

Unexpected identification and characterization of a fungal antimicrobial peptide with a very narrow spectrum of activity directed only against *Clostridium perfringens*

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Mots-Clés : (5 max) : fungal peptides, Non-Ribosomal Peptides (NRPs), cyclodepsipeptide, *Clostridium perfringens*, narrow spectrum antibiotic

Doctorant/post-doctorant Oui Non

Résumer (10-15 lignes max, calibre 12, interligne 1,5) :

Fungi produce various Non-Ribosomal Peptide (NRPs) including cyclic peptides, i.e. cyclodepsipeptides. We tested those peptides on a large panel of micro-organisms as well as their toxicity to human cells. Some cyclodepsipeptides were found active on Gram positive bacteria and fungi but unfortunately were highly toxic limiting their use in medicine. Unexpectedly, one cyclodepsipeptide was found active only against *Clostridium perfringens* (both reference and clinical strains, including resistant ones) at doses of 0.78-1.5 μ M and did not cause induction of resistance after continuous exposure over 30 days. This peptide was furthermore found very safe with no observed toxicity in vitro. Mechanistic approaches showed that this peptide acts through a specific inhibition of the synthesis of proteins only in *C. perfringens*, explaining its selectivity and safety. Finally, ex vivo and in vivo testing confirmed the efficiency and selectivity of this peptide. Taken together, data showed that this peptide displays all the characteristic of a promising antibiotic (i.e. active at nM- μ M range even against resistant strain, not causing resistance, low to no toxicity and active in vivo). Importantly, since the commensal bacteria are known to inhibit *C. perfringens*, the narrow activity of this peptide against *C. perfringens* will make it a major tool in the treatment of this bacterium.

Références :

Olleik H, Nicoletti C, Lafond M, Courvoisier-Dezord E, Xue P, Hijazi A, Baydoun E, Perrier J, Maresca M. Comparative Structure-Activity Analysis of the Antimicrobial Activity, Cytotoxicity, and Mechanism of Action of the Fungal Cyclohexadepsipeptides Enniatins and Beauvericin. *Toxins* (Basel). 2019 Sep 3;11(9):514. doi: 10.3390/toxins11090514. PMID: 31484420; PMCID: PMC6784244.

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