

PhD position in Physical Chemistry applied to biological systems

Project title: Amyloid-cationic peptides for antimicrobial applications

Laboratory : Laboratoire des Biomolécules (LBM) – UMR 7203
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Duration: 3 years, starting in October 1st, 2022 (application to May 17, 2022)

Keywords: Structure-activity relationship, membrane perturbation, peptide aggregation, bacteria mimics

Project description:

Antimicrobial resistance has become one of the major spur to overcome traditional approaches to new drug discovery. Here, we propose a new class of antimicrobials by designing chimera peptides made of an amyloid and a cationic sequence. Thanks to the juxtaposition of both entities, we will fine-tune the membrane-perturbation activities of the new Amy-Cat Pep conjugates as a function of their aggregation state in solution but also at the lipid membrane. As a proof of concept, a first generation of Amy-Cat-Pep has shown highly significant antimicrobial activities towards Gram(+) and Gram(-) bacteria but no hemolytic ones. The interdisciplinary project will center around rational peptide design, cellular assays (antimicrobial and hemolytic activities), structural characterization by CD, FTIR, NMR techniques, and mode of action (membrane poration/insertion) of the conjugates using bacterial lipid models adapted to the biophysical techniques (single-molecule conductance, fluorescence and IR spectroscopies). The interplay of amyloid/cationic sequence will ensure to steer lipid interaction of the Amy-Cat Pep so as to selectively perturb microbial versus mammalian membrane integrity. Finally, the robust mechanistic insights of these new conjugates will contribute to the discovery of efficient antimicrobial peptides with reduced toxicities.

The project will include:

- Peptide synthesis of chimera peptides (Fmoc synthesis)
- Kinetics of amyloid formation (Fluorescence and IR spectroscopies)
- Optimization of bacteria models including peptidoglycans

- Interaction of Amy-Cat-Pep with bacteria mimics (Lipid vesicles, Lipid supported bilayers) (Fluorescence, DLS, TEM, BLM)
- Structural characterization of the chimera peptides in solution and in membrane models (ATR-FTIR, CD, NMR)
- Antibacterial and cytotoxicities tests.

Expected results:

Thanks to an optimized design of the chimera peptides and to the development of biophysical techniques using realistic models of bacteria, we are seeking for a first approach of action mechanism of the amyloid-cat-pep as a new class of antimicrobial peptides.

Profile and skills required:

The candidate must have (or be in the process of obtaining this year) a Master2 degree (or international equivalent) in Chemistry. The candidate must have a good theoretical knowledge in biochemistry/biology. The candidate must be highly committed to pluridisciplinary research project. A first experience in peptide chemistry and/or good knowledge in spectroscopies devoted to peptide structure characterization could be a plus.

Application: The procedure is detailed on the website of the doctoral school ED388

<http://www.ed388.upmc.fr/fr/le-doctorat-a-l-ed-388.html>

Application opening: April 13 , 2022 - Application deadline: May 17, 2022

References:

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