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The Resolution of Inflammation

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Preface

It was with tremendous enthusiasm that we endeavoured to compile and edit this volume for *Progress in Inflammation Research* describing novel findings and developments pertaining to the processes governing the resolution of inflammation. It is perhaps surprising that this topic had, to our knowledge, not previously been covered as a separate subject area in a dedicated monograph given what now seems such an obvious thing to do. Historically, researchers have focussed and have made great advances on the initiation and propagation of inflammation. Little attention had been specifically devoted to elucidating the mechanisms orchestrating the resolution of inflammation, although a variety of mechanisms that limit the inflammatory response had been described (e.g., mediator dissipation and deactivation; exogenous mediator removal or reduction; receptor, cell and tissue desensitisation to mediators; identification of agents with anti-inflammatory potential such as IL-10, IL-1 receptor antagonists, TGF-β, etc).

It is now believed that manipulation of more recently described processes, recognised as being actively involved in resolution, are therapeutically manipulatable for the treatment of inflammatory diseases. Indeed, patients with chronic inflammatory diseases are by necessity treated in order to reduce established and persistent inflammation with the added hope of preventing further progression of the inflammatory response. It has recently become evident that many of the anti-inflammatory agents currently used in the clinical setting influence inflammatory resolution. For example, glucocorticoids have been shown to influence processes now recognised as being important mechanisms allowing resolution to occur; namely glucocorticoids trigger apoptosis (programmed cell death) in most leukocytes (the neutrophil however is a notable exception) and augment apoptotic cell clearance by phagocytes. Similarly, aspirin, the most widely used NSAID, is involved in an unorthodox biosynthetic pathway yielding important lipid mediators (e.g., 15-epi-lipoxin A4 and 15-epi-lipoxin B4) actively involved in the resolution process.

This volume contains major contributions from an international panel of experts who describe the basic processes regulating the resolution of inflammation including apoptosis, macrophage clearance of apoptotic cells and novel pro-resolution lipid

mediators. In addition, there are sections that describe how existing anti-inflammatory drugs such as aspirin and glucocorticoids may influence these resolution processes. There are three chapters devoted to describing fine examples of clinically relevant inflammatory disease areas where much progress has been made in understanding resolution. We feel that we are at the beginning of a rapidly burgeoning and exciting area of inflammation research where new advances are being made in understanding the resolution of inflammation. It is without doubt that continued research will fully elucidate the mechanisms whereby existing anti-inflammatory drugs influence resolution. Furthermore, there is now emerging experimental *in vivo* evidence indicating that by pharmacologically and selectively inducing apoptosis of inflammatory cells, specifically enhancing non-phlogistic clearance of apoptotic cells by phagocytes, and administration of pro-resolution lipids (e.g., lipoxins, resolvins and protectins), inflammatory resolution is achievable. Consequently, we believe that better designed and novel classes of drugs that specifically target resolution processes will be forthcoming in the not too distant future.

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