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EFFECT OF SUCCINATE DEHYDROGENASE DEFICIENCY ON MITOCHONDRIAL FUNCTION

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Succinate dehydrogenase (SDH) connects the tricarboxylic acid (TCA) cycle and the respiratory chain. Mutations in SDH subunits have been associated with tumorigenesis and mitochondrial disease. In this project, we focused on subunit A of SDH (SDHA), primarily associated with inherited mitochondrial disease, and investigated the consequences of its loss or re-expression of mutant variants in HEK cells (SDHA KO). Lack of SDHA led to a downregulation of all SDH subunits and a secondary downregulation of the majority of mitochondrial complex I and IV subunits. Cellular respiratory capacity was severely decreased in the model, SDH-dependent respiration completely abolished and complex I-dependent respiration attenuated, reflecting the downregulation of respiratory chain complexes in general. Finally, the NAD^+/NADH ratio was increased in SDHA KO, indicating complex rearrangement of the TCA. It resulted in higher glycolytic activity and lipid accumulation.

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