Università degli Studi di Napoli Federico II PhD in Biotechnology - 39th cycle

Dr. Ida Palumbo

Development of innovative strategies for the biotechnological exploitation of "Host defense peptides" (HDP)

Tutor: Eugenio Notomista (BIO/10).

Department: Department of Biology - University of Naples “Federico II”, Via Vicinale Cupa Cintia, 21, 80126 Naples NA.

The rapid increase in drug-resistant infections emphasizes the urgent need to develop new antimicrobials. A class of very promising molecules are antimicrobial peptides (AMPs) that kill bacteria damaging their membranes. Very interestingly, in addition to direct antimicrobial activity, they also show several biological activities like anti-inflammatory activity and wound healing enhancement. However, sensitivity to proteases reduces their half-life and limits their therapeutic exploitation. An intriguing solution is to design peptidomimetics mimicking AMPs but resistant to protease like peptoids. To this end, a 13-residue AMP-like peptoid, P13#1, was designed [1]. As expected, P13#1 has all the pharmacologically relevant properties of AMPs but it is more active than natural AMPs themselves: broad range antimicrobial (bactericidal) activity; antibiofilm activity; strong binding to LPS and inhibition of LPS-induced release of pro-inflammatory mediators. Very interestingly, many natural and synthetic AMPs have a cyclic structure (e.g. θ-defensins and bactenecin) that confers higher resistance to proteases, lower conformational freedom and stronger binding to membranes. Accordingly, the first objective of the present PhD project is to design and characterize P13#1-inspired cyclic peptoids and chemically crosslinked bicyclic peptides with improved features. Unfortunately, the polymeric nature of peptides and peptoids makes difficult their administration. The relatively high molecular weight of peptides/peptoids and their “sticky” nature makes difficult obtaining an adequate biodistribution, decreases efficacy and increases local damage and toxicity. Therefore, P13#1 and the new cyclic peptides and peptoids will be used to achieve the second objective of the PhD project i.e. the development of effective delivery systems. In particular, the project aims to develop inhalable nanoparticles to deliver peptides and peptoids directly to the airways and functionalized hyaluronic acid hydrogels to obtain antimicrobial wound dressings.

[1] Cafaro, V.; Bosso, A.; Di Nardo, I.; D'Amato, A.; Izzo, I.; De Riccardis, F.; Siepi, M.; Culurciello, R.; D'Urzo, N.; Chiarot, E.; et al. The Antimicrobial, Antibiofilm and Anti-Inflammatory Activities of P13#1, a Cathelicidin-like Achiral Peptoid. Pharmaceuticals 2023, 16, 1386. https://doi.org/10.3390/ph16101386