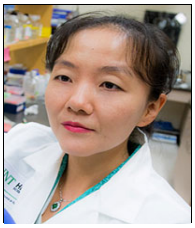

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Using Grapes as a Magic Bullet to Fight Against Free Radicals in the Eye: Application to Cataract Prevention

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Purpose: The main purpose of this study is to investigate if grape powder could protect against *in vivo* ultraviolet (UV) radiation-induced cataract and to study its mechanism of action and identify its targets in the lens.

Methods: The grape powder was provided by the California Table Grape Commission (CTGC). C57BL/6J mice were feed with the regular diet, regular diet supplemented with glucose and fructose, or the grape diet (regular diet supplemented with 5%, 10%, and 15% grape powder) for 3 months. The animals were then exposed to 20.6 kJ/m^2 UV radiation for 15 min to induce cataracts. Two days later, the degree of the cataract and lens morphology was evaluated under dissecting microscope. Glutathione (GSH), free protein thiol (PSH), and protein glutathionylation (PSSG) levels were measured to reflect the oxidative markers. Finally, we also examined the effects of grape powder on the nuclear factor erythroid 2–related factor 2 (Nrf2) pathway and its downstream antioxidant genes in the lens.

Results: We found that 15% grape powder diet could significantly inhibit the onset as well as the severity of UV-induced cataracts. All mice in the regular diet control group developed severe epithelial and superficial anterior subcapsular cataracts two days after the UV radiation. On the other hand, grape powder diet in a dose-dependent manner prevented the lens from UV radiation-induced cataract progression. In the 15% grape powder diet group, the majority of lenses remained largely transparent. The GSH and PSH levels were much higher in the 15% grape powder diet group compared with that of the regular diet control group. The accumulation of PSSG, a marker for protein thiol oxidation, was largely inhibited in the 15% grape powder diet group. Interestingly, we also found that Nrf2 and its downstream targets including SOD, catalase, thioredoxin (Trx), and glutaredoxin 1 (Grx1) were significantly elevated in regular diet control groups due to the UV exposure. However, this UV-induced Nrf2 activation was largely inhibited in all three grape powder diet groups.

Conclusions: Grape powder dose-dependently protected the lens from UV radiation-induced cataract development in mice. Its protective effects may involve directly regulating endogenous Nrf2 and its downstream target detoxifying/antioxidant genes, including SOD1, SOD2, catalase, Trx1, Trx2, Grx1, and Grx2.

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Biography:

I received a BS and MS in Pharmacy from Xinjiang Medical University in Xinjiang, China, and a PhD in Pharmacology from Peking University. I completed my postdoctoral training for four and half years with Dr. Marjorie Lou in biochemistry in the Redox Biology Center at the University of Nebraska-Lincoln. The central theme of my research is to understand the role of oxidative stress defense agents/enzymes and their functional targets and potential therapies in eye diseases. Of primary interest is the age-related macular degeneration (AMD), the most common retinal disorder that affects 25 million people worldwide, yet its pathogenesis remains poorly understood. My lab uses gene knockout and transgenic animals and primary retinal cells as models to elucidate how altered redox signaling and disrupted redox homeostasis contribute to the pathogenesis of AMD. My research emphasizes the effects of oxidative damage and its repair on retinal proteins, in particular the thiol (SH)-containing proteins/enzymes. We also investigate natural product-derived antioxidant compounds that may serve as leads for the development of new pharmaceutical products that may eventually treat AMD. I have coauthored more than 20 peer-reviewed publications in the areas of redox biology.