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Ginsenoside Rc prevents muscle atrophy by targeting TGF-β signaling and nucleolin expression under oxidative stress

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Ginsenoside Rc (gRc), a major component of Panax ginseng, can alleviate muscle damage caused by oxidative stress through its antioxidant effects and enhancement of mitochondrial function. However, the molecular mechanisms and target genes by which gRc mitigates muscle damage are not yet clearly understood. This study aims to elucidate the complex regulatory effects of gRc on the TGF-β pathway by integrating transcriptomic data, in vitro experiments, and molecular docking simulations. First, we analyzed gene sets affected by gRc and H_2O_2, revealing that gRc can potentially inhibit the TGF-β signaling pathway to reduce muscle atrophy. Subsequent in vitro experiments using C2C12 cell lines showed that gRc exhibits similar effects to TGF-β inhibitors under oxidative stress conditions, preventing myotube degradation. Molecular docking simulations further predicted that gRc can bind to TGFBR1, acting as an inhibitor. Transcriptome analysis indicated that gRc inhibits Nucleolin (Ncl), a downstream component of the TGF-β pathway, reducing its expression under oxidative stress. Finally, Nucleolin siRNA transfection experiments confirmed that silencing Ncl can mitigate muscle atrophy caused by oxidative stress. These results demonstrate the potential of gRc to alleviate muscle damage through the TGF-β and Ncl pathways, suggesting its development as a therapeutic agent for sarcopenia and related muscle disorders. This study provides important foundational data for understanding the complex molecular mechanisms of gRc and emphasizes its potential to reduce muscle damage and improve muscle function.