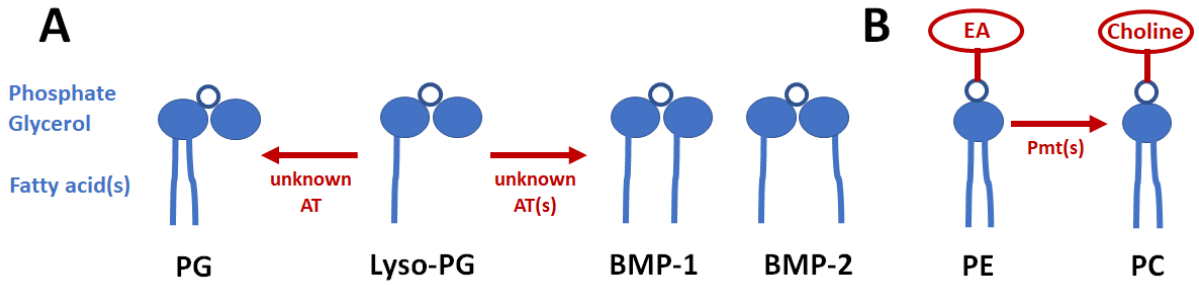
Project Franz Narberhaus

Bacterial phospholipid biosynthesis enzymes

Bacteria constantly rearrange their membrane composition in response to external conditions and nutrient supply. In recent years, it emerged that the repertoire of bacterial phospholipids (PLs) is much more diverse than previously anticipated. The diversity of PLs is particularly large in plant pathogens such as *Agrobacterium tumefaciens* and *Xanthomonas campestris*. These organisms produce a suite of unusual lipids, some of which play a critical role in stress resistance and plant-microbe interaction (1-3).

We are interested in the biosynthesis and biological function of the uncommon PLs Bis(monoacylglycero)phosphate (BMP) and phosphatidylcholine (PC) and (Fig. A and B). BMP is acylated at the glycerol head, which provides two hydroxyl groups for ester linkage of fatty acids. This PL has so far only been described in a few bacteria and neither the transporter(s) for the uptake of the substrate lyso-PG, nor the enzymes responsible for BMP biosynthesis or the biological role of this PL are known (4). The primary goal of this project is the identification and characterization of acyltransferases (ATs) capable of converting the substrate lyso-PG to PG (canonical pathway) or to both possible isoforms of BMP (Fig. A).

A. tumefaciens requires PC for tumor formation on plants (1). PC is produced by several alternative pathways. In the methylation pathway, the head group of the regular bacterial PL phosphatidylethanolamine (PE) is methylated three times to yield PC. These *S*-adenosylmethionine (SAM)-dependent reactions are catalyzed by one or more phospholipid *N*-methyltransferases (Pmts). Bacterial Pmts are cytoplasmic and recruited to the membrane by an N-terminal alpha-helix that binds to anionic lipids (5). Although we have made considerable progress in understanding the mode of action of the phospholipid *N*-methyltransferase PmtA from *A. tumefaciens*, this enzyme has resisted all attempts to reveal its structural details. In a strategy to find more amenable candidates, we conducted database searches and investigated several candidates from thermophilic bacteria (6). These enzymes have similar features as *A. tumefaciens* PmtA and at least three of them can be purified in sufficient amounts for further investigation opening new avenues for an in-depth structure-function analysis of bacterial phospholipid *N*-methyltransferases.



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