DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

Life & Chemical Sciences Seminars

OXPHOS SYSTEM ORGANIZATION UPON ABLATION OF COMPLEX I CORE SUBUNITS

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Siete invitati a partecipare e a diffondere tra i collaboratori

Abstract
Respiratory complex I (CI) is the largest complex of the OXPHOS system, composed of 45 subunits, and its biogenesis requires both nuclear and mitochondria-encoded proteins. CI can associate with CIII and CIV, forming "supercomplexes" (SCs), but their assembly pathways are still controversial. Among CI core subunits, the nuclear-encoded NDUFS3 and the mitochondrial-encoded ND1 are considered the enucleation subunits for the formation of the quinone-binding (Q) and proximal proton pumping (Pp) modules of CI. For this reason, a critical role of ND1 and NDUFS3 in CI biogenesis and in the dynamic organization of supercomplexes has been depicted. In this study, we investigated CI and SCs biogenesis by exploiting unique cell models lacking NDUFS3 or ND1. A residual amount of functional CI was found within SCs in both models and it associated preferentially with pre-$CIII_2$, suggesting that CI and $CIII_2$ interact before their assembly is completed. The absence of NDUFS3 did not compromise neither $CIII_2$ nor CIV steady state levels, whereas a reduction of the assembly/stability of these two respiratory complexes was observed in the lack of full-length ND1. We also demonstrated that the lack of ND1 induces a stall in the multi-step process of CI biogenesis and defined a functional threshold, below which CI and its supramolecular organization is recovered, strengthening the notion that a minimum amount of human ND1 is required for CI and supercomplexes biogenesis. Lastly, a quantitative differential proteomic approach allowed us to identify several putative CI interactors, with a possible role as assembly factors in the early stages of CI biogenesis. Since most of the identified proteins are involved in metabolic pathways, we hypothesize a correlation between such pathways and CI biogenesis.

Biosketch
Luisa Iommarini is a Post-doctoral fellow at Department of Pharmacy and Biotechnology. She spent her career in the field of mitochondrial biochemistry and genetics. She graduated in Industrial Biotechnology at University of Bologna in 2005 working on the biochemical characterization of oncocytic cells harboring mitochondrial DNA mutations. Then, she got her Ph.D. in Cell Biology and Physiology at University of Bologna in 2009, studying the molecular bases and possible therapeutic approaches for mitochondrial optic neuropathies. During her Ph.D. she spent a nearly a year at University of Miami, Miller School of Medicine, where she focused on pharmacological and gene therapy strategies for mitochondrial optic neuropathies. Since 2010, she is a Post-doctoral fellow at Department of Pharmacy and Biotechnology Department, University of Bologna working on the role of respiratory complex I and mitochondrial DNA mutations in regulating tumor progression and OXPHOS structure and assembly. bioenergetics in human pathology, the study of respiratory complexes structure, assembly and function and the analysis of metabolic-based therapeutic strategies for cancer.

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