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0521381878 - Mechanisms in Blood Coagulation Fibrinolysis and the Complement System

Torben Halkier

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This book provides the first comprehensive account of the proteins involved in blood coagulation, fibrinolysis and the complement system. A major section of the book is devoted to each of these three systems, with separate chapters dealing in detail with the structural aspects and the different functional processes. Topics covered in the blood coagulation section include the activation of factors IX and X and prothrombin, and the formation and stabilisation of fibrin. The fibrinolysis section includes the activation of plasminogen, the degradation of fibrin and the regulation of fibrinolysis. The complement system itself is covered in chapters dealing with classical activation, alternative activation, the lytic complex and the regulatory processes involved. In addition, there is a section which deals with special topics, including the kinin system, signal peptides, haemostasis, as well as the evolution of protein structure. This volume will be of use to researchers and advanced students in the fields of haematology, immunology and clinical chemistry.

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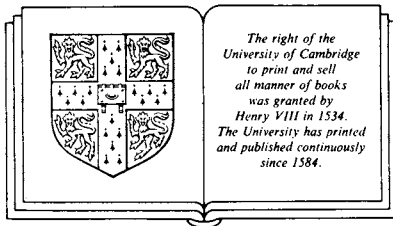
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Mechanisms in blood coagulation fibrinolysis and the complement system

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Foreword

This book was originally prepared as teaching material and as a background compendium in Danish for the final-year undergraduate course 'Mechanisms in blood coagulation, fibrinolysis and the complement system' held at the Department of Molecular Biology and Plant Physiology at the University of Aarhus from 1987 to 1989.

It was initially motivated by the fact that merely reading selected articles in research journals does not provide the student with a sufficient background for the understanding of mechanisms in the three systems referred to in the title. It is no use understanding the fine mechanics of biochemistry, if the overall principles disappear in a mass of details.

Many good reasons can be thought of for compiling a book of this kind, which is both a compendium of components – proteins – and also a guide to the mechanisms by which they act and interact. One reason is that, in spite of the best intentions, a course on the subject in question can easily get out of perspective without some kind of summarising document – the theme is colossal, while the time at the disposal of most students is very limited. Another is that reading original articles can be confusing for one unacquainted with the field; the author hopes that this will not be the case with this book, where the material has been both selected and subjected to a certain amount of pre-digestion. A third reason is the chance to emphasize aspects of particular interest, and a fourth is the possibility of making comparisons and thus of seeing things in a better perspective.

It will, it is hoped, be unnecessary to state that the content of this book reflects more the author's interpretation than it does Completeness or Truth.

It is here appropriate for me to thank Staffan Magnusson* for having introduced me to the field of blood coagulation and for many wide-ranging discussions, just as I should like to thank my students for their patience and help. An especial word of thanks must be addressed to Paul Woolley for his assiduous and expert translation from the original Danish manuscript and

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to Vilhelm Tetens for first suggesting that this book should be addressed to a wider public.

Århus, January 1990.

* The news of the untimely death of Staffan Magnusson reached Århus just before the revised manuscript of this book went to the press.

Introduction









It is a matter of everyday experience that a scratch, a cut or a more serious wound leads to bleeding, and, likewise, that the flow of blood stops in time, as long as the wound was not too large. Blood coagulates; first a scab, or clot, is formed, and later scar tissue. The processes involved are summarised by the terms *coagulation*, *haemostasis* and *fibrinolysis*, and they involve a sizeable collection of proteins acting in an even more sizeable collection of biochemical processes.

The coagulation of blood, and events subsequent to it, can well be regarded as a kind of defence system for stopping holes in complex organisms so as to minimise penetration by foreign bodies and aggressive micro-organisms that later could cause severe damage. However, these do get through sometimes, and penetration by them can result in inflammation at the point of the original damage. A part of the system for combating foreign organisms is the *complement system*, which is the non-specific part of the immune system.

In the following pages, an attempt is made to give an up-to-date picture of our knowledge of the mechanisms of blood coagulation, fibrinolysis and the complement system. The amino-acid sequences of the proteins to be described are summarised in an appendix. The source of the proteins described is usually stated, but where this is not mentioned the proteins are, implicitly, of human origin. Likewise, the physiological systems described are, as far as possible, human.

Many of the proteins that we shall meet in this book have common domains, defined by their amino-acid sequences. In the figures in which the domain structures of individual proteins are shown, standard domain elements will be used, and these are defined in Table 1. For quantitative comparison of homology, the percentage of identical amino-acid residues in the aligned protein chains divided by the number of residues in the shorter chain. In the text this will be referred to as the *degree of identity*.

Table 1.

	Gla-domain
	Growth factor domain
	Kringle domain
	Short consensus repeat (SCR) domain
	Prekallikein/factor XI domain
	Fibronectin type I domain
	Fibronectin type II domain
	Serine proteinase domain