

Next generation lipopeptide antibiotics Al Ayed, U.K.

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Propositions

Accompanying the thesis

Next Generation Lipopeptide Antibiotics

- 1. Ester-to-amide substitution in lipodepsipeptides can be an effective strategy to increase serum stability. (*Chapter 2*)
- 2. Increasing the lipid length of a lipopeptide antibiotic can lead to non-selective membrane disruption and hemolysis. (*Chapter 3*)
- 3. Linear analogues of cyclic cationic lipopeptide antibiotics can exhibit activity comparable to the parent compounds, provided they are prepared as the C-terminal amides. (Chapter 4)
- 4. Genome mining coupled with total synthesis has the potential to speed up the research and development of novel non-ribosomal peptides. (*Chapter 5*)
- 5. The growing threat of antimicrobial resistance can be seen as a silent pandemic. (*Laxminarayan*, *The Lancet*, 2022, 399(10325), 606-607)
- 6. Most areas of modern medicine could not exist without access to effective antimicrobial treatment. (*Blaskovich, ACS Infect. Dis., 2020, 6, 1286–1288*)
- 7. It is prudent to use natural products as a starting point for a synthetic chemistry program to produce antibiotics with attractive properties. (*Lewis, Cell, 2020, 181, 29-45*)
- 8. Predicitve AI models have the potential to speed up drug discovery but are not alternatives to experimental data. (*Mock et al., Nature, 2023, 621, 467-470*)
- 9. Publishing on an open access preprint server such as ChemRxiv before peerreview should be normalized.
- 10. The historical transition from alchemy to modern chemistry symbolizes the human quest for transformation and mastery over the material world.

Karol Al Ayed Leiden, 23 januari 2024