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Dysregulation of Iron Metabolism in X-Adrenoleukodystrophy

ABSTRACT:

X-Adrenoleukodystrophy (X-ALD), a rare neurodegenerative disease, is an intricate peroxisomal disorder caused by the inactivation of the ABCD1 gene. As a result, the encoded protein ALDP, an ATP-binding cassette (ABC) transporter located in the peroxisomal membrane, impairs the peroxisomal beta-oxidation of very long chain fatty acids (VLCFAs). This allows further elongation of VLCFAs resulting in the hyperaccumulation of VLCFAs in plasma and tissues. Oxidative stress due to excess VLCFAs appears early in the neurodegenerative cascade of X-ALD. It has been hypothesized that the oxidative stress induced by VLCFAs is associated with the disruption of iron-sulfur clusters. Iron-sulfur clusters are indicators of cellular iron status. Thus, we predicted that human fibroblast cells with the ABCD1 gene defect would differentially express genes encoding proteins involved in iron import and export in comparison to control fibroblasts. Based on our transcriptional and post-transcriptional *in-vitro* studies on the relative mRNA and protein expression related to iron metabolic functions, we have characterized distinct differences in iron metabolism of patients with X-ALD.