

## Accepted Manuscript

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

Author: Rosella Abeti Ebru Uzun Indhushri Renganathan  
Tadashi Honda Mark A. Pook Paola Giunti



PII: S1043-6618(15)00113-9  
DOI: <http://dx.doi.org/doi:10.1016/j.phrs.2015.05.015>  
Reference: YPHRS 2842

To appear in: *Pharmacological Research*

Received date: 27-2-2015  
Revised date: 4-5-2015  
Accepted date: 15-5-2015

Please cite this article as: Abeti R, Uzun E, Renganathan I, Honda T, Pook MA, Giunti P, Targeting lipid peroxidation and mitochondrial imbalance in Friedreich's ataxia, *Pharmacological Research* (2015), <http://dx.doi.org/10.1016/j.phrs.2015.05.015>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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

Rosella Abeti<sup>1</sup>, Ebru Uzun<sup>1</sup>, Indhushri Renganathan<sup>1</sup>, Tadashi Honda<sup>2</sup>, Mark A. Pook<sup>3</sup> and Paola Giunti<sup>1</sup>

<sup>1</sup>*Department of Molecular Neuroscience, UCL, Institute of Neurology, Queen Square WC1N 3BG, London, UK*

<sup>2</sup>*Department of Chemistry, Stony Brook University, Stony Brook, New York 11794, United States*

<sup>3</sup>*Ataxia Research Group, Division of Biosciences, Department of Life Sciences, College of Health & Life Sciences, and <sup>2</sup> Synthetic Biology Theme, Institute of Environment, Health & Societies, Brunel University London, Uxbridge, UB8 3PH, UK*

*Correspondence must be addressed to: Dr Paola Giunti p.giunti@ucl.ac.uk*

**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: deuterated 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

Download English Version:

<https://daneshyari.com/en/article/5843794>

Download Persian Version:

<https://daneshyari.com/article/5843794>

[Daneshyari.com](https://daneshyari.com)