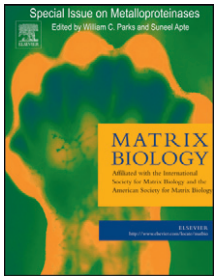
Review



Matrix metalloproteinases in fish biology and matrix turnover

Mona E. Pedersen [1], Tram T. Vuong [1], Sissel B. Rønning [1] and Svein O. Kolset [2]

*1 - **Nofima AS,** Pb 210, NO-1431 Ås, Norway*
*2 - **Department of Nutrition,** Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway*

***Correspondence to Svein O. Kolset:** Department of Nutrition, Institute of Basic Medical Sciences, University of Oslo, Box 1046 Blindern, 0316 Oslo, Norway. Tel.: +47 22851383. s.o.kolset@medisin.uio.no*
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Abstract

Matrix metalloproteinases have important functions for tissue turnover in fish, with relevance both for the fish industry and molecular and cellular research on embryology, inflammation and tissue repair. These metalloproteinases have been studied in different fish types, subjected to both aquaculture and experimental conditions. This review highlights studies on these metalloproteinases in relation to both fish quality and health and further, the future importance of fish for basic research studies.

Introduction

Fish is an important nutrient source in many countries and provides valuable proteins and other nutrients. Fish is also an important world commodity and the quality of such products depends on extensive knowledge of fish physiology and biology, health, slaughter, processing and storage before they reach the consumer. Furthermore, fish is a widely used experimental system to study embryology, effects on the immune system through exposures to bacteria and virus, and effects of environmental factors such as climate, metals and toxins. The zebra fish has been extensively used in experimental biology and molecular biology, and is a valuable supplementary tool to human medical research.

Normal physiological processes in fish, such as development, homeostasis and tissue repair, are dependent on the precise remodelling of the extracellular matrix (ECM), which is composed of proteoglycans (PGs) and fibrous proteins with collagen being the most abundant protein. The ECM provides mechanical support, in addition to signals to the interior of the cell, affecting a variety of cellular responses. The ECM is constantly undergoing changes in response to cellular stimuli, with a well-adjusted interplay between synthesis and deposition of ECM components on one hand, and their proteolytic breakdown on the other.

Matrix metalloproteinases (MMPs) are a major group of proteases that are important for ECM degradation. Typically MMPs consist of a propeptide, a zinc metalloprotease domain, a linker or hinge region, and C-terminal hemopexin domains. MMPs are classified on the basis of their substrate specificities and include collagenases (MMPs 1, 8, 13), gelatinases (MMPs 2, 9), matrilysins (MMPs 7, 11, 26) and stromelysins (MMPs 3, 10). Secreted in latent forms, most MMPs are activated following cleavage by extracellular proteases, some of which being MMPs located at the cell surface known as membrane-type MMPs (MMPs 14, 15, 16, 17, 24 and 25). The human genome has 24 different *MMP*-genes, including a duplicate of *MMP23* [1]. In zebra fish, 26 protease genes have been identified as *MMP*-orthologs [2,3]. Despite the numerical similarities of *MMP*s between zebra fish and mammals, the complexity of the zebra fish *MMP*s is apparently lower. Mammals have three stromelysins (*MMP*s *3*, *10* and *11*), while the zebra fish has only *MMP11*. All the *MT-MMP*s are however present in the zebra fish genome, emphasizing the importance of *MT-MMP*s as regulators of extracellular proteolytic activities [3]. Only a few have been detected, including MMP2,

Table 1. MMPs and inhibitors identified in fish, method of detection and their putative functions.

Putative function	Type of MMP	Method of detection	Species	Ref.
Embryogenesis				
Involved in development	MMP2 and 13, MT-MMPs, TIMP2	mRNA, KO[a] studies, protein, ISH[b]	*Danio rerio* (zebra fish), *Ctenopharyngodon idella* (grass carp), *Ictalarus punctatus* (channel catfish)	[5,6,8,10, 16,46,52],
Cell migration during zebra fish gastrulation	MT-MMP	KO studies	*Danio rerio* (zebra fish)	[7]
Fin and scale regeneration	MMP2 and 9, MT-MMP, TIMP-2	mRNA, ISZ[c]		[17,18]
Retinal and retinotectal development	MT-MMP	mRNA, KO studies	*Danio rerio* (zebra fish)	[19]
Craniofacial development after glucocorticoid exposure	MMP13	mRNA, KO studies IVZ[d]	*Danio rerio* (zebra fish)	[8]
Oocyte growth	MMP11	mRNA, zymography	*Oryzias latipes* (medaka fish)	[20]
Testis development	MMP2, 9, and 13, TIMP 2-a/b	ISZ, mRNA	*Sparus aurata* L. (gilthead seabream)	[22]
Expression and localization in the ovary	MT-MMP	mRNA	*Oryzias latipes* (medaka fish)	[53]
Degradation of ECM in muscle tissue				
Post-mortem tenderization of fish muscle during cold storage	MMP2 and 9	Zymography, western	*Gadus morhua* (atlantic cod), *Anarhichas minor* (spotted wolfish), *Salmo salar* (atlantic salmon), *Cyprinus carpio* (common carp)	[36]
Muscle tenderization post mortem during cold storage	MMPs	Injection with MMP inhibitors in fish	*Paralichthys olivaceus* (Japanese flounder)	[29]
Characterization in skeletal muscle	TIMP2	Real-time reverse zymography de novo peptide sequencing	*Gadus morhua* (Atlantic cod)	[13]
Post-mortem muscle tenderization during chilled storage	Recombinant MMP9	Zymography	*Paralichthys olivaceus* (Japanese flounder)	[31]
Characterization in skeletal muscle	MMP-like	Zymography	*Pagrus major* (red sea bream)	[32]
Normal and soft textured skeletal muscle	MMPs	Zymography	*Salmo salar* (atlantic salmon)	[35]
Inflammation and immune response				
Initial phase of inflammation and later phase with tissue remodelling	MMP9	mRNA, protein zymography	*Cyprinus carpio* (L) (common carp)	[37]
Immune response against bacterial infection	MMP2, 9, and 13, TIMP2-a/b	mRNA	*Danio rerio* (zebra fish), *Ctenopharyngodon idella* (grass carp), *Sparus aurata* L. (gilthead seabream), *Ictalarus punctatus* (channel catfish)	[17,38,39,46]
Inflammation response to salmon louse	MMP9 and 13	mRNA	*Salmo salar* (atlantic salmon)	[42–44]
Wound healing and tissue remodelling	MMP2	mRNA	*Salmo salar* (atlantic salmon), *Oncorhynchus mykiss* (rainbow trout)	[45]
Exposure to gasoline oxygenates	MMP2 and 9	mRNA	*Danio rerio* (zebra fish)	[48]
Biological effects of toxic exposure				
Exposure to polycyclic aromatic hydrocarbons	MMP9	mRNA, protein zymography	*Danio rerio* (zebra fish)	[47]
Exposure to methyl mercury	MMP9	mRNA	*Danio rerio* (zebra fish)	[49]
Exposure to brominated flame retardants	MMP2, 9, and 13	mRNA	*Danio rerio* (zebra fish)	[50]
Exposure to endocrine disruptors	MMP9	mRNA	*Sparus aurata* L. (gilthead seabream)	[51]
Other functions				
Muscle growth and swimming physiology	MMP2 and 9	Zymography	*Piaractus mesopotamicus* (pacu)	[21]

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