RESEARCH ON Nutrition's Health Promoting Factors and Nrf2 AT PUBMED

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Nrf2, a master regulator of detoxification and also antioxidant, anti-inflammatory and other cytoprotective mechanisms, is raised by health promoting factors.

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Abstract: The transcription factor Nrf2, nuclear factor erythroid-2-related factor 2, activates the transcription of over 500 genes in the human genome, most of which have cytoprotective functions. **Nrf2** produces cytoprotection by detoxification mechanisms leading to increased detoxification and excretion of both organic xenobiotics and toxic metals; its action via over two dozen genes increases highly coordinated antioxidant activities; it produces major anti-inflammatory changes; it stimulates mitochondrial biogenesis and otherwise improves mitochondrial function; and it stimulates autophagy, removing toxic protein aggregates and dysfunctional organelles. Health-promoting nutrients and other factors act, at least in part by raising Nrf2 including: many phenolic antioxidants; gamma- and delta-tocopherols and tocotrienols; long chain omega-3 fatty acids DHA and EPA; many carotenoids of which lycopene may be the most active; isothiocyanates from cruciferous vegetables; sulfur compounds from allium vegetables; terpenoids. Other health promoting, Nrf2 raising factors include low level oxidative stress (hormesis), exercise and caloric restriction. **Raising Nrf2** has been found to prevent and/or treat a large number of chronic inflammatory diseases in animal models and/or humans including various cardiovascular diseases, kidney diseases, lung diseases, diseases of toxic liver damage, cancer (prevention), diabetes/metabolic syndrome/obesity, sepsis, autoimmune diseases, inflammatory bowel disease, HIV/AIDS and epilepsy. Lesser evidence suggests that **raising Nrf2** may lower 16 other diseases. Many of these diseases are probable NO/ONOO(-) cycle diseases and Nrf2 lowers effects of NO/ONOO(-) cycle elements. The most healthful diets known, traditional Mediterranean and Okinawan, are rich in **Nrf2** raising nutrients as apparently was the Paleolithic diet that our ancestors ate. **Modern diets are deficient in such nutrients**. **Nrf2** is argued to be both lifespan and healthspan extending…

Ref: https://www.ncbi.nlm.nih.gov/pubmed/25672622 PMID: 25672622 [PubMed - in process] **Free Article**

Martin L Pall *et al.*: **Nrf2, Master Cytoprotection & Detoxification Regulator, is Raised by Many Health Promoting Factors**

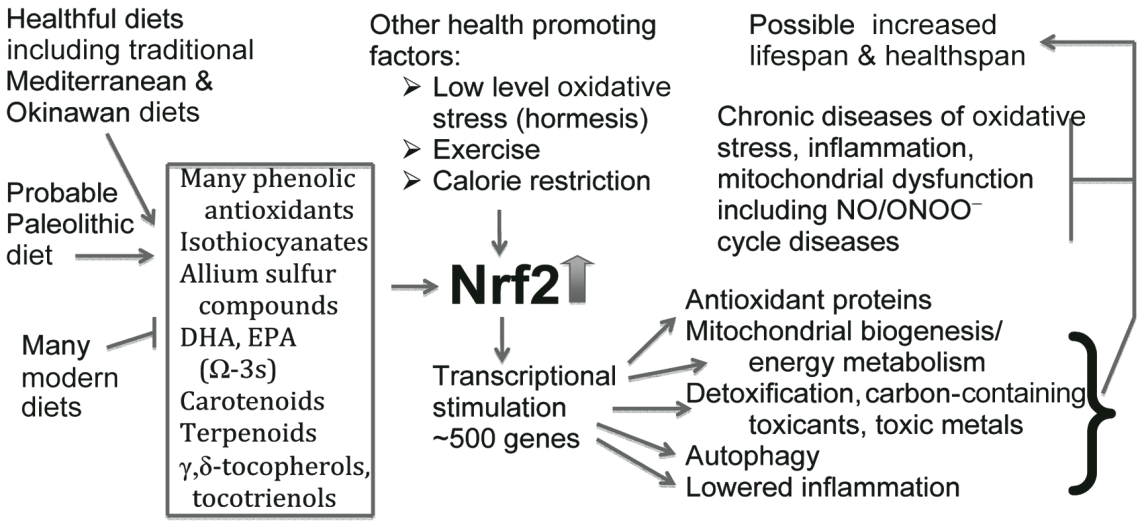


Fig. 1. Outline of the Nrf2 regulatory system.

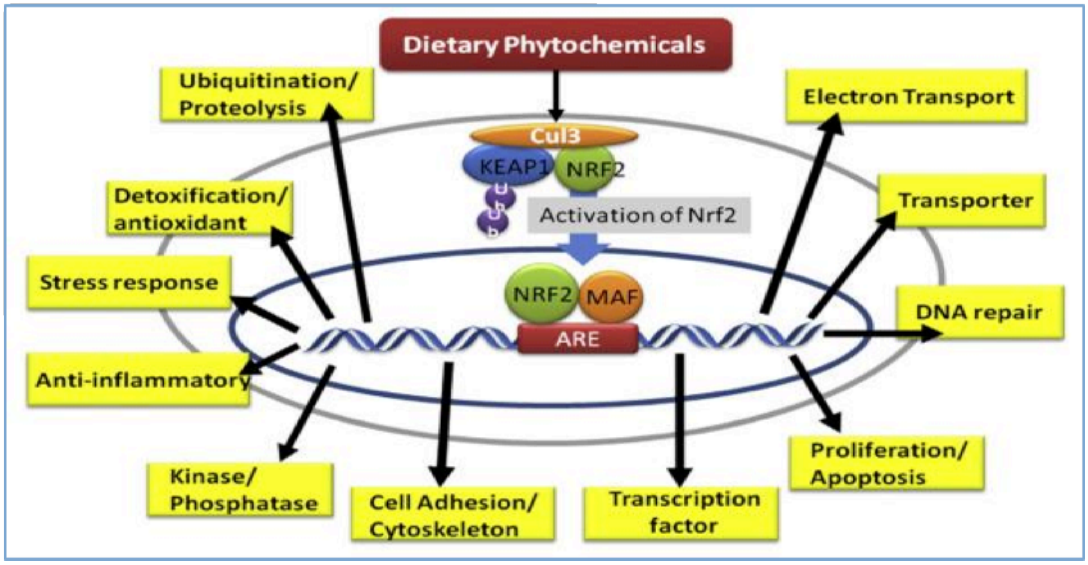
Summary: *"The two most healthful diets known, the traditional Mediterranean and Okinawan diets, and the Paleolithic diet are all thought to be rich in **Nrf2 raising nutrients**, whereas modern diets are deficient in such nutrients. These findings strongly suggest that health-promotion by these diets acts, to a great extent via Nrf2 but that most of us are currently deficient in Nrf2 raising nutrients. Nrf2 acts, in turn via transcription of roughly 500 genes, to raise antioxidant responses, mitochondrial biogenesis and energy metabolism, detoxification of carbon-containing xenobiotics and toxic metals, autophagy of toxic protein aggregates and dysfunctional organelles and greatly lowering many inflammatory responses (**Fig. 1**, lower right). It is not surprising, therefore, that a large number of chronic diseases characterized by oxidative stress, inflammation and often mitochondrial function can be treated and/or prevented by raising Nrf2, at least in animal models (**Fig. 1**, right). Nor should it be surprising that Nrf2 has been proposed to produce both lifespan and healthspan extension, given the many diseases of aging characterized by oxidative stress, inflammation and mitochondrial dysfunction (**Fig. 1**, upper right)."*

"While no doubt it is too early to make a conclusion, it is difficult to escape the suggestion that we may be on the verge of a new literature on health effects of Nrf2 which may well become the most extraordinary therapeutic and most extraordinary preventive breakthrough in the history of medicine. It is our opinion that raising Nrf2 is likely to be the most important health promoting approach into the foreseeable future."

"The stunning apparent breadth of the effects of Nrf2 on diverse diseases produces a challenge for medicine. Medicine has historically focused mainly on the ways in which these various diseases differ from one another, as a way of understanding their differences. However it is possible that these diverse chronic inflammatory diseases all have a similar underlying mechanism and differ from one another primarily in their localization in the body, with the differences in localization being responsible for any differences in their etiologies."

(Note: The entire study is available for review should anyone desire to see the complete study. Please advise.)

The graphic below is from another study cited (Citation #82) by the authors of this study.



Graphic representation of the impact of dietary phytochemicals on the regulation of **Nrf2**-dependent pharmacogenomics. Some of the representative groups of genes are presented.
Ref: https://www.ncbi.nlm.nih.gov/pubmed/23041058