Metallothionein expression and its role in rotenone-induced Complex I-deficient HeLa cells.

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Deficiency of mitochondrial oxidative phosphorylation is a common pathology in several debilitating inherited and acquired metabolic diseases. Deficiency of NADH:ubiquinone oxidoreducatse (complex I) is a model for mitochondrial disease and also the most frequently encountered among this group of diseases. The genotype-phenotype profile of this disease is complicated and the full scope of cell biological consequences of this disease is to a large extent still unclear. Current biochemical and genomics data indicates that the communication between mitochondria and nucleus plays a significant role in the cell biological response and that reactive oxygen species (ROS) not only plays a role in destructive consequences in this disease, but also mediates transcriptional responses. We previously reported a transcriptional profile of complex I deficiency in human fibroblasts (Ref 1) and report here the selective expression of metallothionein type 2A (MT-2A) in rotenone-induced complex I deficient HeLa cells. We also present data that suggests that MT-2A expression significantly increases cell viability, protects against the disease-related production of ROS as well as apoptosis in complex I deficient HeLa cells. We believe that investigating the expression of metallothioneins may not only provide better insight into responses to mitochondria-related diseases, but as metallothioneins can be induced is several ways, also provide exciting new possibilities to the limited therapeutic options that are currently considered for this disease.

[1]Francois H van der Westhuizen, Lambert P van den Heuvel, Roel Smeets, Joris A Veltman, Rolph Pfundt, Ad Geurts van Kessel, Bjrn M Ursing, and Jan Smeitink. Human Mitochondrial Complex I deficiency: investigating transcriptional responses by microarray. Neuropediatrics 34 (1): 14-22 (2003)