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Title: Use of a novel catalytic antioxidant, CTMIO, in a GAA repeat mouse model of FRDA

Cellular stress through an excess of oxygen radicals is a well established feature of Friedreich's Ataxia (FRDA) and therefore antioxidants are an obvious possibility to try and curtail disease progression. However, while some antioxidants have been shown to be effective in preventing heart problems in animal models and FRDA patients, the compounds tested had very limited effects on protecting the nervous system. One reason for this could be that the neurodegeneration in FRDA is not caused by oxidative stress. However, a more likely explanation is that the compounds used in these studies might not have reached the brain cells at concentrations high enough to be effective. Therefore, developing compounds that are not only effective in removing radicals at low concentrations but also can reach the brain cells represents a promising therapeutic approach for FRDA. We are planning to test a novel catalytic antioxidant (CTMIO) in a mouse model of FRDA. Our previous data show that CTMIO was very effective in preventing neurobehavioural problems in a mouse model of another form of ataxia (ataxia-telangiectasia) that is also characterized by oxidative stress. We therefore consider that CTMIO is capable of alleviating the neurological problems that characterize the FRDA mouse model we are planning to use. A protective function of CTMIO would represent a crucial first step in the development of novel, highly active antioxidants that could lead to an effective treatment option for FRDA.