Cardiolipin Synthase, an Essential Enzyme of the Yeast *Schizosaccharomyces pombe,* Is Encoded by a Mitochondrial Fusion Protein

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Cardiolipin (CL) is a unique lipid component of mitochondria in all eukaryotes. CL is essential for the biogenesis, stability, and activity of respiratory chain complexes and for mitochondrial dynamics. Its role in signaling, especially in mitophagy and apoptosis, started to emerge recently. The fission yeast *Schizosaccharomyces pombe* is an important unicellular organism for the study of eukaryotic molecular and cellular biology, in some aspects better resembling higher eukaryotes than its distant cousin, *Saccharomyces cerevisiae*. Unfortunately, little is known about CL biosynthetic pathway in fission yeast.

We identified the C-terminal part of a tandem fusion protein encoded by the S. pombe open reading frame SPAC22A12.08c (with a newly annotated transcript end and newly identified introns) as CL synthase. The N-terminal part of SPAC22A12.08c encodes a protein of unknown function with a predicted hydrolase activity. Mitochondrial tandem proteins have been described in *S. pombe*, *Neurospora crassa*, higher plants, and recently also in *S. cerevisiae*. Interesting question emerged: Why some proteins that function in mitochondria form tandem precursors? We observed a novel mechanism of differential expression of partners of a fusion protein using intron retention. The first part of SPAC22A12.08c fusion protein could be translated from both major SPAC22A12.08c derived mRNAs, with and without intron IV. Functional CL synthase, however, is produced only from the minor SPAC22A12.08c derived mRNA that has intron IV retained. In addition, we provide evidence that *S. pombe* CL synthase is essential in fission yeast.

To understand CL remodeling in *S. pombe* we analyzed fatty acid composition of CL isolated from mitochondria of *S. pombe* strains with deletion of genes those products localize into mitochondria and display possible lipase or acyl-transferase signatures. Unfortunately, these attempts did not lead to identification of the components of *S. pombe* CL remodeling pathway so far.

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