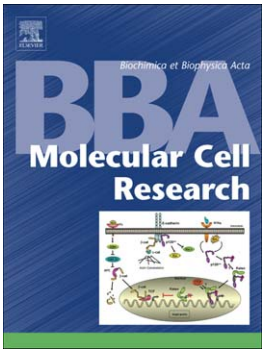


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# New Intracellular Activities of Matrix Metalloproteinases Shine in the Moonlight

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**ABSTRACT (149/150 words)**

Adaption of a single protein to perform multiple independent functions facilitates functional plasticity of the proteome allowing a limited number of protein-coding genes to perform a multitude of cellular processes. Multifunctionality is achievable by post-translational modifications and by modulating subcellular localization. Matrix metalloproteinases (MMPs), classically viewed as degraders of the extracellular matrix (ECM) responsible for matrix protein turnover, are more recently recognized as regulators of a range of extracellular bioactive molecules including chemokines, cytokines, and their binders. However, growing evidence has convincingly identified select MMPs in intracellular compartments with unexpected physiological and pathological roles. Intracellular MMPs have both proteolytic and non-proteolytic functions, including signal transduction and transcription factor activity thereby challenging their traditional designation as extracellular proteases. This review highlights current knowledge of subcellular location and activity of these "moonlighting" MMPs. Intracellular roles herald a new era of MMP research, rejuvenating interest in targeting these proteases in therapeutic strategies.

**Abbreviations**

CCN2/CTGF, connective tissue growth factor; ChIP, chromatin immunoprecipitation; ECM, extracellular matrix; ERK, extracellular signal-regulated kinase; GADPH, glyceraldehyde-3-phosphate dehydrogenase; GPI, glycophosphatidylinositol; HMGB1, high mobility group box 1; IFNα, interferon-alpha; IκB-α, inhibitor of kappa B-alpha; IL, interleukin; JNK, c-Jun N-