# Potent MMP-12 Inhibitors as a Therapy for COPD and Asthma

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## BACKGROUND

According to the World Health Organization, chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide. COPD is caused by genetic and environmental factors such as smoking and air pollution; and it is characterized by progressive airflow obstruction associated with inflammation and emphysema.

MMP-12 expression is highly expressed in COPD patients and its activity in turn causes the destruction of alveolar walls in the lung. This lung damage leads to emphysema, thus making MMP-12 a compelling target for pharmacological intervention. Not only is MMP-12 implicated in COPD but elevated MMP-12 levels are also observed in asthma disease progression thus making it a target for asthma therapies.

## BRIEF DESCRIPTION

Prof. Maurizio Pellecchia and his colleagues at the University of California, Riverside (UCR) have developed novel MMP-12 inhibitors with single-digit nanomolar activity. These agents, are highly selective for MMP-12 with appreciable inhibition of only MMP-3. When compared to a known MMP-12 inhibitor, MMP408, the UCR MMP-12 inhibitors are 5 times more potent than MMP408.

To examine their efficacy, the UCR MMP-12 inhibitors were tested in a well-established murine model of elastase-induced emphysema. After treatment, it was determined that the mice treated with the MMP-12 inhibitors exhibited significantly less lung damage than the controls.

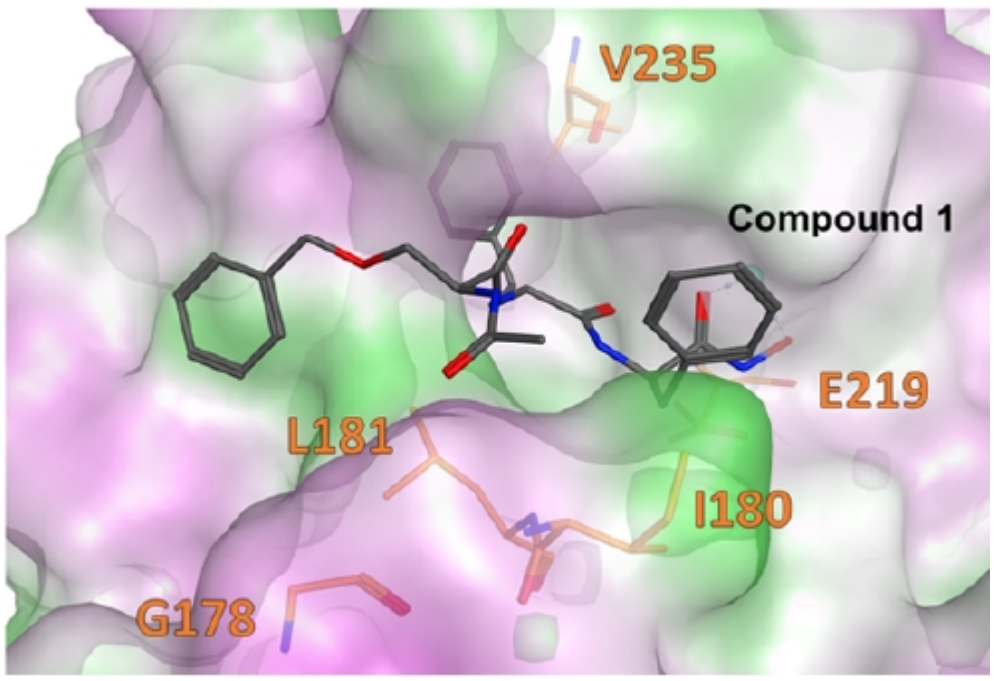



**Fig. 1** Docked geometry of one of the UCR MMP-12 inhibitors in complex with MMP-12.

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## OTHER INFORMATION

### KEYWORDS

chronic obstructive pulmonary disease, COPD, MMP-12, emphysema

### CATEGORIZED AS

- Medical
  - Disease: Respiratory and Pulmonary System

### RELATED CASES

2021-808-0

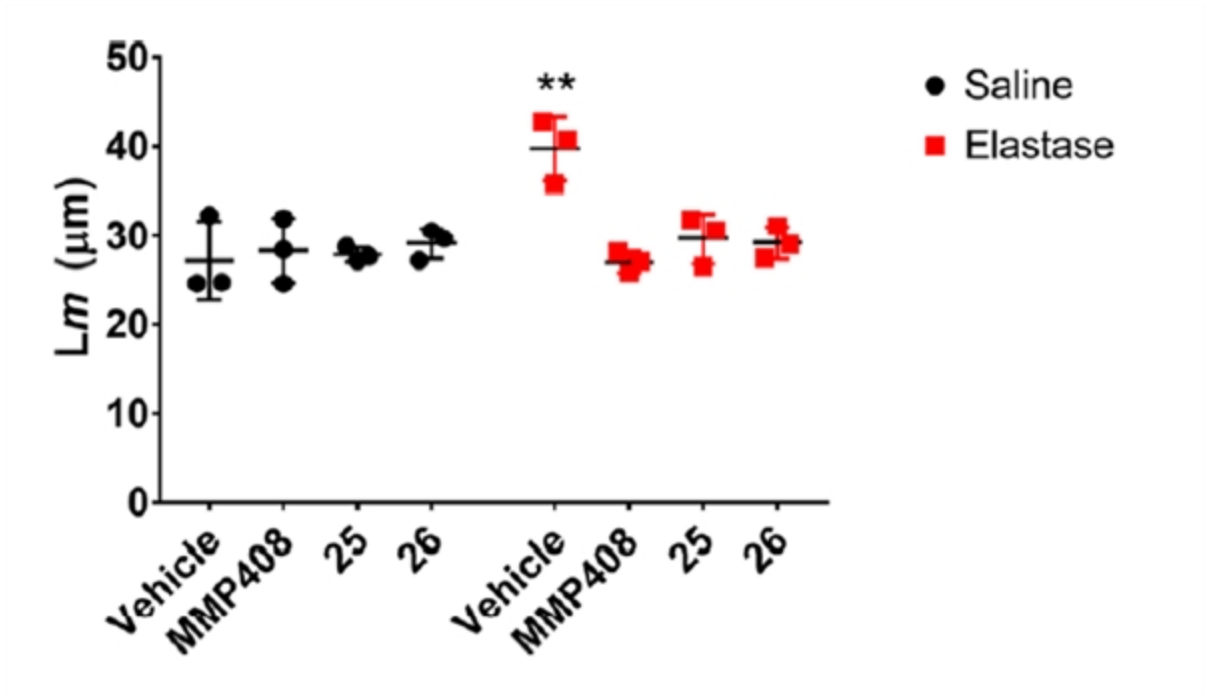



**Fig. 2** Effects of MMP-12 inhibition on lung tissue destruction in a murine model of elastase-induced emphysema. Mice were challenged with a single intranasal instillation of porcine pancreatic elastase (PPE), then treated daily for 7 days with vehicle control or MMP-12 inhibitors MMP408, compound 25, or compound 26. After 21 days, the mice were examined and data gathered on how they responded. Mice exposed to PPE but treated with MMP-12 inhibitors (MMP-408, compound 25, or compound 26) exhibited a significant decrease in emphysema-like pathology compared to PPE + vehicle-treated mice, with measurements for mice treated with PPE + MMP-12 inhibitors exhibiting no significant differences compared to the control, saline treated mice.

## APPLICATIONS

MMP-12 inhibitors may be developed as a COPD or asthma therapy

## PATENT STATUS

| Country | Type | Number | Dated | Case |
|---|---|---|---|---|
| United States Of America | Issued Patent | 11,732,007 | 08/22/2023 | 2021-808 |

## RELATED MATERIALS

- Baggio C., et al. Therapeutic Targeting of MMP-12 for the Treatment of Chronic Obstructive Pulmonary Disease. J Med Chem., Article ASAP (2020). - 10/27/2020

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