viewed initially as a proinflammatory cytokine due to its ability to promote the development of IFN-γ-secreting T helper cells. However, later studies showed that IL-27 can limit the development of immune responses, and can antagonize the actions of IL-6. The authors discuss the importance of these two cytokines in the diagnosis, stratification and treatment of inflammatory arthritis.

Collectively, these reviews present a selection of the accumulating evidence regarding the intricate balance between inflammation and immune resolution. Increasing our knowledge regarding the key molecular and cellular mechanisms underlying these two processes will enable researchers to find ever more sophisticated ways to tip the balance in favour of one or the other.

References

1 David T, Ling SF, Barton A. Genetics of immune-mediated inflammatory diseases. Clin Exp Immunol 2018; **193**:3–12.
2 Alivernini S, Tolusso B, Ferraccioli G, Gremese E, Kurowska-Stolarska M, McInnes IB. Driving chronicity in rheumatoid arthritis: perpetuating role of myeloid cells. Clin Exp Immunol 2018; **193**:13–23.
3 Crowley T, Buckley CD, Clark AR. Stroma: the forgotten cells of innate immune memory. Clin Exp Immunol 2018; **193**:24–36.
4 Jones GW, Hill DG, Cardus A, Jones SA. IL-27: a double agent in the IL-6 family. Clin Exp Immunol 2018; **193**:37–46.

