

TEIXOBACTIN THE TREATMENT OF AN ACHILLES HEEL?

The first time I heard about Maine was by watching *Murder, She Wrote*. This was an American television series, starring Angela Lansbury [as you read, this 89 year old woman is still actively interpreting Madame Arcati on stage in *Blithe Spirit*] as detective Jessica Fletcher. Fletcher was a resident of Cabot Cove, a coastal town in Maine; the fictional 'Cabot Cove' name was derived from the name of an actual inlet in Kennebunkport, Maine. However, this year I encountered Maine in a very different context ... *Nature*. A most interesting article, accessible on www.nature.com hails Maine as the cradle of a new antibiotic, teixobactin.

As you know, modern antibiotics have been heralded by the marketing of penicillin in the 1940s. Although Sir Alexander Fleming, who discovered penicillin, warned of the dangers of resistance way back in his Nobel prize speech in 1945, few would have thought of such resistance to be the achilles heel of antibiotics back then. Nonetheless, it has resulted in a shortfall of medical armamentarium when dealing with infections. We are partly to blame for this, considering the overuse of antibiotics, illegal over-the-counter selling of antibiotics as well as agricultural misuse. Actually, last December the UK has published

Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations, where it is being predicted that by 2050, antibiotic resistance would cost the world up to €88,000,000,000,000 and a reduction of 2% to 3.5% in global GDP - www.jpiaamr.eu. This initiative has been heralded by the UK's Prime Minister, David Cameron.

Returning to teixobactin, researchers at the National Institutes of Health and the German government have developed a new technology, the iChip, which is a lattice of tiny wells. Researchers dip the chip in a bacterial sample [diluted soil] mixed with agar to trap cells in each well, after which it is covered with a permeable membrane to lock the sample inside. The iChip is then placed in the bacteria's original environmental habitat [soil]. Using this technique, the researchers were able to screen 10,000 bacteria, previously unculturable. This is how they discovered a new bacteria, *Eleftheria terrae* which is the source of teixobactin, an 11-residue, macrocyclic depsipeptide. This was found to be a novel inhibitor of cell wall synthesis by binding to a highly conserved motif of lipid II (precursor of peptidoglycan) and lipid III (precursor of cell wall teichoic acid), leading to lysis of vulnerable bacteria. It seems to work on Gram-positive bacteria only, including MRSA and mycobacterium tuberculosis.

Teixobactin's next step is clinical trials in order to investigate the safety and efficacy of the medicine. Although the process may take up to 15 years, in this case, I assume that modelling and simulation will be used to extrapolate and interpolate safe and effective drug doses in diverse clinical conditions. This will shorten the authorisation process.

However, the million dollar question is the following ... if teixobactin ever manages to reach the market, will it be prostituted like all the other antibiotics which have previously been heralded as game-changers? ❌

Pan Ellul