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Title: Targeting lipid peroxidation and mitochondrial imbalance in Friedreich's ataxia.

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Abstract

Friedreich's ataxia (FRDA) is an autosomal recessive disorder, caused by reduced levels of the protein frataxin. This protein is located in the mitochondria, where it functions in the biogenesis of iron-sulphur clusters (ISCs), which are important for the function of the mitochondrial respiratory chain complexes. Moreover, disruption in iron biogenesis may lead to oxidative stress. Oxidative stress can be the cause and/or the consequence of mitochondrial energy imbalance, leading to cell death. Fibroblasts from two FRDA mouse models, YG8R and KIKO, were used to analyse two different categories of protective compounds: deuterised poly-unsaturated fatty acids (dPUFAs) and Nrf2-inducers. The former have been shown to protect the cell from damage induced by lipid peroxidation and the latter trigger the well-known Nrf2 antioxidant pathway. Our results show that the sensitivity to oxidative stress of YG8R and KIKO mouse fibroblasts, resulting in cell death and lipid peroxidation, can be prevented by d4-PUFA and Nrf2-inducers (SFN and TBE-31). The mitochondrial