

SFB Guest Lecture Series

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Biosynthesis of Bis(monoacylglycero)phosphate

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Bis(monoacylglycero)phosphate (BMP) is a low abundant, negatively charged phospholipid. BMP is compartmentalized in intraluminal vesicles of late endosomes/lysosomes, where it plays an important role in organelle maturation, lipid degradation, and cholesterol sorting. Under pathophysiological conditions, BMP accumulates in genetic and drug-induced lysosomal storage diseases. In addition, it has been identified as a cofactor for viral infections and recent data suggest that BMP plays a key role in the pathogenesis of antiphospholipid syndrome. Despite its pivotal functions, the biosynthesis of this peculiar lipid is still elusive.

Published data suggest that phosphatidylglycerol (PG) is the precursor lipid of BMP, which we confirmed with isotope-labelled PG in cell-based experiments. Notably, we observed that the acylation of PG, leading to the formation of acyl-PG, precedes BMP synthesis suggesting that acyl-PG formation is the first step of BMP synthesis. To identify enzymes catalyzing this reaction, we screened a lipid hydrolase library for acyl-PG synthase activity. This screening identified two enzyme families converting PG into acyl-PG. Specific enzymes also produced BMP through the hydrolysis of acyl-PG. Overall, our data indicate that BMP synthesis is catalyzed through overlapping pathways.