Università degli Studi di Napoli Federico II

PhD in Biotechnology - 37th cycle

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Combined genetic/chemical-modification strategies to improve biological stability and activity of recombinant Host Defence Peptides.

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The rapid increase in drug-resistant infections is a serious challenge to antimicrobial therapies. A class of very interesting molecules that could help solve the bacterial resistance problem are antimicrobial peptides (AMPs) which target microbial membranes and, often, intracellular targets. AMPs, in addition to direct antimicrobial activity, show several biological activities like anti-inflammatory activity and wound healing enhancement. For this reason, they are more appropriately termed Host Defense Peptides (HDPs) [1]. Even if HDPs have great medical and industrial potential, due to their peptidic nature, they have limited stability, a drawback that has so far limited their exploitation. HDP usually have a short half-life due to their rapid degradation by proteolytic enzymes produced by many bacteria but present also in almost all the biological fluids [2].

The general aim of present PhD project is the development of strategies to improve biological stability and activity of HDPs in general and of recombinant HDPs in particular. This goal will be pursued trough three different but complementary strategies:

- PEGylation and/or PASylation of the HDPs.
- Multimerization of the HDPs.
- Preparation of recombinant HDPs with modified N- and C- termini.

These three strategies could be easily combined to prepare vary stable peptides.

After the appropriate chemical modification procedures, the modified peptides will be characterized to evaluate their antimicrobial activity, toxicity, biological stability and immunomodulatory activity.

References

[1] Hancock RE, Sahl HG, Antimicrobial and host-defense peptides as new anti-infective therapeutic strategies, Nat. Biotechnol. 24 (2006) 1551–1557.

[2] Kumar P, Kizhakkedathu JN, Straus SK. Antimicrobial Peptides: Diversity, Mechanism of Action and Strategies to Improve the Activity and Biocompatibility In Vivo. Biomolecules. 2018 Jan 19;8(1):4.