

## Nrf2 signaling in health and disease

Niki Chondrogianni

Institute of Chemical Biology, National Hellenic Research Foundation, Athens, Greece

Email: [nikichon@iee.gr](mailto:nikichon@iee.gr)

Ageing is a complex process affected by both genetic and environmental factors, characterized by a gradual failure of functionality, reduced stress response and resistance, leading to enhanced probability for age-related diseases and mortality. Proteasomes are constituents of the cellular proteolytic network that maintain protein homeostasis through regulated proteolysis of normal and abnormal (in any way) proteins. Proteasome activation in human primary cells and the model organism *Caenorhabditis elegans* has resulted in cellular and organismal lifespan extension and in deceleration of protein aggregation in Alzheimer's (AD) and Huntington's (HD) nematode models. SKN-1, the homolog of Nrf2 in *C. elegans* has been at least partially implicated in the regulation of these positive effects. A dietary triterpenoid, namely 18 $\alpha$ -glycyrrhetic acid (18 $\alpha$ -GA) that activates SKN-1/Nrf2, has been shown to promote similar beneficial effects in human primary cells and in *C. elegans*. Lately, we have also shown that the same Nrf2 activator protects human primary cells from MMC-induced genotoxicity through the ERK/Nrf2 pathway. Our results reveal an additional beneficial effect of the Nrf2 activator 18 $\alpha$ -GA, suggesting that this important phytochemical compound is a potential candidate in preventive and/or therapeutic schemes against conditions (such as aging) or diseases that are characterized by both oxidative stress and DNA damage. Our work identifies new bioactive compounds with anti-ageing and/or anti-aggregation properties or reveals additional beneficial properties on already known bioactive compounds.



**Niki Chondrogianni** is a Director of Research at the Institute of Chemical Biology, National Hellenic Research Foundation. She focuses on the genetic and environmental factors that govern ageing, longevity and age-related diseases with emphasis on proteasome regulation. She is seeking for compounds that may act as proteasome activators and thus may serve as anti-ageing agents while dissecting at the same time the involved molecular pathways. She is equally interested in identifying compounds than can decelerate protein aggregation and thus the progression

of proteinopathies with emphasis on Alzheimer's disease using *C. elegans* as a model in combination with human cells of neuronal origin and murine primary neurons. Various molecular pathways have been revealed to be involved in such beneficial results including the Nrf2/SKN-1 pathway. She is a national and international patent holder that resulted in the development of novel anti-ageing products that act through the activation of the proteasome system (two relative product series in the national/international market).