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Editorial

Editorial: Antibacterial targets for the 21st century

The discovery of life-saving antibiotics and their mechanisms of action has been one of the great success stories of bio-organic chemistry in the 20th century: from penicillin to erythromycin, chloramphenicol, streptomycin, and vancomycin. However, the "golden age of antibiotic discovery" has passed, and the rate of antibiotic discovery in the last 30 years has slowed to a trickle, at the same time as dramatically worsening levels of antibiotic discovery. As is well-documented elsewhere, high-throughput screening programs based on genomic drug targets in the 1990s were surprisingly unsuccessful, and several commercial and regulatory factors have led to many pharmaceutical companies reducing or stopping their antibacterial R&D programmes.

In the face of emerging multiply-resistant bacterial pathogens, notably Gram-negative organisms such as *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, and *Escherichia coli*, it is therefore important that academic research groups persevere in the search for new targets for antibacterial drug action, and employ new tools for drug discovery for the known targets. This Special Issue contains a series of review articles on current efforts in bio-organic chemistry, biochemistry and microbiology to identify and study promising targets and new approaches for antibacterial drug discovery.

One of the best known targets for antibacterial chemotherapy has been the assembly of the bacterial cell wall, notably the peptidoglycan layer containing a unique structure not found in eukaryotes. Gobec and co-workers describe recent efforts to identify potent inhibitors of the earlier cytoplasmic enzymes MurA-F on the peptidoglycan biosynthetic pathway, and Roper and co-workers describe recent studies on the transglycosylase activity of penicillin-binding proteins on the cell surface, for which crystal structures emerged in 2007. Recent studies have shown that the later enzymes of peptidoglycan biosynthesis are co-localised with bacterial cell division proteins, and van den Blaauwen and co-workers describe the development of chemical inhibitors for FtsZ and other cell division proteins involved in this multi-enzyme complex. The biological modification and recycling of peptidoglycan have also emerged as possible antibacterial targets: Clarke and co-workers describe molecular studies on peptidoglycan acetylation and de-acetylation; and Fisher and Mobashery describe recent chemical biology studies on the cellular peptidoglycan recycling machinery.

The lantibiotic family of non-ribosomal peptides have proved a rich area of bio-organic chemistry research for over 20 years, the article by Tabor describes the impact that chemical synthesis in particular has had in lantibiotic research in recent years. Two emerging areas of research are then described: Bolhuis and Aldrich-Wright describe antibacterial agents that target DNA, including recently discovered transition metal-based agents; Williams and co-workers then describe "the art of antibacterial warfare" via chemical intervention in bacterial quorum sensing. Finally, Fishwick and co-workers describe the application of new methods for structure-based drug design, which will help to yield lead compounds for recalcitrant enzyme targets and new targets that emerge from research. If the levels of antibacterial drug resistance continue to increase, as seems likely, the chemical biology/microbiology interface needs to find new antimicrobial targets and therapeutic agents, and to identify new strategies for utilising the targets that we already know about, and we hope that these articles help to stimulate research in this important area.

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