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Matrix Metalloproteinases in Tissue Remodelling and Inflammation

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Editors

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Preface

Matrix metalloproteinases (MMPs), or matrixins, belong to the metzincin superfamily of metalloproteinases. MMPs are proteolytic enzymes believed to be implicated in many physiological and pathological processes mainly associated with inflammatory reaction. MMPs are zinc and calcium dependent enzymes being able to degrade virtually all extracellular matrix components. MMP synthesis and functions are regulated by transcriptional activation, post-transcriptional processing (release of pro-domain, cell surface shedding), and control of activity by a family of endogenous inhibitors collectively known as tissue inhibitors of metalloproteinases (TIMPs). Upon stimulation, many cell types have been identified as producers of MMPs and TIMPs in a context of inflammatory process, strongly suggesting the involvement of MMPs in numerous inflammatory diseases. This mainly includes respiratory pathologies but also diseases of various organs such as liver, central nervous and cardiovascular systems.

From the previous book edited in the same series *Progress in Inflammation Research* by Kevin M.K. Bottomley, David Bradshaw and John S. Nixon in 1999 entitled: *Metalloproteinase as targets for anti-inflammatory drugs*, a spectacular increase in the studies of the role of metalloproteinases on the inflammatory process has been published.

The aim of this new volume is to provide new advances regarding the involvement of MMPs in various diseases associated with the inflammatory process. Moreover, the recent development of selective and non-selective inhibitors of MMPs would also provide new insights in the knowledge of the relationship between activation of inflammatory cells and tissue remodelling and propose new therapeutic possibilities to the treatment of inflammatory disease.

The first five chapters are devoted to the airway diseases including acute lung injury and acute respiratory distress syndrome, asthma, chronic obstructive pulmonary disease, pulmonary fibrosis and cystic fibrosis. It is now well established that chronic inflammatory response can become detrimental to the airways, causing degradation of the extracellular matrix in the lung. Matrix metalloproteinases are thought to play a critical role in this degradation, and has been the subject of intense

research. Two chapters are devoted to the role of MMP and chronic inflammation in cardiovascular diseases. These chapters define cardiac remodelling and pulmonary arterial hypertension, describe MMP-dependent mechanisms that stimulate the remodelling process, and explore future directions and therapeutic potentials in terms of MMP inhibition.

One chapter is devoted to the involvement of MMPs and inflammatory disorders in the central nervous system. Indeed, metalloproteinases, as key modulators of extracellular matrix homeostasis, play a role in the cascades leading to neuronal cell death and tissue regeneration. Yet they may have a detrimental or beneficial role depending on the type and the stage of brain injury.

The last chapter is devoted to the metalloproteinase and extracellular matrix remodelling in inflamed and fibrotic livers. Extracellular matrix remodelling is a complex mechanism of synthesis and degradation of matrix components. Depicting these mechanisms opens the path to the identification of biomarkers and targeted drugs for the reversion of inflamed/fibrotic scar towards a normal architecture and the restoration of normal liver functions.

We thank Hans Detlef Klüber of Birkhäuser Verlag AG for his patience and expert assistance in the preparation of this volume. We are also profoundly grateful to the authors who have contributed to this volume which we believe will provide an important advance in the field of metalloproteinase, extracellular matrix remodelling and chronic inflammatory process.

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