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#### Abstract -

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# The complexity of the Nrf2 pathway: beyond the antioxidant response.

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### Abstract

The NF-E2-related factor 2 (**Nrf2**)-mediated signalling pathway provides living organisms an efficient and pivotal line of defensive to counteract environmental insults and endogenous stressors. **Nrf2** coordinates the basal and inducible expression of antioxidant and Phase II detoxification enzymes to adapt to different stress conditions. The stability and cellular distribution of **Nrf2** is tightly controlled by its inhibitory binding protein Kelch-like ECH-associated protein 1. **Nrf2** signalling is also regulated by posttranslational, transcriptional, translational and epigenetic mechanisms, as well as by other protein partners, including p62, p21 and IQ motif-containing GTPase activating protein 1. **Many studies have demonstrated that Nrf2** is a promising target for preventing carcinogenesis and other chronic diseases, including cardiovascular diseases, neurodegenerative diseases and pulmonary injury. However, constitutive activation of **Nrf2** in advanced cancer cells may confer drug resistance. Here, we **review** the molecular mechanisms of **Nrf2** signalling, the diverse classes of **Nrf2 activators**, including bioactive nutrients and other chemicals, and the cellular functions and disease relevance of **Nrf2** and discuss the dual role of **Nrf2** in different contexts.

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**KEYWORDS:** Activator; Antioxidant; Kelch-like ECH-associated protein 1 (Keap1); NF-E2-related factor 2 (**Nrf2**); Nutrients; ROS

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