Controlling the interactions between lipid nanoparticles and bacteria for the delivery of antimicrobials

Brendan Dyett[1], *Thomas Meikle*[1], *Biserka Lakic*[1], *Priscila Cardoso*[2], *Céline Valéry*[2], *Calum J. Drummond*[1], *Charlotte E. Conn**[1]

[1]School of Science, STEM College, RMIT University, Melbourne 3001
[2]School of Health and Biomedical Science, STEM College, RMIT University, Melbourne 3001
charlotte.conn@rmit.edu.au

The overuse and misuse of antibiotics has led to the growing threat of antimicrobial resistance, declared as one of the top 10 global public health threats by the WHO. Antibiotic resistant bacteria, causing diseases such as urinary tract infections and sexually transmitted diseases, have now been detected in every country in the world, with superbugs (multi- or pan-resistant bacteria) of particular concern. Gram-negative bacteria, in particular, can develop resistance to antibiotics due to an external lipid membrane, which hinders the transport of antibiotics. One way to overcome this issue is to encapsulate the antibiotic in a lipid-based nanocarrier, which can facilitate drug transport across this membrane, Figure 1. In this talk I will discuss our recent studies determining the uptake of cubosomes, lipid-based nanocarriers of cubic symmetry, into gram-positive and gram-negative bacteria.[1] Fundamental differences in the uptake mechanism between these types of bacteria can assist in the design of novel cubosomes, targeted to a particular bacterial strain. The ability of cubosomes to deliver a range of antimicrobials, including antimicrobial peptides[2,3] and metal nanocrystals[4], will be described. Finally, the ability of cubosomes to target intracellular infections is exemplified with the delivery of the anti-tubercular drug rifampicin to intracellular TB infection.

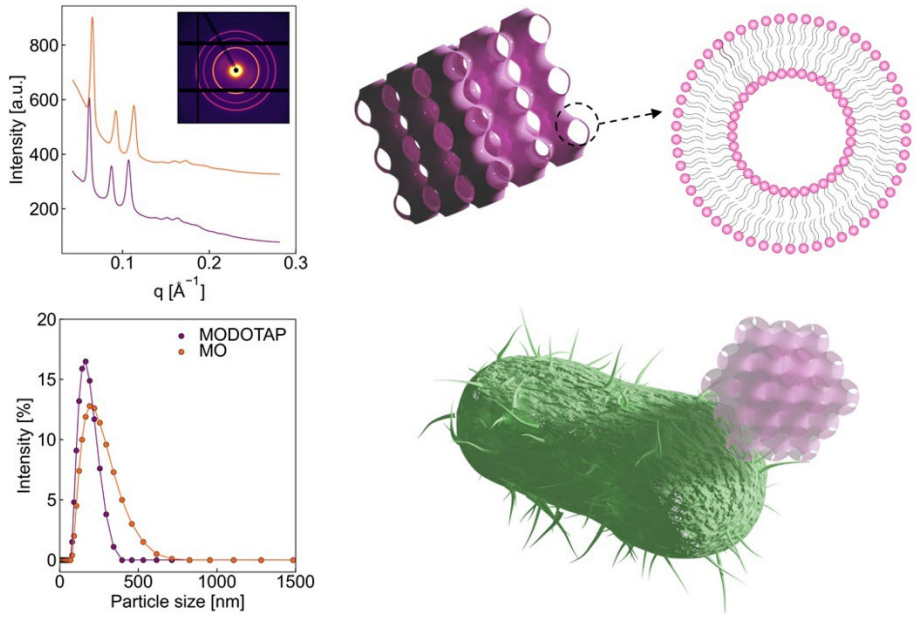

Figure 1: Schematic illustration of cubosome interaction with the bacterial cell surface. 1-D SAXS patterns and DLS of cubosome structure and size. Reproduced from [1]

References

[1]Dyett BP, et al. *ACS Applied Materials & Interfaces* **2021**, 13(45), 53530-40.
[2]Cardoso P, et al. *Frontiers in Chemistry* **2022,** 10, 1009468
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[4]Meikle TG, *ACS Applied Materials & Interfaces* **2020**, 12(6), 6944-54.