Reshaping the Antibiotic Fidaxomicin

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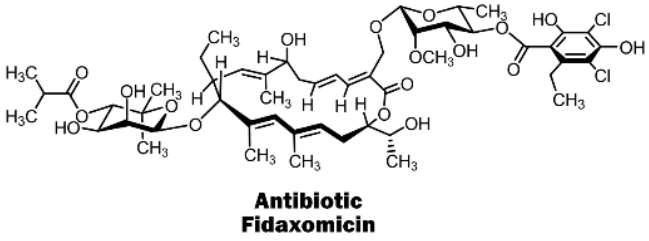
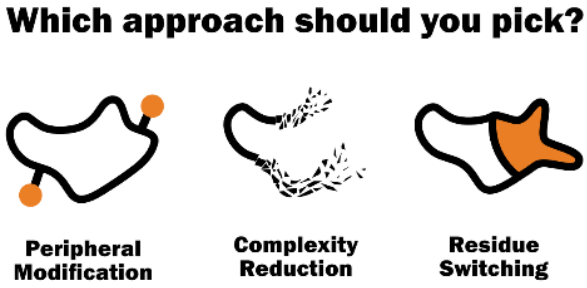
Natural products become drugs in different ways. The natural product itself can turn out to be sufficiently potent, safe, and bioavailable to treat disease (*e.g.* vancomycin, paclitaxel). However, modification of the natural product structure is often necessary to improve physicochemical properties, spectrum of activity, or counter resistance. We are interested in the natural product antibiotic fidaxomicin, which is used to treat infections in the gut.[1] Exploring several different approaches, such as peripheral modification[2,3], complexity reduction[4], and residue switching[5] we studied how modifying the structure of fidaxomicin affects bioactivity. In this talk we share the lessons learned for the discovery of novel antibiotics.



Antibiotic Fidaxomicin



[1] A. Dorst, E. Jung, K. Gademann, *CHIMIA* **2020**, *74*, 270–273.
[2] E. Jung, A. Kraimps, S. Dittmann, T. Griesser, J. Costafrolaz, Y. Mattenberger, S. Jurt, P. H. Viollier, P. Sander, S. Sievers, K. Gademann, *ChemBioChem* **2023**, *24*, e202300570.
[3] A. Dorst, R. Berg, C. G. W. Gertzen, D. Schäfle, K. Zerbe, M. Gwerder, S. D. Schnell, P. Sander, H. Gohlke, K. Gademann, *ACS Med. Chem. Lett.* **2020**, *11*, 2414–2420.
[4] E. Jung, M. Hunter, A. Dorst, A. Major, T. Teofilovic, R. Müller, K. Gademann, *Helv. Chim. Acta* **2024**, e202400013.
[5] E. Jung, T. Griesser, J. Costafrolaz, Y. Mattenberger, S. Dittmann, A. Dorst, A. Major, D. Dailler, D. Schäfle, S. Sievers, P. H. Viollier, P. Sander, K. Gademann, **2024**, *submitted*.