

# Teixobactin: A Novel Antibiotic in Treatment of Gram Positive Bacterial Infections

ARUNAVA KALI

Sir,

Antimicrobial resistance have emerged as a serious concern worldwide. In spite of the best effort in developing novel antimicrobial agents employing advanced techniques like computer-aided drug design, proteomics, genomics, combinatorial synthesis and high-throughput screening, there is lack of newer antibiotics in the process of development [1]. Environmental microbiota has been an essential source of several antimicrobial agents. In a press release on 7<sup>th</sup> January, 2015, NovoBiotic Pharmaceuticals announced the discovery of teixobactin, a novel antibiotic from a previously uncultured and undescribed soil –bacteria belonging to  $\beta$ -proteobacteria provisionally named *Eleftheria terrae*, using isolation chip (iChip) method [1,2]. iChip uses an assembly of three (central, top and bottom plates) flat hydrophobic plastic polyoxymethylene plates containing multiple through-holes and polycarbonate membranes to compose an array of miniature diffusion chambers [3]. Each chamber is likely to capture a single cell when the assembly is dipped into a suitably diluted bacterial mixture. This novel method is being utilized to isolate and characterize microbes from unexplored environmental niche and the discovery of teixobactin could be considered as its first success [1].

Teixobactin is a cyclic depsipeptide containing an unusual amino acid enduracididine [1]. It is the first new class of antibiotic which acts on unique targets in cell wall synthesis pathway. It binds to a highly conserved non-peptide motif of peptidoglycan precursor (lipid II) and teichoic acid precursor (lipid III), resulting in inhibition of cell wall synthesis and subsequent lysis. It has shown excellent activity against a wide range of gram positive bacteria, including multidrug resistant organisms such as Methicillin-resistant *Staphylococcus aureus* (MRSA), Vancomycin Intermediate *S. aureus* (VISA), Vancomycin – resistant enterococci (VRE), *Clostridium difficile*, *Streptococcus pneumoniae* and *Mycobacterium tuberculosis* [1]. However, it has inherent limitation against gram negative bacteria

pertaining to their cell wall composition. Unlike other cell wall inhibitor antibiotics, it does not act on protein targets which may readily develop mutational resistance on continuous drug exposure. In fact, the absence of resistant mutants of *Staphylococcus aureus* and *M. tuberculosis* after prolonged exposure of teixobactin in sublethal concentration, have generated immense interest on its development and introduction for clinical use [1,2].

It has been effective in sepsis, pneumonia and soft tissue infection in animal model with a very low PD<sub>50</sub> (50% protective dose) for MRSA in comparison to Vancomycin [1]. Since it has no deleterious action against mammalian cells due to lack of target sites and not been found to cause serious toxicity, haemolysis or DNA damage, it is likely to have wide therapeutic window. However, it has to prove its safety in human clinical trials. Although it has been expectantly described as ‘game-changing’ antibiotic because of its novel site of action precluding development of mutational resistance [4], it may not prevent resistance due to impermeable thickened cell wall which curtails its access to lipid II and lipid III, particularly in case of injudicious clinical use due to increasing drug promotion and marketing. In conclusion, the isolation of teixobactin from soil using iChip not only marks the development of a new antibiotic class with low risk of acquiring resistance, but also opens up infinite possibilities to discover useful molecules from unexplored strata of microbial kingdom.

## REFERENCES

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### PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Microbiology, Mahatma Gandhi Medical College & Research Institute, Pondicherry, India.

### NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Arunava Kali,  
Assistant Professor, Department of Microbiology, Mahatma Gandhi Medical College and Research Institute,  
Pillaiyarkuppam, Pondicherry-607 402, India.  
E-mail: ak.arunava@gmail.com

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