

Yin yang

A balancing act for oxidative stress

Kenneth Maiese

Department of Neurology and Neurosciences; University of Medicine & Dentistry of New Jersey;
New Jersey Medical School; Newark, NJ USA

Derived from classical Chinese philosophy and with frequent applications in Chinese medicine, “yin yang” has grown into an interesting concept that may have a number of applications. The term is usually used to depict the existence of polarizing or opposing forces in nature. Yet, the concept of “yin yang” can be much more involved, especially in biological systems, and pertain to events that not only are intimately connected, but also have significant repercussions upon each other. Interestingly, one does not need to search far in biology and medicine to learn of the concept of “yin yang.” For example, nicotinamide, which is the amide form of vitamin B3 (niacin), is a robust cytoprotectant that can scavenge reactive oxygen species during oxidative stress and increase survival of both neuronal and vascular cells during multiple injury paradigms that include anoxia, excitotoxicity, ethanol toxicity, and elevated glucose. Furthermore, nicotinamide also may limit inflammatory injury, protect against trauma, and improve cognition under some conditions. However, there is another side to nicotinamide that is relevant to the concept of “yin yang” and involves opposing forces with sirtuins. It appears that reduced concentrations of nicotinamide may be necessary to increase cell longevity to permit activity of sirtuins. Elevated concentrations of nicotinamide block the activity of sirtuins, agents that have been tied to increases in longevity and cellular protection such as during metabolic disorders with diabetes mellitus. Therefore, in relation to the biology of cell survival and cell longevity, a complex relationship exists between nicotinamide and sirtuins that require a careful balance to maximize cell survival and extend cell longevity.

In this issue of *Oxidative Medicine and Cellular Longevity*, we present a unique group of papers that bring home the role of “yin yang” for our readers. In the review paper by Bouayed and Bohn, the authors take direct aim at the concept of “yin yang” in bringing to light the sometimes unrecognized and unexpected effects of exogenous antioxidants. Exogenous dietary antioxidants, such as vitamin C, vitamin E, carotenoids, and polyphenols, are necessary for the proper functioning of the endogenous cellular antioxidant system, but under certain conditions exogenous agents also may yield pro-oxidant behavior. As a result, the authors outline the intimate connections between oxidant and antioxidant pathways and the need to better align these systems. In the next review by Attia, the author describes the challenges of drug development and unexpected consequences that may arise following clinical approval and use of drug treatments as a result of unexpected opposing forces of nature. Attia provides striking insight to adverse drug reactions, especially those that are idiosyncratic in nature, and how knowledge and modulation of reactive metabolic pathways that may ensue with drug activation may prevent unintended adverse consequences during future clinical drug deployment. Sayed-Ahmed et al. extend this concept of finely controlling opposing cellular pathways in their original work using a model of hepatocellular carcinoma. They show that initiation of hepatocellular carcinoma results in the generation of reactive oxygen species and the concomitant reduction of antioxidant pathways, but that specific and directed strategies such as with thymoquinone that can oppose specific oxidant stress pathways can prevent the generation of hepatocellular carcinoma. Remarkably, opposing cellular pathways also involve metabolic pathways in individuals that may not have extensive disease as shown by the unique clinical study in non-diabetic males by Tahara et al. The authors show for the first time that insulin resistance promotes elevated serum levels of advanced glycation end products yet is inversely correlated with testosterone resulting in low testosterone levels in diabetic men. Interestingly, application of exogenous therapeutic strategies may not always upset the homeostasis of intrinsic cellular pathways through the development of reactive metabolic pathways but rather through the elimination of essential molecules. For example, colleagues of Fatani et al. illustrate for us that deficiency in carnitine, an essential cofactor for β -oxidation of long-chain fatty acids in the myocardium, occurs during Fanconi Syndrome and can result in ifosfamide-induced cardiotoxicity requiring the supplementation of carnitine to prevent this disorder. Gautam et al. introduce an additional level of scrutiny for the concept of “yin yang” to inform us with their novel clinical study of lymphocytes in individuals of progressive ages that external factors such as aging should also be recognized in scenarios that can alter the balance between the opposing forces of oxidant generation and antioxidant scavenging in biological pathways. In our final article for this issue, Lee et al. identify a unique relationship between neurons and astrocytes that allow neurons to transfer α -synuclein to astrocytes and trigger the production of inflammatory factors that may injure neurons. Yet, this observation represents only one side of the coin and in the true spirit of the concept of “yin yang,” we learn that some factors released from α -synuclein-stimulated astrocytes can impart protection upon neurons. Our papers in this issue of *Oxidative Medicine and Cellular Longevity* bring to the forefront the concept of “yin yang” in complex biological systems. Although the origins of this concept may have originated with the advent of medical care in ancient civilizations, it is no less relevant than it is now to fully understand and develop effective therapeutic strategies for modern medicine.

Correspondence to: Kenneth Maiese; Email: maieseke@umdnj.edu
Submitted: 08/16/10; Accepted: 08/16/10
Previously published online: www.landesbioscience.com/journals/oximed/article/13340
DOI: 10.4161/oxim.3.4.13340