Coordination of membrane lipid biogenesis in photosynthetic cells.

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Photosynthetic membranes (= thylakoids) constitute the most abundant membrane system on earth and their functioning is the primary source of sugars for the complete food chain in the biosphere. Thylakoid membranes are formed within a subcellular organelle called the chloroplast, which is limited by two envelope membranes. Chloroplast membranes are unique since they are extremely poor in phospholipids, containing up to 80% of mono- and digalactosyldiacylglycerol. These galactolipids are synthesized by specific enzymes of the chloroplast envelope, called MGDs and DGDs. An important question is the coordination of galactolipid syntheses with lipid neosyntheses, conversions and trafficking occurring in other membrane compartments of the cell. Monogalactosyldiacylglycerol null mutants are lethal, reflecting the primary importance of photosynthetic membranes. Dissection of lipid homeostasis in plants would benefit of specific inhibitors of MGDs (MGD1, MGD2, MGD3) for chemical genetic strategies in combination with conventional genetic approaches. We have screened 24,000 molecules allowing the identification of a new scaffold of inhibitors of MGDs. Inhibition of MGDs is competitive relatively to diacylglycerol. We synthesized 250 chemical analogues to determine the substructure responsible for the inhibition. Best inhibitors are called galvestines. Use of galvestine-1 at the level of specific cells allows the dose-dependent down-tuning of the membrane biogenesis of chloroplast membranes, and allows novel studies to comprehend the morphogenesis of this complex membrane structure.

How can we relate the complex cellular homeostasis of lipids (neosyntheses in different membrane compartments, conversions, transfers) with the biogenesis / morphogenesis of subcellular organelles like the chloroplasts? A dialogue between the chloroplast and the endomembrane system allows the coordination of synthetic pathways. This dialogue can be interrupted by small molecules like galvestines. Interrupted biogenesis of thylakoids allows the study of intermediate states, which could not be studied until now.