

## Pharmacognosy, Phytochemistry & Natural Products

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## Natural product-derived ectosteric inhibitors of cathepsins

Cysteine cathepsins are potent extracellular matrix-degrading proteases that have been implicated in various skeletal, vascular and respiratory pathologies. Highly potent active site-directed inhibitors have been developed and tested in preclinical and clinical studies. Whereas they are highly effective in slowing down the destructive matrix degradation process, they also have serious side effects which can be attributed to the inhibition of the regulatory functions of the target protease. We have developed a strategy where only the pathologically relevant degradation of collagen and elastin is inhibited without interfering with the other proteolytic functions of the protease. These inhibitors are named ectosteric inhibitors which bind outside of the active site and either block the binding of therapeutically relevant substrates, ligand binding and or protease oligomerization needed for the degradation of extracellular matrix proteins. Natural product libraries appear to be a rich source of such inhibitors. Using various plant extracts and purified compound libraries, we identified potent ectosteric inhibitors which specifically inhibit the collagenase and elastase activities of cathepsins. The talk will discuss the strategy of the identification of ectosteric inhibitors, their mechanism and efficacy in *in vivo* models. Emphasis will be given to compounds identified in traditional Chinese Herbal Medicine used in skeletal and cardiovascular diseases.

## **Biography**

Dieter Bromme has received his Doctoral degree from the University of Halle-Wittenberg (GDR) in 1983. Prior to his appointment as Professor at the Faculty of Dentistry at the University of British Columbia, Vancouver and Canada Research Chair in Proteases and Diseases in 2004, he was a Research Officer at the Biotechnology Research Institute in Montreal, Canada, a Project Leader at Khepri Pharmaceuticals in South San Francisco and a Professor at the Mount Sinai School of Medicine in New York. His research interest is focused on mammalian lysosomal cysteine proteases where he has published almost 180 research papers and book chapters.

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