Integrative Modulation of Reproductive Longevity and Chronic Stress Resilience in Caenorhabditis elegans via Dual Antioxidant-Induced SIRT1-FOXO3 and Nrf2-Keap1 Axis Activation and Epigenomic Stabilization Using Resveratrol and Astaxanthin

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Infertility affects over 186 million people globally and is mechanistically linked to oxidative stress-induced mitochondriopathy, genomic instability, and chronic inflammation. These pathologies interact reciprocally and are the initiators of reproduction aging, embryonic perturbation, and systematic degeneration, as well as of Alzheimer's, Parkinson's, PCOS, Type 2 Diabetes, and cardiovascular disease. Despite continuous technological progress, assisted reproduction technologies (ARTs) remain limited and largely fail to rectify bioenergetic and epigenetic deficiencies behind the pathologies. Caenorhabditis elegans is utilized in this research as the model to examine the influence of the redox modulator and mitochondrial bioenergetic enhancer compounds resveratrol and astaxanthin on reproduction lifespan and oxidative stress tolerance. Resveratrol activates SIRT1 to promote mitochondrial biogenesis, FOXO3-antioxidant signaling, and p53-genomic stability, while astaxanthin activates the Nrf2-Keap pathway to promote glutathione metabolism and suppress pro-inflammatory cytokines. Experimentations utilized antioxidant-saturated E. coli, NGM plate administration, and H2O2-stress exposure to 75 experiment plates (15 each of resveratrol, astaxanthin, combination, control, and toxicity). Microscopy, AI-assisted lifespan analysis, paired t-tests, Tukey HSD post-test analysis, and nonlinear regressions determined the combinational therapy to improve reproduction lifespan and stress tolerance significantly ($p < 0.00001$). Chronic stressor model simulations determined metabolically reprogrammed and epigenetically recalibrated responses as primary resilience mechanisms to predict the therapeutic use of this strategy for reproduction and chronic stress-induced degenerative diseases.

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