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Cardiolipin metabolism and its causal role in the etiology of the inherited cardiomyopathy Barth syndrome

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Highlights

- Mutations in the TAZ gene, encoding the cardiolipin remodelling enzyme tafazzin, are causal for the inherited cardiomyopathy Barth syndrome.
- Defective tafazzin function results in a plethora of mitochondrial defects including mitochondrial morphology, electron transport chain formation and function, and an increase in reactive oxygen species production.
- A mitochondrial quality control AAA protease contributes to the Barth syndrome phenotype by degrading mutant tafazzin proteins, and works together with tafazzin to ensure that misformed and reactive oxygen species producing mitochondria are effectively degraded by mitophagy.

Abstract

Cardiolipin (CL) is a phospholipid with many unique characteristics. CL is synthesized in the mitochondria and resides almost exclusively within the mitochondrial inner membrane. Unlike most phospholipids that have two fatty acyl chains, CL possesses four fatty acyl chains resulting in unique biophysical characteristics that impact several biological processes including membrane fission and fusion. In addition, several proteins directly bind CL