SYNTHESIS OF NOVEL LIPID I AND LIPID II ANALOGS

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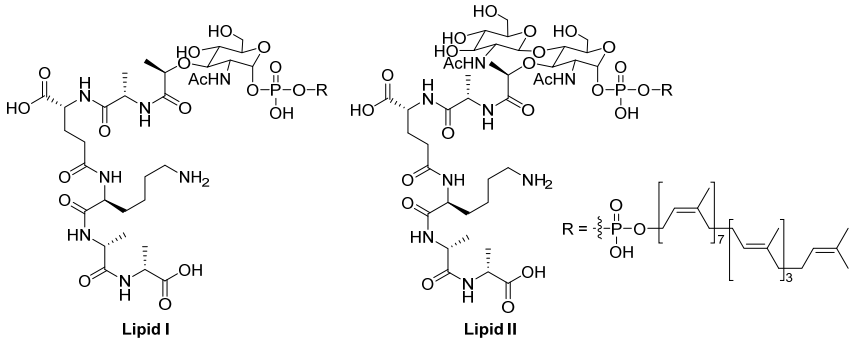
Antibiotic resistance is rising and represents an enormous danger for the human health. Many antibiotics inhibit the peptidoglycan biosynthesis resulting in an imperfect bacterial membrane leading to bacterial death. The main cell membrane precursors are valuable tools to understand the enzymes involved in peptidoglycan synthesis and their interaction with antibiotics.[1] However, isolation of the key biosynthetic precursors Lipid I and Lipid II, which differ in the glycosylation pattern, is very difficult.[2] Therefore, synthetic approaches are vital for a reliable supply. This also opens the possibility to access analogs as chemical tools for biological questions. The structure of these cell wall precursors is characterized by a *N*-acetyl-muramyl-pentapeptide linked via pyrophosphate bride to a hydrocarbon chain. Lipid II features an additional β-(1-4)-linked *N*-acetylglucosamine compared to Lipid I. Natural Lipid I/II has a 55-carbon undecaprenol chain, rendering synthesis, analytics and also biological experiments, where detergents have to be used to prevent aggregation and precipitation, more difficult.[1,2] Thus, shorter Lipid I/II analogs, bearing a shorter terpene sequence are very attractive. Despite certain advances, the development of a more efficient strategy for Lipid I/II synthesis remains an important research question, in particular to enable for a reliable and scalable access, which is also directly amenable to designed analogs. This poster will discuss novel approaches for Lipid I and Lipid II synthesis developed in our group.



[1] D. Münch, H. G. Sahl, *Biochim. Biophys. Acta - Biomembr.* **2015**, *1848*, 3062–3071.

[2] S. Ha, E. Chang, M. Lo, H. Men, P. Park, M. Ge, S. Walker, *J. Am. Chem. Soc.* **1999**, *121*, 8415–8426.