Analysis of the angucycline biosynthetic gene cluster in Streptomyces sp. QL37 and implications for lugdunomycin production

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Stellingen

Propositions accompanying the thesis

Analysis of the angucycline biosynthetic gene cluster in *Streptomyces* sp. QL37 and implications for lugdunomycin production

1. The capacity of a strain to produce lugdunomycin does not correlate to the phylogeny of the producer (Chapter 3).

2. The observation that multiple biosynthetic gene clusters (BGCs) may specify a single compound has major implications for synthetic biology approaches (Chapter 4).

3. Screening for the presence of orthologues of *lugOIII* and *lugOV* in angucycline BGCs can lead to the discovery of novel rearranged angucyclines (Chapter 5).

4. Transcriptional activation of the *lug* gene cluster by the SARP regulator LugRV can be employed to increase angucycline production (Chapter 6).

5. To obtain insight into the regulatory network and biosynthesis of a natural product, transcriptomics data should be the foundation of follow-up research questions (Amos *et al.*, 2017, PNAS 114: E11121-E11130).

6. Blocking the production of a single natural product can have unexpected consequences for other pathways for specialized metabolism and for growth (Singh *et al.*, 2009, *J Ind Microbiol Biotechnol* 36:1257-1265, Culp *et al.*, 2019, *Nat Biotechnol* 37: 1149-1154).

7. Mass spectral molecular networking is ideally suited for the discovery of novel metabolic intermediates, providing insight into the biosynthesis pathway of a natural product (Zhu *et al*., 2020, *Chem Commun* 56: 10171-10174; Iorio *et al*., 2021, *Sci Rep*:5827).

8. The rich chemical diversity of angucyclines offers a huge enzymatic toolbox for combinatorial (bio)synthesis (Fewer and Metsä-Ketelä, 2020, *FEBS, J.* 287: 1257-1259, Kharel *et al*., 2012 *Nat Prod Rep* 29 :264).

9. Aristotle said that the whole is often more interesting than the sum of its parts. This thesis shows that this applies well to collaborations between biologists and chemists.

10. Do not compare your yoga poses to those of other yogis, especially when a pose is difficult. The same rule applies to a PhD trajectory.

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