Next generation bacitracin: reimagining a classic antibiotic

Buijs, N.P.

Stellingen

Behorende bij het proefschrift

Next Generation Bacitracin: Reimagining a Classic Antibiotic

1. Chemical synthesis is a critical tool in drug discovery as a chemist's toolbox contains more than just twenty amino acids. (*this thesis*)

2. The originally published route to synthesise bacitracin A is unsuitable for the preparation of analogues. It is therefore important to keep an open mind for alternative methods rather than repeatedly attempting to replicate the same protocol. (*Chapter 2*)

3. Crystallographic insights are a crucial tool in drug design, and are directly responsible for the development of the next generation bacitracin analogues. (*Chapter 4*)

4. Although attempts to replace bacitracin's zinc chelating N-terminal aminothiazoline moiety with more chemically stable motifs led to a marked loss in antibacterial activity, the commensurate inclusion of hydrophobic residues may recover that lost potency and thereby open the door for bacitracin's use as a systemic drug. (*Chapters 3, 4*)

5. Nature doesn't necessarily produce good drugs, but it does produce good starting points.

6. The current economic incentives to tackle the rise of antimicrobial resistance are insufficient, creating a serious threat to global health. "Compared with drugs for other diseases … antibiotics perform poorly in economic decision models and are therefore less likely to be selected by pharmaceutical companies for continued development." (E. Power, *Clin. Microbiol. Infect.*, 2006, **12**, 25–34)

7. The scientific community should be glad that we don't always listen to the opinions of reviewers. In fact, Solid-Phase Peptide Synthesis was originally criticised by a reviewer as a "travesty…, not chemistry at all, a concept which should be suppressed by the community." (G. R. Marshall, *Biopolym. - Pept. Sci. Sect.*, 2008, **90**, 190–199)

8. The re-examination of decades old antibiotics using modern techniques has in many cases revealed the mechanisms that underpin some of nature's best bactericidal strategies. (U. Theuretzbacher *et al*, *J. Antimicrob. Chemother.*, 2015, **70**, 2177–2181)

9. When comparing the abilities of chemists and Nature to produce biomolecules, the vast array of structures that Nature can produce within the constraints of an aqueous, pH 7, 37 °C environment, surely leads one to conclude that chemists must be rather bad at chemistry.

10. Nothing will ever be perfect, but often they are good enough. "The best way to find a mistake in a manuscript is to hit submit." – Prof. dr. Nathaniel I. Martin

11. Organic chemistry is to analytical chemistry what cooking is to baking.

12. Pressuring PhD students into taking all their holiday days may be counterproductive if the goal is to reduce stress.

Ned Peter Buijs

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