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S E M I N A I R E

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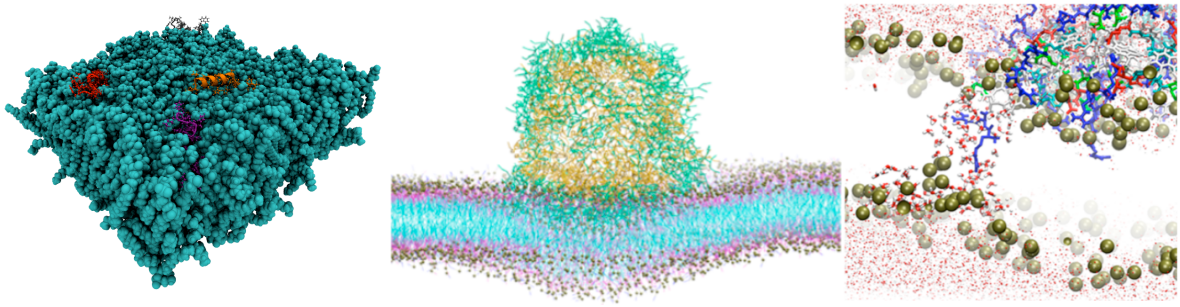
« Sequence activity relationship studies of antimicrobial peptides enlighten drug discovery »

The 2016 Review on Antimicrobial Resistance[1] (AMR) predicts that, unless action is taken, around 10 million deaths per year will be attributable to AMR by the year 2050. Action recommended by the review is two-fold: 1) that the inappropriate use of existing antimicrobials should be reduced so that their utility endures for longer and; 2) new antimicrobials must be made available that are effective against drug-resistant bacteria. The pipeline of new antibiotics is limited however, hence the potential of numerous alternatives to antibiotics – "noncompound approaches (i.e. products other than classic antibacterial agents) that target bacteria or approaches that target the host" – is being actively investigated.[2] Antimicrobial peptides (AMPs) are a potential alternative to classical antibiotics that are yet to achieve a therapeutic breakthrough for treatment of systemic infections.

In this talk, I will present the work that we have been doing in investigating the mechanisms of action of antimicrobial peptides on model lipid membranes using classical molecular dynamcis simulations. In doing so, I will primarily focus on the work we have been doing over the last several years investigating how minor changes to the sequence of antimicrobial peptides affects their potency and their mechanism of action. [3-5] Additionally, I will present our recent work investigating the structure and antimicrobial activity of a pseudocapsid formed of antimicrobial peptides.[6] As each of these projects have significantly benefitted from an interdisciplinary approach, I will also provide a brief description of the experimental work that has done by our various collaborators to compliment the simulations we have conducted in both cases.



References
[1] O'Neill, J. (2016). Tackling drug-resistant infections globally: final report and recommendations. 1st ed. [ebook]
[2] Czaplewski, L. et al (2016) Alternatives to antibiotics—a pipeline portfolio review. *Lancet. Infect. Dis.* **16**, 239-251.
[3] Amos, S. B. A. et al (2016) Antimicrobial peptide potency is facilitated by greater conformational flexibility when binding to gram-negative bacterial inner membranes. *Sci. Rep.* **6**, 37639..
[4] Manzo, G. et al (2019) Minor sequence modifications in temporin B cause drastic changes in antibacterial potency and selectivity by fundamentally altering membrane activity. *Sci. Rep.* **9**, 1385.
[5] Manzo, G. et al (2019) Temporin L and aurein 2.5 have identical conformations but subtly distinct membrane and antibacterial activities. *Sci. Rep.* **9**, 10934.
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Mercredi 17 mars 15h00