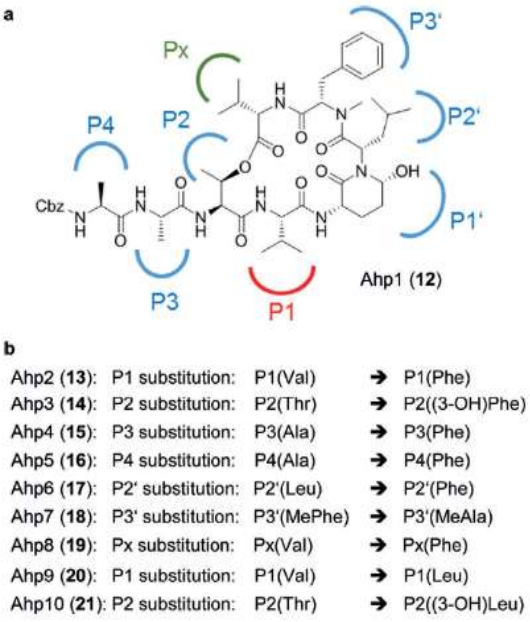
HTRA inhibitors

Novel Ahp-cyclodepsipeptide-based HTRA inhibitors

Invention

High Temperature Requirement A (HTRA) proteins are serine proteases of the S1 family (trypsin/chymotrypsin-like). HTRA1 is supposed to play a role in macular degeneration, and HTRA2 has been associated with cell death in reperfusion-ischemia. Therefore, HTRA proteins might represent novel therapeutic targets. However, currently no inhibitors with drug-like characteristics and thus promising potential for pharmaceutical development are available. Researchers of the University of Duisburg-Essen have now demonstrated that Ahp-cyclodepsipeptides represent a suitable scaffold for generating target-tailored inhibitors of serine proteases. They have developed a practical mixed solid- and solution-phase synthesis that allows the customized synthesis of Ahp-cyclodepsipeptides and thus tailored inhibitor synthesis. The applicability of this approach was shown by the generation of the most potent human HTRA1 as well as HTRA2 protease inhibitors to date (see figure). Inhibitory potency of the synthesized substances was proven in binding studies and cell-based assays.



Structure of synthesized HTRA protease-tailored Ahp-cyclodepsipeptide:
a) Chemical structure of Ahp1 and its corresponding binding mode;
b) Overview on the sequence modifications underlying Ahp2-Ahp10;
Taken from figure 3 of Köcher, S., *et al.* (2017).

Commercial Opportunities

Ahp-cyclodepsipeptides constitute a novel class of HTRA inhibitors and are thus qualified to be further developed as “first-in-class” drugs for that target. On behalf of the University of Duisburg-Essen, PROvendis offers the invention for licensing and research collaboration to interested companies.

Current Status

In case of interest we will be pleased to inform you about the patent status.

Relevant Publications

Köcher, S., et al. (2017) Tailored Ahp-cyclodepsipeptides as potent non-covalent serine protease inhibitors. *Angew. Chem. Int.* Ed. Engl. 56: 8555-8558.

An invention of the University of Duisburg-Essen.

Competitive Advantages

- First-in-class inhibitors for HTRA
- Novel promising drug target for various indications

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Technology concept formulated

Industries

- Pharmaceutical Industry

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