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Human LACE1 Functions Pro-Apoptotic and Interacts with Mitochondrial YME1L Protease

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Abstract : Cellular function depends on mitochondrial function and integrity that is therefore maintained by several classes of proteins possessing chaperone and/or proteolytic activities. In this work, we focused on characterization of LACE1 (lactation elevated 1) function in mitochondrial protein homeostasis maintenance. LACE1 is the human homologue of yeast mitochondrial Afg1 ATPase, a member of SEC18-NSF, PAS1, CDC48-VCP, TBP family. Yeast Afg1 was shown to be involved in mitochondrial complex IV biogenesis, and based on its similarity with CDC48 (p97/VCP) it was suggested to facilitate extraction of polytopic membrane proteins. Here we show that LACE1, which is a mitochondrial integral membrane protein, exists as part of three complexes of approx. 140, 400 and 500 kDa and is essential for maintenance of fused mitochondrial reticulum and lamellar cristae morphology. Using affinity purification of LACE1-FLAG expressed in LACE1 knockdown background we show that the protein physically interacts with mitochondrial inner membrane protease YME1L. We further show that human LACE1 exhibits significant pro-apoptotic activity and that the protein is required for normal function of the mitochondrial respiratory chain. Thus, our work establishes LACE1 as a novel factor with the crucial role in mitochondrial homeostasis maintenance.

Keywords : LACE1, mitochondria, apoptosis, protease
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