

Supplementation of selenium-enriched yeast attenuates age-dependent transcriptional changes of heart in mitochondrial DNA mutator mice

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ABSTRACT

Background: Age is a major risk factor in developing heart diseases and has been associated with profound transcriptional changes in mammalian tissues. Low tissue selenium has recently been linked to several age-related diseases, including cardiovascular disease. This study investigated the global effects of age and dietary supplementation of selenium on heart transcriptional profiles in POLG mutator mice.

Methods: Heart transcription profiles from young (2-month-old) and old (13-month-old) animals fed either a control diet or a diet supplemented with 1.0 mg selenium from selenium-enriched yeast (SP)/kg diet were obtained and validated using microarray and real-time RT-PCR techniques.

Results: Aging led to significant transcriptional changes, where the expression of 1942 genes in old animals was changed by a fold change larger than 2.0, when compared to young animals. Age-regulated genes are associated with cardiovascular system development, immune and inflammatory response, and cellular oxidative stress response. Multiple genes linked with cardiomyocyte apoptosis, hypertrophy, and cardiac fibrosis, such as *Myh7*, *Lcn2*, *Spp1*, and *Serpine1*, were significantly up-regulated in old animals. SP supplementation also caused significant transcriptional changes in the heart, especially in old mice where many age-dependent transcriptional changes were totally or partially reversed by SP. Upstream regulator analysis further indicated that genes for *Foxo1* and *Foxo3*, two transcriptional regulators involved in the regulation of cardiac muscle remodeling, were significantly activated by SP, suggesting that Foxo-mediated transcriptional activities play important roles in the anti-aging properties of SP.

Conclusions: Results of this study indicate that SP supplementation attenuated age-related transcriptional changes in the heart of old POLG mice, which implies a potential clinical application of dietary selenium in preventing decline of cardiac function in old animals.

Key words: Aging, heart, gene expression, selenium