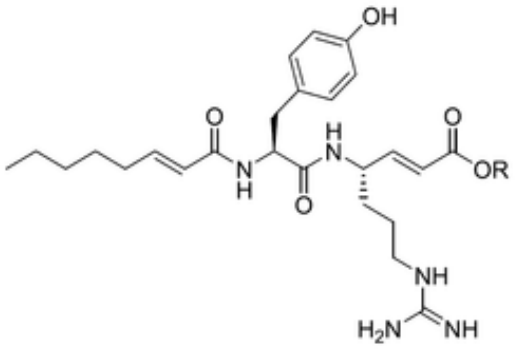
Technology Offer

Barnesins – novel natural small molecules as highly specific cysteine protease inhibitors

Reference Number 10-00107

Challenge

Proteases play an important role in various metabolic processes. Cysteine proteases constitute a specific subclass thereof and are named after the cysteine residue of their catalytic active site. Alteration of activity level or concentration of cysteine proteases has been found to be associated with various diseases as with Cruzain or Falcipain in parasitic infections (Chagas' disease resp. malaria), Cathepsin S in rheumatoid arthritis, Calpain in muscular dystrophy, Cathepsin K in osteoporosis, Cathepsin B in Alzheimer´s diseases or Cathepsin K and L in cancer. This observation turn cysteine proteases into promising drug targets while their inhibitors make ideal potential drug candidates.



Barnesin A

Technology

Provided is Barnesin A, a newly discovered natural small molecule isolated from the Epsilonproteobacterium *Sulfurospirillum barnesii,* and derivatives thereof. The new lipopeptide is equipped with a vinylogous arginine residue. Barnesin A shows a highly specific inhibitory activity against cysteine proteases. First results obtained with a selection of cysteine proteases indicated an IC50 in the low micromolar range for Papain and Ficin and an IC50 in the two-digit nanomolar range for Cathepsin B, which makes it a promising drug candidate for the treatment of metastatic cancers and neurological disorders, especially for Alzheimer´s disease. Moreover, the invention comprises the gene cluster for the biosynthesis and an efficient route for the chemical synthesis of the molecule. A first derivative with improved activity has already been synthesized.

Commercial Opportunity

Barnesin A and derivatives thereof are offered for licensing or co-development.

Development Status

For a first selection of therapeutically relevant cysteine proteases *in vitro* data are available, Evaluation of further relevant enzymes is ongoing. Based thereon SAR studies will be conducted.

Patent Situation

A European Patent application with priority of February 2018 has been filed.

Further Reading

Rischer *et al*. (2018). *ACS Chem Biol. Jun 25 (2018)[Epub ahead of print]:* Biosynthesis, Synthesis, and Activities of Barnesin A, a NRPS-PKS Hybrid Produced by an Anaerobic Epsilonproteobacterium.Marton Siklos *et al.* (2015), *Acta Pharmaceutica Sinica B* 5.6 (2015): 506-519.

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