

## NOVEL ANTIBIOTICS

Dr Matthew Cooper of the Department of Chemistry has developed a revolutionary approach for targeting antibiotics to the bacterial cell membrane. Novel antibiotics have been developed with high potency against vancomycin-resistant *Enterococci* and *Staphylococci*.

### Uses:

- New antibiotic therapies

### Benefits:

- Effective against a broad range of antibiotic-resistant bacteria
- Demonstrated for vancomycin. Potential to be applied to other antibiotics including  $\beta$ -lactams

For further information please contact:

Dr Iain Thomas

✉ [iain.thomas@enterprise.cam.ac.uk](mailto:iain.thomas@enterprise.cam.ac.uk)

☎ +44 (0)1223 760339

Cambridge Enterprise Limited, University of Cambridge  
Hauser Forum, 3 Charles Babbage Road, Cambridge, CB3 0GT, UK  
[www.enterprise.cam.ac.uk](http://www.enterprise.cam.ac.uk)

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## Background

Microorganisms have successfully developed resistance to every approved antibiotic to date. Bacterial resistance can arise through a number of mechanisms, but in many cases mutation of the target site reduces antibiotic activity due to reduced binding.

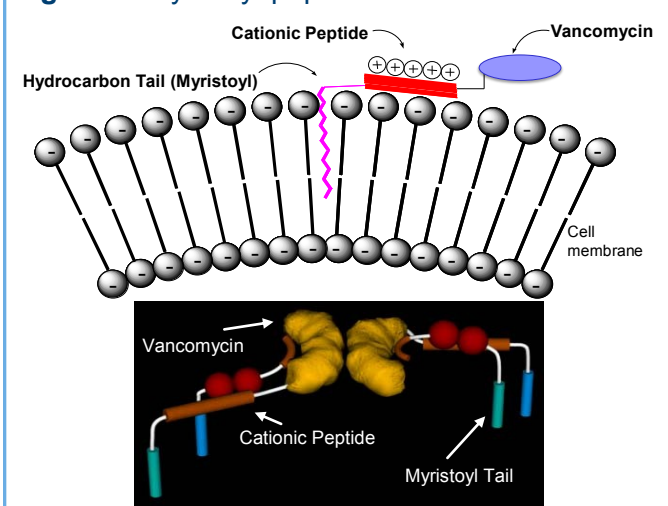
Vancomycin is currently the antibiotic of *last resort* against almost all Gram-positive bacteria. The emergence of vancomycin-resistant strains (e.g. vancomycin-resistant *enterococcus* (VRE)) and the increasing prevalence of hospital-acquired infections has given rise to the urgent need for improved antibiotics.

## Technology

Gram-positive bacteria have a unique membrane composition and Dr Matthew Cooper has developed a novel strategy for targeting vancomycin to these cell membranes. The technology—the myristoyl-peptide switch—comprises three parts (Fig 1):

- A hydrocarbon tail (myristoyl) that inserts into the cell membrane
- A cationic peptide that adheres to cell surface
- A linker to vancomycin

**Figure 1: Myristoyl-peptide switch**



Localising the antibiotic to the cell membrane is key to overcoming resistance, as it results in an enhanced concentration of antibiotic at the site of peptidoglycan cell wall biosynthesis.

A number of potent test compounds have been characterised with excellent antibacterial activities against clinically relevant bacteria (including VRE, methicillin-resistant *S. aureus* (MRSA) and glycopeptide intermediate-resistance *S. aureus* (GISA)) and comparable to existing standards of care (Table 1).

**Table 1: Efficacy of myristoyl-peptide antibiotics**

Antibiotic	VanA MIC (µg/ml)	VanB MIC (µg/ml)	Minimum inhibitory concentration (MIC) for test compounds APT2036 and A P T 3 0 8 8 against the VRE strains VanA and VanB.
Vancomycin	2048	512	
Teicoplanin	64	0.5	
LY333328	1	1	
CBP-Vancomycin	12	12	
Linezolid	4	4	
Synercid	2	1	
Daptomycin	4	1	
<b>APT2036</b>	<b>8</b>	<b>4</b>	
<b>APT3088</b>	<b>2</b>	<b>0.3</b>	

## Commercialisation

This technology has been successfully used with vancomycin and should prove applicable to other antibiotics. There is great potential to revive antibiotic treatment for diseases in which they are no longer prescribed due to enhanced resistance.

We are seeking a commercial partner interested in licensing this technology for development of new antibiotics. This technology is protected by 2 patents (**WO0236612** and **WO07103548**) and comprises a portfolio of over 300 glycopeptide compounds. Filing is pending on a third patent.