Effect of mitochondrial complex I inhibition on Fe-S cluster protein activity

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Iron-sulfur (Fe-S) clusters are small inorganic cofactors formed by tetrahedral coordination of iron atoms with sulfur groups. Present in numerous proteins, these clusters are involved in key biological processes such as electron transfer, metabolic and regulatory processes, DNA synthesis and repair and protein structure stabilization. Fe-S clusters are synthesized mainly in the mitochondrion, where they are directly incorporated into mitochondrial Fe-S cluster-containing proteins or exported for cytoplasmic and nuclear cluster-protein assembly. In this study, we tested the hypothesis that inhibition of mitochondrial complex I by rotenone decreases Fe-S cluster synthesis and cluster content and activity of Fe-S cluster-containing enzymes. Inhibition of complex I resulted in decreased activity of three Fe-S cluster-containing enzymes: mitochondrial and cytosolic aconitases and xanthine oxidase. In addition, the Fe-S cluster content of glutamine phosphoribosyl pyrophosphate amidotransfer