

Preface

Proteases act as positive or negative effectors of numerous biological processes, either as nonspecific catalysts of protein degradation or highly selective agents controlling physiological events. Many biological pathways involving protease activity have been characterized, and a wealth of information is available. Five classes of proteolytic enzymes are recognized on the basis of their catalytic mechanism: aspartic, cysteine, metallo-, threonine, and serine peptidases. With the advent of whole genome sequencing, this classification system has expanded by the necessity to encompass the diverse catalytic repertoire found in nature. Much work remains to define the diversity of proteolytic events in biological systems and their spatial and temporal distribution in health and disease. This volume contains seven chapters contributed by leaders in their field and provides illustrative examples of the key role of proteases in biological processes, and how proteolytic function and regulation can be harnessed to define new strategies of therapeutic intervention. The reader will find these chapters both stimulating and informative.

In Chapter 1, Antalis, Bugge, and Wu discuss the exciting group of membrane-anchored serine proteases that have emerged as crucial contributors to processes related to development and maintenance of homeostasis.

In Chapter 2, Zogg and Brandstetter review the assembly of multiprotein complexes in blood coagulation, with emphasis on their structural organization, modes of action, and regulation, and outline therapeutic opportunities for the treatment of hemophilia and thrombosis.

In Chapter 3, Lancellotti and De Cristofaro detail the structural and functional properties of ADAMTS13, a disintegrin and metalloprotease involved in the pathogenesis of thrombotic microangiopathies via processing of matrix components.

In Chapter 4, Di Cera reviews the structure, function, and regulation of thrombin and how this knowledge has led to the rational engineering of thrombin variants with intriguing anticoagulant and antithrombotic properties, both *in vitro* and *in vivo*.

In Chapter 5, Olson and Gettins offer an extensive review of protein inhibitors of the serpin superfamily, detailing their structural and kinetic properties and how this knowledge may lead to engineering variants with desired specificity toward protease targets for therapeutic applications.

In Chapter 6, Yang, Hill, and Rosenberg discuss the multiple roles of metalloproteases in neurological disorders, especially their ability to open the blood-brain barrier and degrade the extracellular matrix around blood vessels, and outline the advantages of more specific inhibitors.

In Chapter 7, Troy, Akpan, and Jean deal with the regulation of caspases in the nervous system and discuss their function in the context of neurodegenerative diseases like Alzheimer's and cerebral ischemia.

I thank all the authors for their excellent contributions and their efforts to submit outstanding chapters by the stringent deadlines agreed with the publisher. Expert editorial assistance from Tracey Baird, Senior Administrative Assistant, is gratefully acknowledged and was key to the timely execution of this project.

September 1, 2010

ENRICO DI CERA

St. Louis, Missouri