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Inhibitors of Prostasin

Background

Prostasin is a prostate-abundant serine protease originally discovered in human seminal fluid. Prostasin mRNA is found in normal prostate epithelial cells, but is not expressed in invasive prostate cancer lines. Expression of prostasin in invasive cancer lines reduces the invasiveness of cells in vitro. Prostasin is also known to be an activator of the epithelium sodium channel, in vitro, and is present in tissues that absorb Na^+ such as kidneys, colon, lung, and salivary glands. The proper regulation of the epithelial sodium channels is crucial to maintaining sodium balance, extracellular fluid volume, and blood pressure. Serine proteases are inhibited by a group of inhibitors called serpins. Serpins work by mimicking the 3-D structure of a normal substrate of the protease. These inhibitors can then be instrumental in such diseases as cystic fibrosis and chronic obstructive pulmonary disease (COPD).

Application

This invention relates to inhibitors of prostasin and their use in the treatment of diseases or dysfunctions which result from disorders of prostasin function or regulation.

Invention

A novel serine protease inhibitor designated PN-1, which has been shown to inhibit prostasin.

Advantages

PN-1 is an irreversible inhibitor of prostasin.

PN-1 could be used to treat such disease as cystic fibrosis and chronic obstructive pulmonary disease, which are known to have sodium channel dysregulation.

Lead Inventor

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Selected References

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