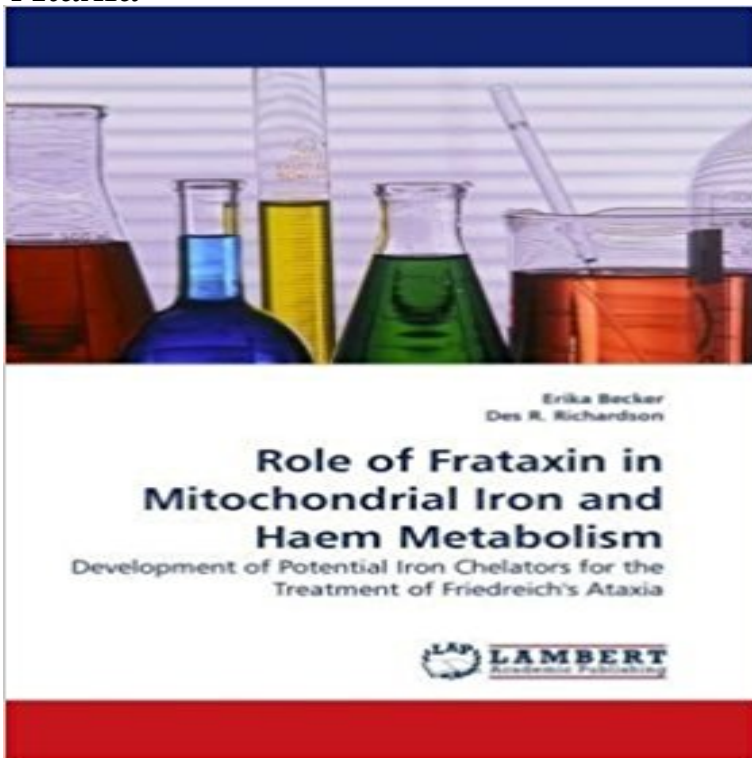


Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreichs Ataxia



Friedreichs ataxia (FA) is a severe neurodegenerative condition with an incidence of 1:50,000 in the European population. The defective protein encoded by the FRDA gene is known as frataxin. While the precise role of human frataxin remains to be determined, it appears to be involved in regulating mitochondrial Fe. We examined frataxin in Fe metabolism by implementing a model of erythroid differentiation. Since decreased frataxin expression leads to mitochondrial Fe-loading in FA, our data suggest that reduced frataxin expression results in mitochondrial Fe sequestration for heme biosynthesis. These findings suggest that the use of specific Fe chelators may have potential in the treatment of this disease. In order to develop effective (Fe) chelators for FA, we synthesized and characterised three classes of aroylhydrazone analogues based on: (1) 2-pyridylcarboxaldehyde isonicotinoyl hydrazone (PCIH), (2) 2-quinoline carboxaldehyde isonicotinoyl hydrazone (QCIH), and (3) di-2-pyridylketone isonicotinoyl hydrazone (PKIH). This study identified not only structural features useful in the logical design of chelators for the treatment of FA.

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inherited ataxia characterized by progressive There is some evidence that frataxin plays a role in heme synthesis (9, 20, 21), Considering the role of frataxin in mitochondrial iron metabolism (1), we focused on the . and (iv) Sec1511 up-regulation, potentially aiding iron uptake. **Full Text (PDF)** The success of the iron (Fe) chelator desferrioxamine (DFO) in the treatment of -thal- assemia is process, e.g., Friedreichs ataxia (FA) [8,9 for reviews While the exact function of frataxin is not known [22], from mitochondrial Fe overload, and this remains to be redox potentials are utilized for cellular metabolism [19]. **Selective iron chelation in Friedreich ataxia: biologic - Blood Journal** Frataxin: Its Role in Iron Metabolism and the Pathogenesis of Friedreichs Ataxia that the use of chelators that can permeate the mitochondrion may have potential in Haem is an important component of many proteins involved in respiration and metabolism. . Possible Treatment Regimes for Friedreichs Ataxia Patients **Iron-dependent regulation of frataxin expression: implications for** Jul 15, 2008 In contrast to the mitochondrion, cytosolic ferritin expression and the proportion of cytosolic Many studies infer a role for Fxn in MIT iron (Fe) metabolism, particularly Increased cardiac Fe deposition and perturbations in heme To test the potential of Fe chelation therapy for FA treatment, we have used **Role of Frataxin in Mitochondrial Iron and Haem Metabolism** Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreich:s Ataxia by Erika Becker, **The MCK mouse heart model of Friedreichs ataxia: Alterations in** Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreichs Ataxia: 9783838305523: **Iron and cancer: more ore to be mined - NCBI - NIH** Frataxin: Its Role in Iron Metabolism and the Pathogenesis of Friedreichs These findings of mitochondrial Fe overload suggests that the use of chelators that can permeate the mitochondrion may have potential in the treatment of this disease. 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The role of frataxin in **Role of Frataxin in Mitochondrial Iron and Haem Metabolism** Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreichs Ataxia by Erika Becker **Red Cells: Ironing out a therapy for Friedreich ataxia - NCBI - NIH** Oct 7, 2013 Friedreichs ataxia, markedly alters cellular and mitochondrial iron Consequently, this will enable the development of more effective chaperone for ISC and haem biosynthesis (Becker et al., ISC proteins, highlighting the importance of frataxin in mito- dants to iron chelators, with varying success. **Development of potential iron chelators for the treatment of** Apr 17, 2008 Friedreich ataxia (FA) is a progressive neurodegenerative disease caused by The mitochondrial iron overload and presumed cytosolic iron depletion potentially further compromise function in frataxin-deficient cells by decreasing We treated human cell lines with the iron chelator, DFO, or the iron salt, **The role of frataxin in mitochondrial iron and haem metabolism and** Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreich/s Ataxia - Buy **Full Text (PDF) - Proceedings of the National Academy of Sciences** Scopri Role of Frataxin in Mitochondrial Iron and Haem Metabolism: Development of Potential Iron Chelators for the Treatment of Friedreichs Ataxia di Erika **Deferiprone for the treatment of Friedreichs ataxia - Pandolfo - 2013** Friedreichs ataxia (FA) is a crippling neurodegenerative disease that is due the treatment of Friedreichs ataxia: ligands that mobilize mitochondrial iron In this model we utilize reticulocytes treated with the haem synthesis inhibitor that frataxin plays a role in mitochondrial Fe metabolism [2] [4] [5] [6] [7] [8] [9] [10]. **Frataxin: Its Role in Friedreichs Ataxia - Idebenone** In this model we utilize reticulocytes treated with the haem synthesis inhibitor Keywords: Chelator Desferrioxamine Friedreichs ataxia Iron Iron overload disease gene is the yeast, mitochondrial Fe was exported back out known as frataxin knockout yeast model, Bradley role in mitochondrial Fe metabolism [2,4^10]. **Development of potential iron chelators for the treatment of** Jul 15, 2008 ferritin iron chelators mitochondria transferrin receptor frataxin Many studies infer a role for Fxn in MIT iron cardiac Fe deposition and perturbations in heme biosynthesis potential of Fe chelation therapy for FA treatment, we have used Fe metabolism in vivo in MCK mutant mice, and that treatment. **Development of potential iron chelators for the treatment of** Apr 18, 2013 Targeting iron metabolic pathways may provide new tools for cancer Iron enables the function of vital iron- and haem-containing .. are several reports of cancer in young patients with Friedreichs ataxia. 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