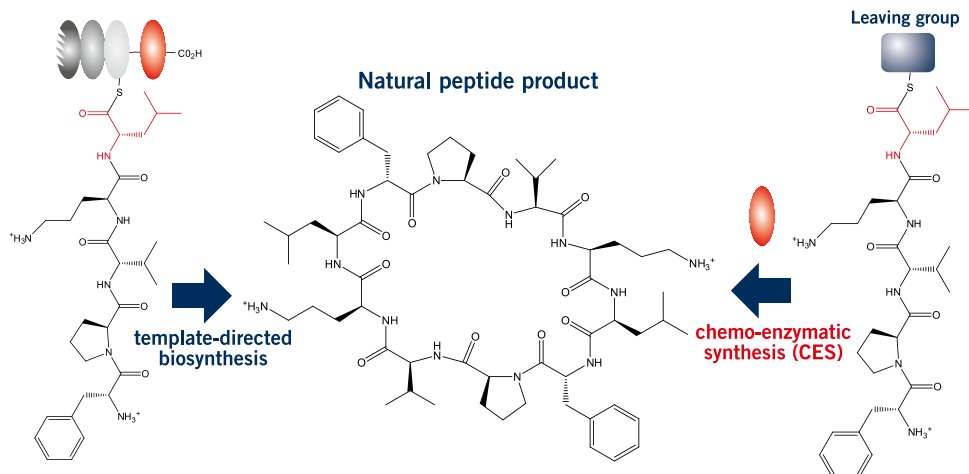


# Cyclic Peptides: Optimization of natural peptide drugs

## The innovation

The innovative platform technology presented here allows for the first time the chemo-enzymatic synthesis of highly-potent cyclic peptide agents and the fast and efficient generation of combinatorial natural product libraries.

Cyclic peptides are among the most effective agents to control pathogenic germs, fungal infections as well as for cancer treatment, and hence are of outstanding relevance for drug discovery. Since 1980, two thirds of all newly-approved drugs were natural products or derivatives thereof. Prominent representatives of cyclic peptide drugs are antibiotics like Daptomycin and Pristinamycin as well as the antimycotic agent Caspofungin. In Nature, cyclic peptides are synthesized by various microorganisms. However, their biosynthesis does not occur via the ordinary protein biosynthesis machinery, the ribosome, but rather on large multi-enzyme complexes. Accordingly, this class of substances shows a relatively high structural diversity. In the past, this diversity prohibited or at least significantly hampered the synthesis of corresponding natural product derivatives, requiring time-consuming and costly synthesis and/or tedious retrieval of appropriate drug candidates. Within the scope of the ongoing R&D projects, the tools for the straightforward and efficient genera-



tion of a wide range of tailor-made, combinatorial libraries of cyclic peptides are developed and available for exclusive licensing.

The new innovative process of chemo-enzymatic synthesis involves the synthesis of linear precursor peptides, which are subsequently coupled to reactive leaving groups and finally enzymatically and hence with highest region- and stereo-selectivity - converted to the active cyclic peptide. Since there are hardly any constraints concerning the applied building blocks, the implementation of this new technology provides first-time access to a nearly unlimited set of novel, proprietary natural product analogs and is particularly attractive for the

optimization of pharmaceutical properties of cyclic peptide agents.

Proof-of-concept for the successful implementation of this new technology has already been provided by the synthesis and optimization of the natural peptide antibiotic Tyrocidine A. Within a relatively small library of less than 200 compounds, derivatives with considerably improved therapeutic indices (>40fold) could be identified with a very high hit rate (>3%, standard procedures in comparison: <0.01%). Given the high potency of the natural lead compounds, this innovative technique can be adopted with comparable efficiency for optimization of the most diverse, cyclic peptide agents.

## Keywords

- „Red“ biotechnology
- Chemo-enzymatic synthesis
- Combinatorial libraries
- Drug discovery
- Antibiotics
- Oncologics
- Antimycotics

## Advantages at a glance

- Easy and efficient synthesis of natural cyclic peptide agents and derivatives thereof
- Highest regio- and stereo-selective synthesis (enzyme-catalyzed)
- Generation of biocombinatorial peptide libraries
- Generation of innovative, proprietary peptide drugs
- Improvement of pharmacological properties
- Cost savings

To acquire a licence for this new technology, please don't hesitate to contact us!



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## Areas of application

- Biotechnological drug discovery and drug optimization
- Pharmaceutical Industry (antibiotics, antimycotics, oncologics etc.)

## Patent status

The invention is covered by a patent family that was internationally filed, has already been granted in EP and is owned by ZYRUS Beteiligungsgesellschaft mbH & Co. Patente I KG. The application was filed in July 2003.