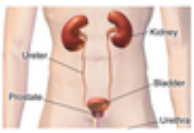
Technology Offer

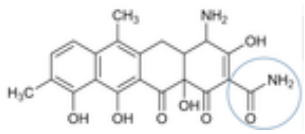
# Novel Chelocardin Derivatives – resistance breaking atypical tetracyclines with broad-spectrum antibiotic activity

Reference Number 02-00315

## Challenge

Multidrug resistant (MDR) bacteria, which are associated with nosocomial but also with community-acquired infections, are a current threat to public health. Especially pathogens belonging to the ESKAPE species (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa,* and *Enterobacter spp.*) are the leading cause of concern. Thus, for example hospital acquired infections (HAI) like complicated urinary tract infection (cUTI) or complicated intra-abdominal infection (cIAI) lack efficient antimicrobial therapy and result in high mortality rates. Therefore, the demand for novel antibiotic substances with resistance breaking properties remains high.




*Carboxamido-Deacetyl-Chelocardin for treatment of urinary tract infection*

## Technology

Provided is a broad-spectrum antibiotic lead candidate with significantly improved activity against all Gram-negative pathogens of the ESKAPE panel. The compound is based on the atypical tetracycline Chelocardin (CHD) originally discovered in the 1970s with proven efficacy in humans. CHD offers a structurally altered aromatization pattern with an unusual planar structure, providing an uncommon mode of action (MoA). CHD not only targets protein biosynthesis but also corrupts the integrity of the bacterial membrane. Due to this dual mode of action CHD retains activity against tetracycline-resistant strains and probably slows down the development of new resistance mechanisms. The newly developed CHD-analog Carboxamido-Deacetyl-Chelocardin (CDCHD) shows fourfold efficacy compared to CHD against a broad spectrum of tetracycline resistant pathogens and has improved activity against ESKAPE pathogens, including ESBL-producing *E.coli* and *K. pneumoniae* involved in cUTI or cIAI. Therefore, CDCHD is a promising antibiotic drug candidate applicable for an injectable therapeutic for treatment of cUTI or cIAI. Furthermore, the invention covers the gene cluster ensuring the cost-effective production of the drug and providing an invaluable tool for combinatory biosynthesis for the generation of further novel improved CHD-analogs.

## Commercial Opportunity

The invention is offered for licensing or co-development.

## Development Status

PK/PD data are available for CDCHD; in a cUTI study in mice efficacy of treatment in bladder and kidneys could be proven; preclinical testing is under way. Analoging through bioengineering and semi-syntheses is ongoing.

## Patent Situation

Patents were granted in EP and US (priority of 2009); a new European patent application covering the complete gene cluster was filed in December 2017 (EP17210536) .

## Further Reading

Stepanek et al. 2016. Dual mechanism of action of the atypical tetracycline chelocardin.Biochim Biophys Acta. 2016 Jun;1864(6):645-654.
Lesnik et al. 2015. Construction of a new class of tetracycline lead structures with potent antibacterial activity through biosynthetic engineering. Angew. Chem. Int. Ed., 2015, 54, 3937-40.

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