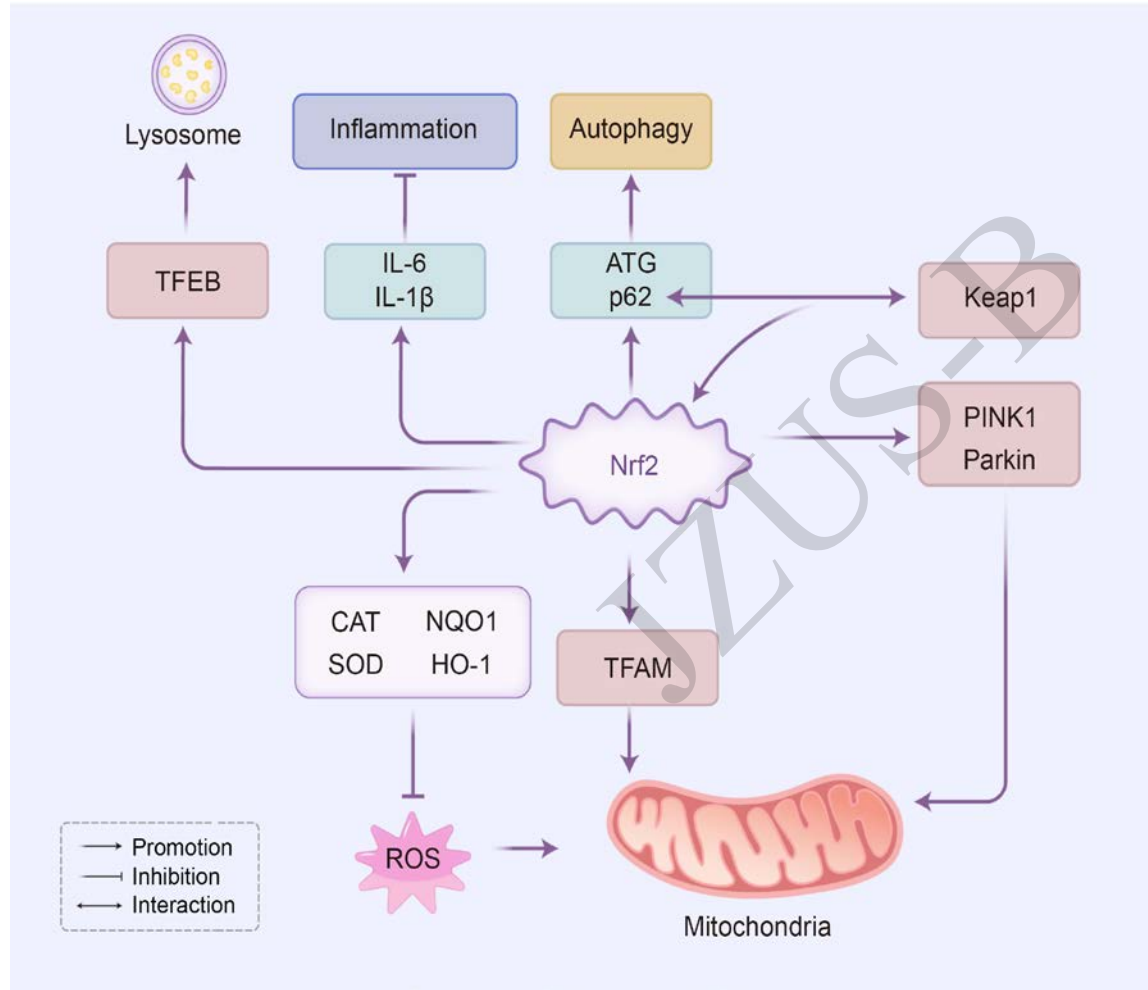


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Nrf2 signaling pathway and its molecular regulatory mechanism

Key words: Nuclear factor erythroid 2-related factor 2 (Nrf2); Kelch-like ECH-associated protein 1 (Keap1); Oxidative stress; Mitochondrial function; Inflammation; Autophagy

Research Summary



This review provides a comprehensive analysis of the dual regulatory role of Nrf2 in both normal physiological and pathological conditions, focusing on the molecular mechanisms by which it modulates mitochondrial function, oxidative stress, inflammation, and autophagy.

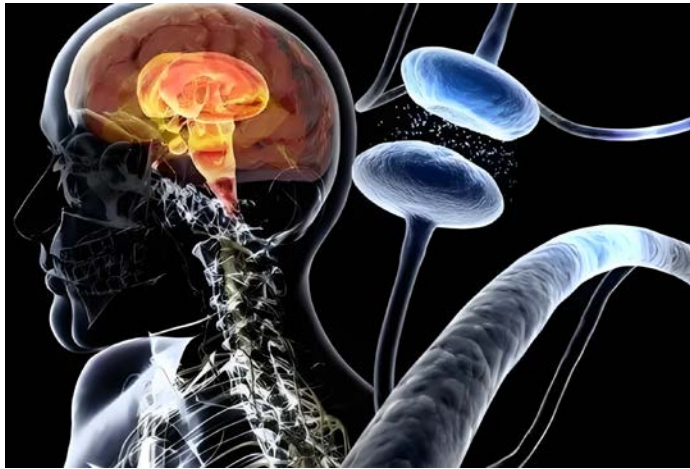
Innovation points

The review summarizes the current knowledge on the effects of various synthetic and natural compounds, such as flavonoids and resveratrol, on Nrf2 activity.

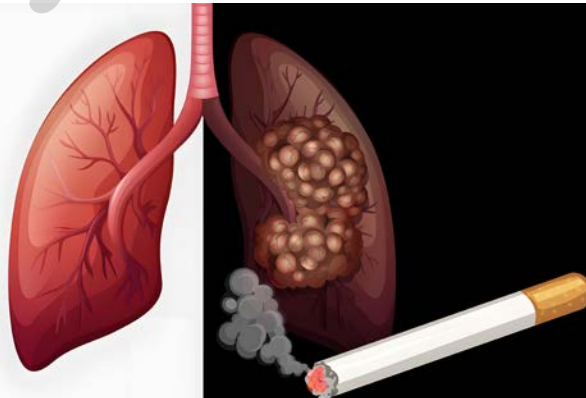
Drug	Mechanism
Genistein	Increasing the phosphorylation of PI3K p85 synergistically enhances the expression of HO-1 at mRNA and protein levels (Huang et al., 2023)
Catechins	Acting on the Nrf2 pathway, reducing ROS levels, inducing ARE-mediated expression of antioxidant genes, including phase II detoxifying enzymes (Yang et al., 2022)
Luteolin	Keap1/Nrf2/HO-1 signaling pathway; suppressing Nrf2 activation by modulating p47 ^{phox} and p22 ^{phox} expression; inducing a decrease in Nrf2 expression, resulting in reduced binding of Nrf2 to ARE; and depletion of reduced glutathione (Hayakawa et al., 2025; Yang et al., 2020; Tang et al., 2011)
Resveratrol	Increasing Nrf2 gene expression; upregulating downstream antioxidant enzymes such as SOD, glutathione peroxidase (GPX), and CAT (Majhi et al., 2023)
Sulforaphane	Keap1/Nrf2 pathway, promoting its nuclear translocation; inducing Nrf2/ARE/Prdx6 activity; inducing antioxidant enzyme expression; increasing mitochondrial biogenesis; and preventing dopaminergic neuronal loss (Shore et al., 2024)
Tert-Butylhydroquinone	Keap1/Nrf2 /ARE signal pathway; stimulates transcription of phase 2 genes (Satoh et al., 2009)
Metformin	Keap1/Nrf2 pathway and enhancing mitophagy; suppressing Nrf2 expression and activating p53 and AMPK pathways; Keap1/Nrf2/HO-1 signal pathway (D. Sun et al., 2024; Duan et al., 2025; Tang et al., 2022)

Innovation points

The review also explores the therapeutic potential of Nrf2 in neurodegenerative diseases, cancer, diabetes, and other disorders, laying a foundation for the development of Nrf2-targeted pharmacological interventions.



Type 1 and Type 2
Diabetes



Healthy Lung

Lung Cancer