Universiteit Leiden
The Netherlands

Anthracycline biosynthesis in Streptomyces: engineering, resistance and antimicrobial activity

Hulst, M.B.

STELLINGEN

behorende bij het proefschrift

Anthracycline biosynthesis in *Streptomyces*: engineering, resistance and antimicrobial activity

1. Substrate acceptation by DoxA is rate limiting during biosynthesis of *N,N*-dimethylated anthracyclines (Chapter 3).

2. Streptomycetes harbour not only cryptic biosynthetic pathways but also cryptic resistance mechanisms (Chapter 4).

3. Doxorubicin-derived anticancer compounds may be a promising source of antimicrobials (Chapter 5).

4. Well-controlled 1 ml *Streptomyces* fermentations are suitable for correlating protein expression and metabolic profiles, as a primer for natural product discovery (Chapter 6).

5. The fact that DNA-intercalating compounds can protect against phages sheds new light on their role in nature (Kronheim et al., 2018, *Nature*, **564**, 283–286)

6. Understanding the biological role of anticancer compounds in producer strains will help to improve production titres and discover new bioactive metabolites.

7. In the search for truly novel antimicrobials, we may have to look in entirely different parts of the chemical space (Zhao et al., 2024, *Nature*, **629**, 165–173).

8. The development of CRISPR-based technologies accelerates innovations in the field of *Streptomyces* biology and engineering (Tong et al., 2019. *Proc. Natl. Acad. Sci. U.S.A.*, **116**, 20366–20375; Bai et al., 2024, *ACS Synth. Biol.*, **12**, 3143–3147).

9. Not only antibiotic discovery but also stewardship is crucial to continue to treat infectious diseases in the future.

10. To capitalise on the progress of artificial intelligence in the field of biology, it is essential to improve the proficiency of biologists in coding.

Mandy B. Hulst
Leiden, 20 June 2024