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Dissecting the distinct functions of mitochondria

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Mitochondria are the major site of energy production in the cell. An interesting and unique feature of the Electron Transport Chain (ETC) is that it is regulated under dual genetic control. Whereas the majority of the proteins that constitute the ETC are encoded by the nuclear DNA, 13 proteins are encoded by the Mitochondrial DNA (mtDNA). It is important to note, that mutations in mtDNA lead to very different phenotypes, suggesting that mitochondrial perturbations must manifest beyond bioenergetics. Other two salient functions of mitochondria are their biosynthetic capacity and their role as signaling organelles. We hypothesize that biological outcomes derived from these functions of mitochondria are also involved in the mechanisms mediating mitochondrial-associated diseases. However, it is not fully understood the involvement of distinct mitochondrial functions in the regulation of key cellular processes such as proliferation. In this study, HEK293 cells stably expressing a dominant negative form of the mtDNA polymerase POLG were used to eliminate mtDNA from cells in culture in a doxycycline-dependent manner as a model to dissect the importance of the different mitochondrial functions. First, the metabolic changes that occur during loss of mtDNA were studied by analyzing the whole cell metabolome profile to identify unique pathways activated during mitochondrial dysfunction. Next, the TCA cycle function and the mitochondrial membrane potential in cells with mtDNA loss were independently restored to elucidate the final consequences derived from the mitochondrial ability to carry out biosynthetic processes and to overall communicate with the rest of the cell.

Biography

Inmaculada Martinez-Reyes received her BA in Pharmacy and completed her PhD in Molecular Biology under the guidance of Jose Manuel Cuezva at University Autonoma of Madrid, Spain. During her Doctorate studies, she focused on the role of mitochondria in cancer. She was awarded a Postdoctoral Fellowship from Ramon Areces Foundation of Spain to perform her Postdoctoral training in Navdeep Chandel's laboratory at Northwestern University. She is currently studying fundamental biology related to mitochondrial metabolism in hopes of finding new therapies for mitochondrial-associated diseases including cancer. She has published papers in outstanding journals and participated in numerous international conferences.

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