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Small-molecule inhibitors of bacterial metallo- β -lactamases

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Citation

Hajmohammadebrahimtehrani, K. (2020, December 16). *Small-molecule inhibitors of bacterial metallo- β -lactamases*. Retrieved from <https://hdl.handle.net/1887/138734>

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Issue Date: 2020-12-16

Propositions

1. Small size and simplicity of structure, makes nitrilotriacetic acid analogs ideal candidates for further MBL inhibitor development.
Thesis chapter 2
2. Chemoenzymatic approaches provide access to structurally diverse aminocarboxylic acid MBL inhibitors that are otherwise difficult to produce via conventional synthetic means.
Thesis chapter 3
3. The propensity of thiols to readily form disulfides in solution makes them unlikely candidates for clinical use as MBL inhibitors.
Thesis chapter 4
4. Innovative strategies such as prodrug approaches can be applied to address the selectivity and stability issues associated with small-molecule MBL inhibitors.
Thesis chapter 5
5. The ability of selected cyclic boronates to inhibit both SBLs and MBLs may ultimately contribute to the realization of their therapeutic potential.
Antimicrob. Agents. Chemother. 2017, **61**, e02260-16
6. The majority of MBL inhibitors act by either strongly binding zinc in the solution and making it inaccessible for the MBLs, or by binding the active site zinc as well as the adjacent amino acid residues.
Trends Pharmacol Sci. 2018, **39**, 635–647.
7. The structure of the cephalosporin core allows for chemical modification at multiple positions to enhance potency, broaden the spectrum of activity, and provides access to β -lactamase-triggered prodrugs.
Foye's principles of medicinal chemistry, 6th ed
8. Early profiling of metal binding affinity using methods such as isothermal titration calorimetry is crucial in MBL inhibitor development in order to minimize adverse effects associated with promiscuous metal-binding.
Wade et al. 2020. Submitted to *ACS Infect. Dis.*
9. The new generation of lipidated glycopeptides derived from vancomycin and teicoplanin offer new hopes in tackling infections caused by the vancomycin resistant gram-positive pathogens.
Martin et al., 2019 Dutch Patent application filing
10. The students' creativity to solve scientific problems makes their supervision a pleasant experience, as long as the supervisor is aware of the students' creativity in doing things wrong.
11. Teamwork and group mentality are vastly different and yet, the former can easily turn into the latter.