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# Preface

The complement system, first described more than a century ago, was for many years the ugly duckling of the immunology world, but no more. Complement in recent years has blossomed into a fascinating and fast moving field of immediate relevance to clinical scientists in fields as diverse as transplantation biology, virology, and inflammation. Despite its emergence from the shadows, complement retains an unwarranted reputation for being “difficult.” This impression derives in large part from the superficially complicated nomenclature, a relic of the long and tortuous process of unraveling the system, of naming components in order of discovery rather than in a systematic manner. Once the barrier of nomenclature has been surmounted, then the true simplicity of the system becomes apparent.

Complement comprises an activation system and a cytolytic system. The former has diverged to focus on complement to distinct targets—bacteria, immune complexes, and others—so that texts now describe three activation pathways, closely related to one another, but each with some unique features. The cytolytic pathway is the same regardless of the activation process and kills cells by creating pores in the membrane. Complement plays an important role in killing bacteria and is essential for the proper handling of immune complexes. Problems occur when complement is activated in an inappropriate manner—the potent inflammation-inducing products of the cascade then cause unwanted tissue damage and destruction.

Complement’s renaissance has been driven in large part by the discovery of the complement regulatory molecules and the realization that these molecules and other agents can provide effective anticomplement agents for use in therapy. As newer and better anticomplement agents become available, the requirement for laboratories to assess complement activation in clinical samples and to monitor the effects of anticomplement agents will grow.

*Complement Methods and Protocols* aims to provide a comprehensive source of up-to-date protocols for the study of the complement system, both for the basic scientist interested in understanding the mechanisms of activation and the clinical scientist wishing to quantify complement activation. In the first

chapter, the complement system is briefly reviewed to set the stage for the methods chapters to follow. The next two chapters describe methods for purifying complement components, using classical chromatography and immunoaffinity approaches, respectively. Chapters 4 to 6 describe methods for the functional analysis of complement components, regulators, enzymes, and complexes, including a detailed description of the generation of the depleted sera essential for complement assays. Methods for measurement of complement activation fragments and complexes deposited on cells, in tissues, or in biological fluids are detailed in Chapters 7 to 10. Chapter 11 provides an overview of screening methods for identifying and assessing complement deficiency and Chapter 12 a detailed account of methods needed to assess deficiency of C1 inhibitor. Other clinically relevant protocols for analysis of complement autoantibodies, immune complexes, and complement allotypes are provided in Chapters 13 to 15. Chapter 16 departs from the main theme of the book to describe protocols for generating gene-deleted mice, included here because of the enormous influence such methods are now having on complement research. The final chapter reviews complement deficiencies in experimental animals, listing the different complement deficiencies defined in animals and the experimental models in which these deficient animals have been examined.

I am grateful to my friends and colleagues who have contributed to this volume for their willingness to make time in their busy schedules. In particular, I wish to thank the members of the Complement Biology Group in Cardiff, many of whom have contributed chapters to this volume and others who have reviewed parts of the manuscript or contributed to the tedious task of assembling the appendices. I promise I won't do it again in a while! Finally, thanks to The Wellcome Trust for their continued and generous support of complement research in Cardiff.

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