

Preface

For some time, we had in mind to write together on the role of proteases and anti-proteases in inflammation. We had considered different options over the years, but concretization was still a long way from our busy schedules. The idea of this book arose in 2009, at the ninth World Congress on Inflammation in Tokyo. We met there at the booth held by Springer Verlag (at that time Birkhenhouse Verlag) with Pr. Vincent Lagente, who had just published in the same series and was presenting his most recent volume. The enthusiasm of Pr. Lagente and the persuasiveness of the publisher representative convinced us that a book on Proteases and their Receptors in Inflammation was the best way to shed some light on the crucial role the protease-anti-protease balance appears to play in inflammatory diseases. We thus embarked on this project, associating colleagues and friends to contribute to the 13 chapters of this book. Each contributor has been a key scientific player in raising new knowledge on the role of proteases, and we want to express here our most sincere gratefulness for the time and energy they spend on their chapters, providing this volume with their invaluable expertise.

The existence of proteases has been known for centuries. Their control and the use of proteolytic activity have occupied a place of choice very early in the everyday life of human beings. Back to the Antiquity, the properties of proteases were exploited by humans for their food processing. As such, rennet, a natural complex of enzymes mainly composed of proteases produced in the stomach of many mammals to digest their mother's milk, was used in the production of cheese. A reference to this enzymatic activity can be found in Homer's classic, the Iliad, and likewise the philosopher Aristotle wrote several times about the process of milk curdling [1]. Along the same lines, wheat flour, a major component of bread, contains gluten, an insoluble protein indigestible by a number of individuals and that affects loaf processing yield. Proteinases from *Aspergillus oryzae* have been identified very early on and used to modify wheat gluten, inducing a limited proteolysis. The proteolytic treatment of the dough facilitated its handling and machining, and resulted in increased loaf volumes [2]. Proteases have also been used by other civilizations. For instance, people from the Pacific Islands have used

for centuries the juice of the papaya fruit as a tenderizer for meat. It is now known that the protease papain is the active component accounting for this effect [1]. Papain is nowadays merchandized as a powder, and sold as meat tenderizer. This protease is also recommended as a home remedy treatment for insect stings or bites, because of its ability to degrade insect protein toxins. This story of papain has led two scientists: the French Réaumur (1683–1757) and the Italian Spallanzani (1729–1799), to hypothesize and demonstrate that gastric juice (full of proteases) are responsible for food digestion, through a complex process, now attributed to the protease pepsin.

Proteases are everywhere from prokaryotes to eukaryotes, from virus to bacteria and in all human tissues, playing a role in many biological functions ranging from digestion, fertilization, development, to senescence and death. The innate immune response to all types of aggression and tissue damage constitutes one of the major function in which proteases play a role. Almost 14,000 entries in PubMed are reported to the keywords “proteases and inflammation”. While the role of proteases in inflammation-associated tissue damage was considered for years merely as a degradative role, where proteases would serve as “cleaners” or “spoilors” of the inflammatory site, the discovery of receptors for proteases has highlighted proteases as true signaling molecules that actively participate to inflammatory signals.

In the present book, the first two chapters are devoted to resume the type of signals proteases might send to cells and how those signals might be modulated by protease inhibitors in the context of inflammation. Then, the role and expression of different types of proteases: Kallikreins, proteases from inflammatory cells, and Matrix Metalloproteases at sites of inflammation is addressed in the following three chapters. Six chapters are devoted to discuss the role of proteases in specific organ inflammatory diseases: the lungs, the gastro-intestinal tract, the skin, the joints, or specific inflammation-associated events: fibrosis, coagulation, pain. Because proteases are not only produced by the host, but as stated before, also by microorganisms, it appeared important to have a special chapter focusing on the role of microbial proteases in the inflammatory response to infection. Finally, the last chapter discusses the different pathways by which protease receptor signaling terminates, thereby ending protease signaling events.

As editors, we are profoundly indebted to the chapter authors, and we want, once again, to express our gratitude for the contribution they made to this volume, providing this book with the most advance knowledge in this field.

We also want to thank Hans Detlef Kluber of Springer Verlag, for his enthusiasm, his patience, and his expert assistance in the preparation of this volume. A special thank to Ursula Gramm for her editorial and coordinator help.

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Proteases and Their Receptors in Inflammation

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2011, XIV, 310 p., Hardcover

ISBN: 978-3-0348-0156-0