A Supramolecular Approach to Combatting Antimicrobial Resistance

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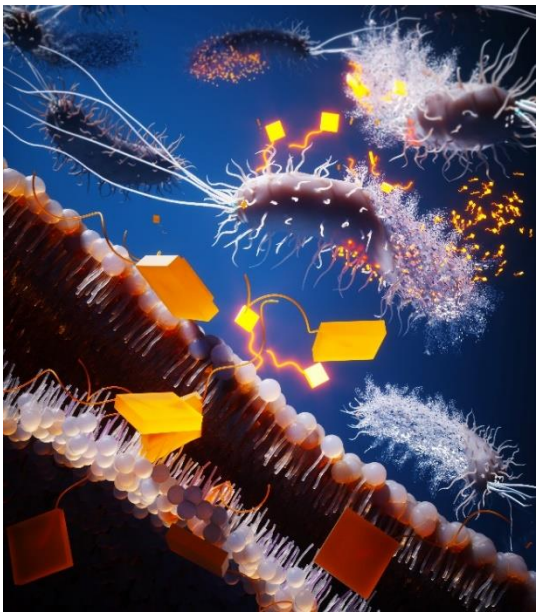
Antimicrobial Resistance (AMR) has been widely recognised as a top priority public health threat by the World Health Organization (WHO) and by Governments around the world, where the majority of our antimicrobial therapies may be obsolete by 2050.[1] There is, therefore, an urgent need for new antimicrobial drugs that exhibit a distinct mechanism of action from currently available treatment options.

Our recent work harnesses the principles of supramolecular chemistry, which explores non-covalent interactions between molecules, to develop novel strategies for combating AMR. Supramolecular chemistry has long been a fundamental area of study but has now reached a level of maturity that is finding significant real-world applications, most notably in medicinal chemistry.[2] However, the development of new antimicrobial agents that exploit this approach has received little attention.

We have focussed on the design of receptor molecules capable of disrupting cellular ion homeostasis in bacteria. Squaramides are particularly useful in this regard due to their strong H-bond donating ability and their synthetic versatility that translates to facile tuning of their physicochemical properties.[3] This talk will summarise some of our efforts to design easily accessible, and functionally rich squaramides for use as ion receptors and transporters and report on our progress towards the application of these ion transporters as a new class of antimicrobial agents.[4,5]



References

1. Bassetti, M., Poulakou, G., Ruppe, E., Bouza, E., Van Hal, S. J., Brink, A., *Intensive Care Med.,* **2017***,* 43, 1464–1475.
2. Davis, J. T., Gale, P. A., Quesada, R., *Chem. Soc. Rev.,* **2020**, 49, 6056.
3. Marchetti, L.A., Kumawat, L.K., Mao, N., Stephens, J.C., Elmes, R.B.P., *Chem*, **2019**, 5, 1398-1485.
4. Brennan, L. E., Kumawat, L. K., Piatek, M. E., Kinross, A. J., McNaughton, D. A., Marchetti, L.A, Geraghty, C., Wynne, C., Tong, H., Kavanagh, O. N., O'Sullivan, F., Hawes, C. S., Gale, P. A., Kavanagh, K., Elmes, R.B.P., *Chem*, **2023**, 9, 3138 – 3158.
5. Brennan, L. E., Luo, X., Mohammed, F. A., Kavanagh, K., Elmes, R.B.P., *Chem. Sci.,* **2025**. In Press. DOI: 10.1039/D4SC01693A