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Exploring the chemical space of natural products from *Streptomyces* using multi-omics approaches

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Propositions accompanying the thesis
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approaches

1. When applying heterologous expression for natural product discovery, it is important to consider the possibility that the biosynthesis of a molecule may be encoded by more than one gene cluster (Chapter 1)
2. Platforms that integrate computational tools with high-throughput laboratory techniques offer the potential to complement traditional methods by facilitating the discovery of previously uncharacterized natural products. (Chapter 2)
3. The fact that Diels-Alder reactions are thermodynamically favorable does not necessarily imply the absence of a protein (enzyme) capable of facilitating the spatial alignment of the two precursors (Chapter 3)
4. The co-occurrence of BGCs for angucyclines and for isomaleimycin in several streptomycetes suggests that lugdunomycin evolved long ago and may therefore have an important biological role (Chapter 3).
5. Finding putative Diels-Alderase is highly challenging due to the multifunctional nature of the candidate enzymes (Jeon BS *et al.*, 2017, *Chem rev*, 117: 5367-5388).
6. Well-studied microbes continue to serve as valuable sources of new natural products, provided that modern and complementary approaches are utilized in their study (Li Y, *et al.* 2022, *Angew Chem Int Ed Engl* 61: e202208573).
7. An open-access library of natural product-producing microbes is important to accelerate drug discovery in academia worldwide (Cook MA, *et al.*, 2023, *J Ind Microbiol Biotechnol* 50: kuad042).
8. Strain prioritization introduces bias, demanding a holistic approach that extends beyond taxonomy and genome mining (Martinet L, *et al.*, 2020, *Biomolecules* 10: 1027).
9. The statement that 'we tend to forget that no computer will ever ask a new question' is also applicable to artificial intelligence [based on Grace Hopper (1906-1992), Computer Scientist and United States Navy Rear Admiral].
10. In medieval times, aluminium was considered the metal of kings and queens because it was thought to be scarce. Once we learned how to mine it, it became as common as the foil we use to wrap sandwiches. The same transformation should happen with mining microbes for new antibiotics.