Antioxidant Pathway as Potential Therapy for Alzheimer's Disease

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Oxidative stress is the imbalance between reactive oxygen species and antioxidants in a cell. Often this imbalance is caused by an increase of reactive oxygen species (ROS) leading to dyshomeostasis of the cellular redox balance. Oxidative stress is a major component of several chronic diseases including cardiovascular diseases, cancer and neurodegenerative diseases like Parkinson's and Alzheimer's diseases. To mitigate the damage caused by oxidative stress our cells are capable of producing their own antioxidants. One cellular mechanism involves the nuclear factor-erythroid 2-related factor (Nrf2) antioxidant pathway which can be activated in the presence of ROS. To better understand how this pathway works, it is important to track Nrf2 during activation of this pathway. Here we test three different plasmids designed to either force expression of "tagged" proteins in the Nrf2 pathway, or to provide a readout mechanism for the level of Nrf2 activation. These experiments lend support for the efficacy of using these tools to better understand the Nrf2 pathway.

Introduction

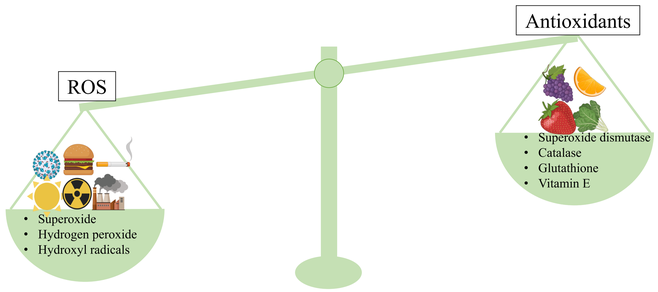


Figure 1. Imbalance between reactive oxygen species (ROS) and antioxidants leads to oxidative stress

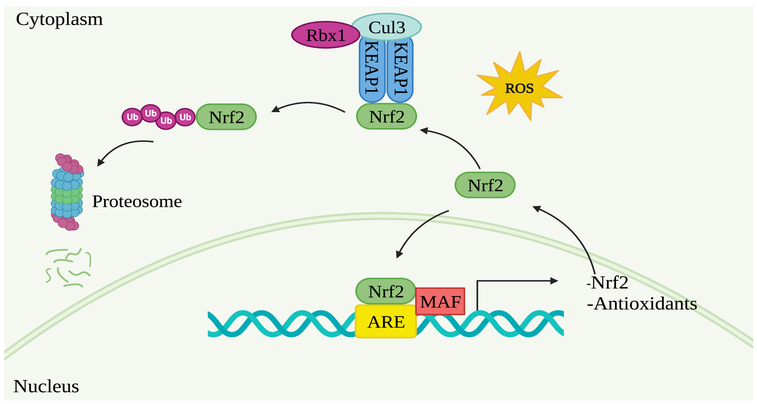
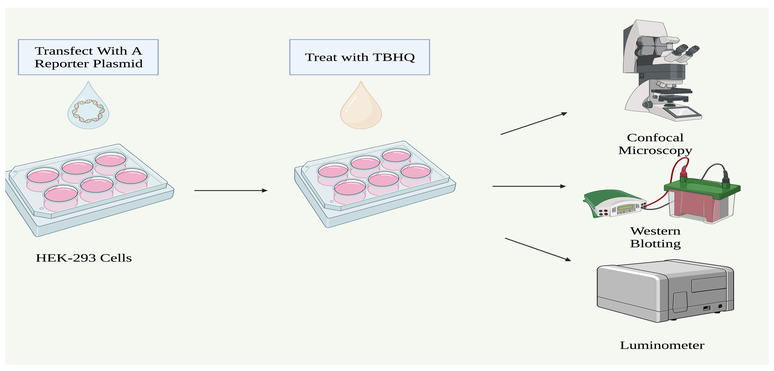


Figure 2. The Nrf2 pathway

Methods



Results

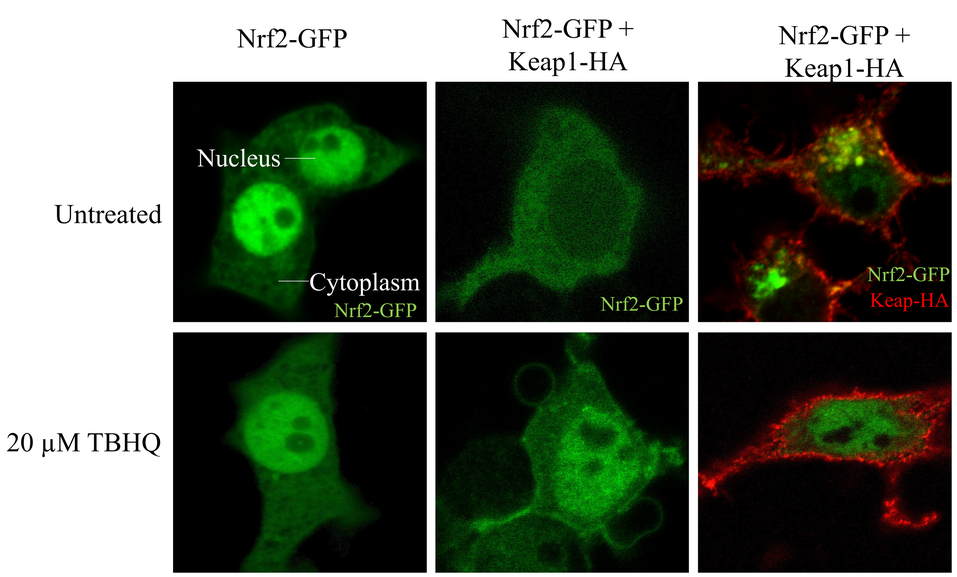


Figure 3. Nuclear localization of Nrf2 after TBHQ treatment

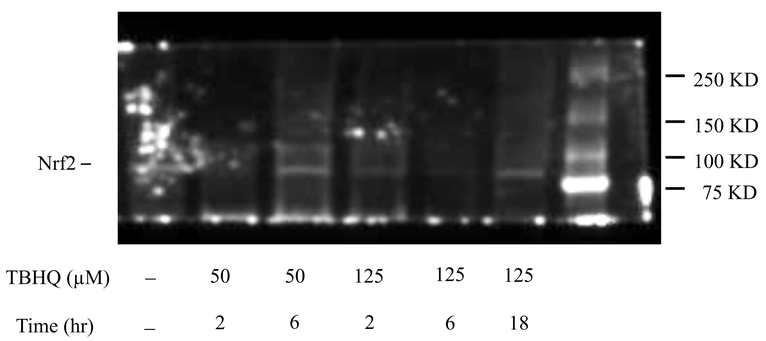


Figure 4. TBHQ appears to disrupt the interaction between Keap1 and Nrf2.

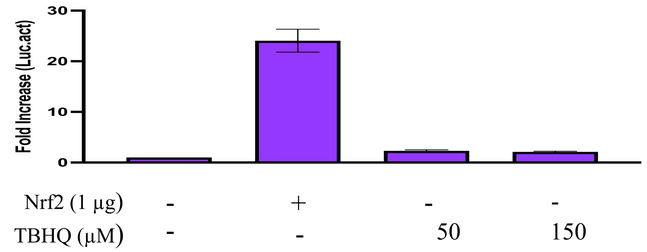


Figure 5. TBHQ has no significant affect on Nrf2 activity. The bars represent means ± SEM, N = 3.

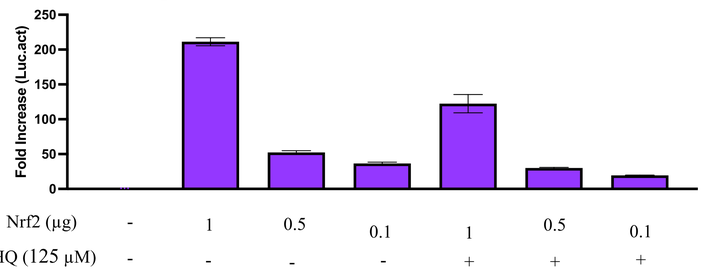


Figure 6. TBHQ has no significant affect on Nrf2 activity after overexpression of Nrf2. The bars represent means ± SEM, N = 3.

Conclusion

- Nrf2-GFP overexpression likely overloads normal proteasomal degradation and leads to accumulation of Nrf2 in the nucleus.
- Overexpression of both Nrf2 and Keap1 allows for some sequestration of Nrf2 in the cytoplasm.
- Treating co-transfected cells with TBHQ results in Nrf2 translocation into the nucleus.
- TBHQ does not lead to significant increase in Nrf2 activity assessed by the luciferase assay.

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