SELENIUM-DEPENDENT GLUTATHIONE PEROXIDASE 4 REGULATION OF FERROPTOSIS: APPLICATIONS IN GRAFT SURVIVAL AND ONCOLOGICAL THERAPY

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Introduction: Selenium is a fundamental micronutrient required for biosynthesizing glutathione peroxidase 4, a key antioxidant enzyme responsible for maintaining cellular redox homeostasis. Its primary biochemical function is reducing lipid hydroperoxides to alcohols, effectively inhibiting ferroptosis - a form of regulated cell death characterized by iron-dependent lipid peroxidation. In tissue engineering, the viability of a graft is critically challenged by ischemia-reperfusion injury, where reintroduction of oxygen generates high levels of reactive oxygen species. This study evaluates the potential of the selenium-glutathione peroxidase 4 axis in protecting healthy transplanted tissues while simultaneously targeting residual malignant cells.
Materials and Methods: A systematic review of molecular research was conducted using databases such as PubMed, ScienceDirect, Google Scholar and Wiley Online Library (2015–2026). The analysis focused on the metabolic pathways of selenoproteins and their role in preventing membrane damage. Data from the *Saccharomyces cerevisiae* eukaryotic model were utilized to assess the dose-dependent effects of selenium genomic integrity and mitochondrial respiration. Additionally, we reviewed current evidence regarding the autophagy-mediated turnover of GPX4 and the impact of selenium availability on enzymatic stability.
Results: The data demonstrate a clear hormetic effect of selenium compounds, defined as a dual-phase response where physiological doses provide cellular protection while supra-optimal concentrations induce toxicity. At physiological levels, selenium upregulates glutathione peroxidase 4 activity, significantly reducing malondialdehyde levels - a definitive biomarker of oxidative damage -thereby enhancing graft survival. Conversely, excessive inorganic sodium selenite exhibits pro-oxidant properties by interacting with thioredoxin reductase 1. This interaction converts the enzyme into a pro-apoptotic inducer, triggering lethal oxidative stress specifically in malignant cells. By utilizing biomimetic scaffolds for controlled delivery of selenium, it is possible to maintain an antioxidant environment for tissue regeneration while inducing selective ferroptotic death in cancer cell populations.
Conclusions: The selenium-glutathione peroxidase 4 pathway is a critical target for optimizing outcomes in regenerative medicine and oncology. Modulating this axis provides a dual-action strategy: stabilizing cellular integrity of engineered grafts and establishing a metabolic safety net against tumor recurrence. Integrating selenium-enriched biomaterials represents a significant advancement in the development of safer and more effective protocols for tissue transplantation and post-oncological recovery.
Keywords: Selenium, glutathione peroxidase 4, ferroptosis, oxidative stress, graft survival.