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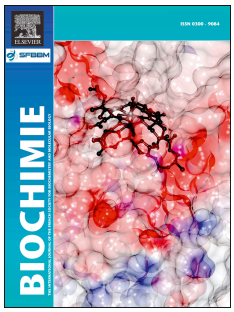

Proteases decode the extracellular matrix cryptome

Sylvie Ricard-Blum, Sylvain D. Vallet

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Proteases decode the extracellular matrix cryptome

Sylvie Ricard-Blum[a], **Sylvain D. Vallet**[a]

[a]UMR 5086 CNRS - Université Lyon 1, 7 Passage du Vercors, 69367 Lyon Cedex 07, France
s.ricard-blum@ibcp.fr, sylvain-daniel.vallet@ibcp.fr

Corresponding author:
Sylvie Ricard-Blum
UMR 5086 CNRS - Université Lyon 1
7 Passage du Vercors, 69367 Lyon cedex 07, France
Phone number: +33(0)437652926
e-mail: s.ricard-blum@ibcp.fr

Abstract

The extracellular matrix is comprised of 1100 core-matrisome and matrisome-associated proteins and of glycosaminoglycans. This structural scaffold contributes to the organization and mechanical properties of tissues and modulates cell behavior. The extracellular matrix is dynamic and undergoes constant remodeling, which leads to diseases if uncontrolled. Bioactive fragments, called matricryptins, are released from the extracellular proteins by limited proteolysis and have biological activities on their own. They regulate numerous physiological and pathological processes such as angiogenesis, cancer, diabetes, wound healing, fibrosis and infectious diseases and either improve or worsen the course of diseases depending on the matricryptins and on the molecular and biological contexts. Several protease families release matricryptins from core-matrisome and matrisome-associated proteins both *in vitro* and *in vivo*. The major proteases, which decrypt the extracellular matrix, are zinc metalloproteinases of the metzincin superfamily (matrixins, adamalysins and astacins), cysteine proteinases and serine proteases. Some matricryptins act as enzyme inhibitors, further connecting protease and matricryptin fates and providing intricate regulation of major physiopathological processes such as angiogenesis and tumorigenesis. They strengthen the role of the extracellular matrix as a key player in tissue failure and core-matrisome and matrisome-associated proteins as important therapeutic targets.

Keywords: Bioactive fragments, Cryptome, Extracellular matrix, Matricryptins, Proteases

Abbreviations: ADAM: A disintegrin and metalloproteinase, ADAMTS: A disintegrin and metalloproteinase with thrombospondin motif, ATP: Adenosine triphosphate, BMP-1: Bone morphogenetic protein-1, CUB: Complement C1r/C1s, Uegf, Bmp1, ECM: Extracellular matrix, EGF: Epidermal growth factor, FN: Fibronectin, MMP: Matrix metalloproteinase, mTLD: mammalian Tolloid, mTLL: mammalian Tolloid-Like, SPARC: Secreted Protein Acidic and Rich in Cysteine, TIMP: Tissue inhibitor of metalloproteinases, TRAF: Tumor-necrosis-factor-receptor-associated factor.