302 Matriptase inhibitor as a disease modifying therapy for osteoarthritis

Asset Overview

Product Type	Small molecule
Indication	Osteoarthritis
Current Stage	Lead Identification / Optimization
Target(MoA)	Inhibitor of Matriptase
Brief Description	• An effective 'disease-modifying OA drug' would target a detrimental protein present in an OA joint but not the normal joint • Our research has enabled the validation of matriptase as a therapeutic target for osteoarthritis
Organization	LifeArc

Differentiation

□ **Tackling Osteoarthritis: Matriptase Inhibitor**

- Matriptase gene expression was significantly elevated in OA cartilage compared with neck of the femur (NOF) cartilage, and matriptase was immunolocalized to OA chondrocytes.
- Matriptase alone caused significant collagenolysis from OA cartilage, which was metalloproteinase-dependent.
- Matriptase also induced MMP-1, MMP-3, and MMP-13 gene expression.

□ **Differentiation in the Development Pipeline and Market Place**

- In clinical study on an interleukin-1 (IL-1) inhibitor, there was no significant clinical improvement that had been reported in either trial compared to the placebo control.
- Small molecule inhibitors designed to inhibit a target that has DMT potential with systemic effects being limited by local delivery.

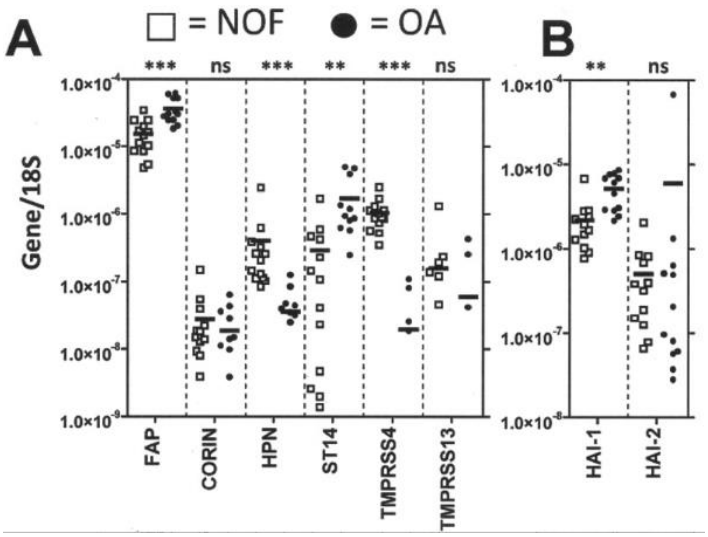
□ **Commercial Potential of Disease-Modifying Therapy (DMT)**

- Few Disease-Modifying Therapies (DMT) are being developed. Most "competition" emerges from analgesics with innovative MOAs—including anti-nerve growth factors (anti-NGFs), a new class of opioids (CR845), an intra-articular formulation of capsaicin (CNTX-4975).
- Prevalence is rising. Diagnosed Prevalent Population (Symptomatic) (7MM), from 36M (2016) to 41M (2026). An effective 'Disease-Modifying OA drug' will deliver structural alteration of the disease linked to clinical benefit.

302 Matriptase inhibitor as a disease modifying therapy for osteoarthritis

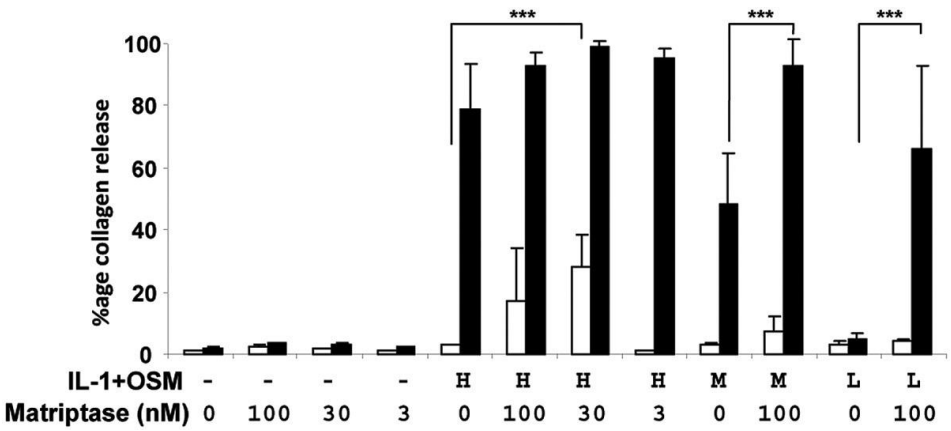
Key Data

Elevated matriptase gene expression in OA tissue



A and B, Elevated matriptase (ST14) expression in osteoarthritis (OA) cartilage. Gene expression levels of several membrane proteinases (A) or hepatocyte growth factor activator inhibitor type 1 (HAI-1) and HAI-2 (B) (analyzed in a separate set of samples, where n = 12 for both OA and neck of femur fracture [NOF]) were assessed in hip cartilage obtained from patients with OA (n = 13) or in normal control cartilage obtained from patients with NOF (n = 12).

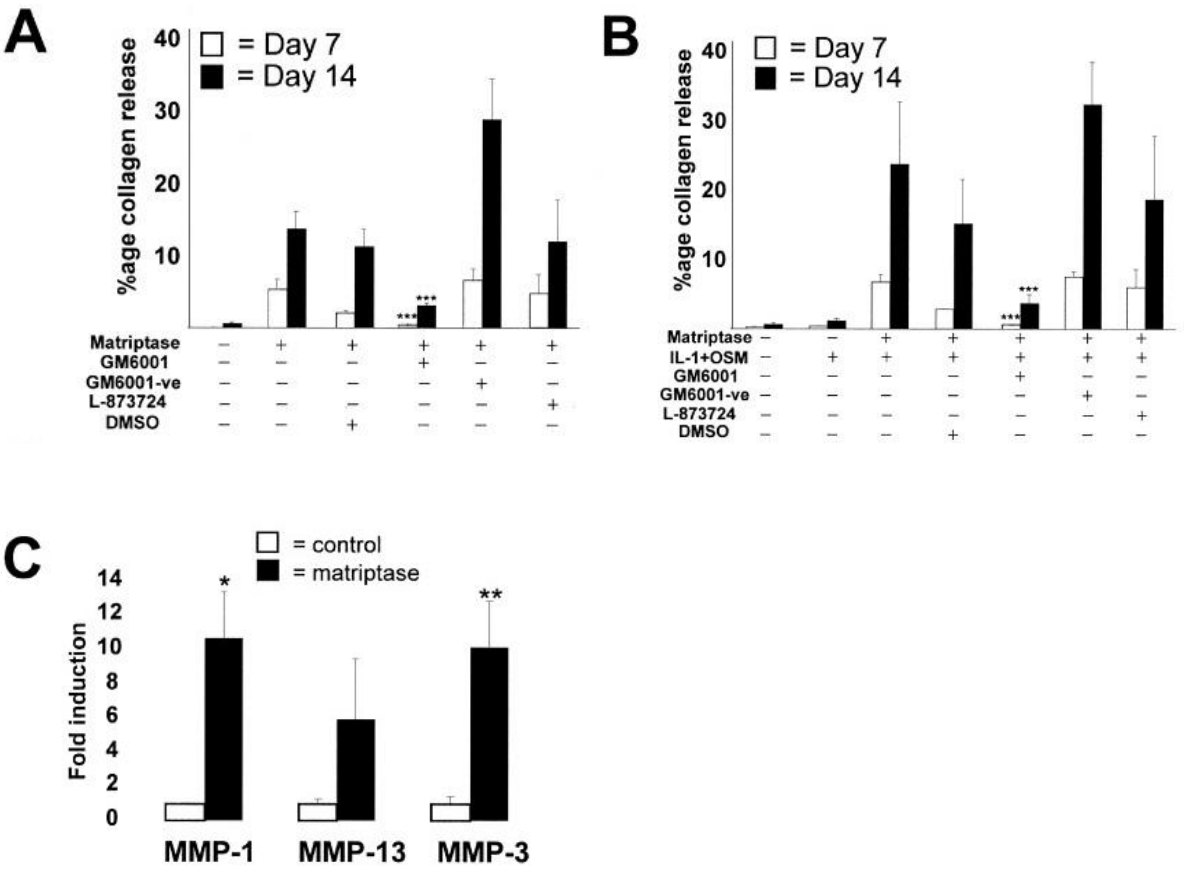
Enhanced cytokine-induced cartilage collagenolysis by matriptase



Bovine cartilage explants were incubated with interleukin-1 (IL-1) plus oncostatin M (OSM) with or without matriptase (100 nM unless indicated otherwise) for 14 days, with fresh medium, cytokines, and reagents used on day 7, as appropriate. The concentrations of IL-1 plus OSM used are as follows: high (H; 1 ng/ml plus 10 ng/ml), medium (M; 0.6 ng/ml plus 6 ng/ml), and low (L; 0.25 ng/ml plus 2.5 ng/ml). Collagen release by day 7 (open bars) and cumulative day-14 release (closed bars).

Matriptase inhibitor as a disease modifying therapy for osteoarthritis

Enhanced osteoarthritis (OA) cartilage collagenolysis by matriptase



A and B, Human OA cartilage explants were incubated with control medium with or without matriptase (100 nM), with or without IL-1 plus OSM (1 ng/ml plus 10 ng/ml), and with or without GM6001 (or its negative control; both 10 μM) or L-873724 (10 nM) for 7 days. The collagen release by day 7 and cumulative release by day 14 were determined by hydroxyproline measurement and expressed as a percentage of the total for each treatment. A, Matriptase as prime stimulus. B, Matriptase plus IL-1 plus OSM as prime stimulus. Bars show the mean and SD results from at least 3 separate experiments (n = 4 samples). C, RNA isolated from the day-7 cartilage was subjected to real-time polymerase chain reaction for matrix metalloproteinase (MMP) gene expression.

302 Matriptase inhibitor as a disease modifying therapy for osteoarthritis

Intellectual Property

Patent No.	
Application Date	
Status	미공개
Country	

Contact Information

Contact Person	Zhi Zhang
Email	zhi.zhang@lifearc.org
URL	https://www.lifearc.org/licensing-opportunity/matriptase/