

## Novel inhibitors of NorA efflux pump for combating antimicrobial resistance

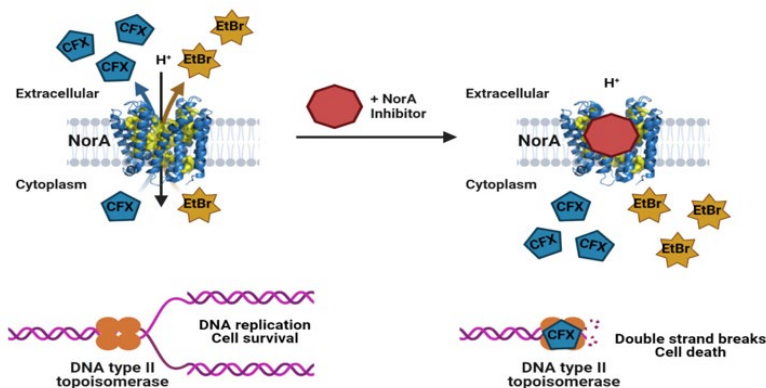
These novel compounds could be used in the treatment of antibiotic resistant bacterial infections and demonstrate that inhibitors of NorA efflux can prevent the emergence of further resistant strains.

### Problem addressed

Antimicrobial resistance (AMR) is a leading cause of death worldwide and has been identified by the World Health Organisation (WHO) as one of largest threats facing global health and development. The development of inhibitors of resistance mechanisms would allow the use of existing drugs in combination therapy as a method of targeting resistant bacteria.

### Proposed solution

Efflux pumps represent the first-line mechanism of resistance for many bacteria, whereupon extrusion of the drug reduces the intracellular concentration below the level of therapeutic efficacy. Inhibition of the protein NorA would prevent the efflux of antibiotics such as ciprofloxacin, increasing their efficacy and hence reducing the emergence of resistance. Use of these novel compounds of NorA inhibitors may be used to resensitise bacteria to fluoroquinolone antibiotics or as a combination therapy with a fluoroquinolone antibiotic to treat a bacterial infection.



### Technology overview

This invention identifies novel compounds to tackle antimicrobial resistance (AMR). Through a novel high-throughput phenotypic screen, the researchers have identified the first potent and druglike inhibitors of the *Staphylococcus aureus* (*S. aureus*) NorA multidrug efflux pump, a key driver of clinical resistance to antibiotics such as ciprofloxacin. The inventors have developed novel compounds to provide a potent *in vivo* tool to validate NorA as a therapeutic target in murine bacteraemia models, and subsequently establish a chemical series suitable for future development for combination therapy with existing antibiotics. The inventors have further established compounds with potent activity *in vitro* models.

### Benefits

- Treatment of bacterial infections.
- Can prevent the emergence of resistant strains.
- Exhibit superior potency and low toxicity over other NorA inhibitors.
- Potent inhibitors that re-sensitised methicillin-resistant *S. aureus* (MRSA) to the antibiotic ciprofloxacin.
- Validates NorA as a therapeutic target and establishes a chemical series suitable for future development for combination therapy with existing antibiotics.

Dr Luis A. Gomez-Sarosi

Industry Partnerships and  
Commercialisation Executive –  
Natural Sciences

e: l.gomez-sarosi@imperial.ac.uk

t: +44 7593 505908

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## Intellectual property information

NorA inhibitors is protected by UK patent application: GB2319181.0

## Inventor information

Janine Gray , [Edward Tate](#), Elizabeth Ledger, [Thomas Burden](#), [Andrew Edwards](#)