

Title: RNA-sequencing exploration on *SIR2* and *SOD* genes in *Polyalthia longifolia* leaf methanolic extracts (PLME) mediated anti-aging effects in *Saccharomyces cerevisiae* BY611 yeast cells

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Abstract: *Polyalthia longifolia* is well-known for its abundance of polyphenol content and traditional medicinal uses. Previous research has demonstrated that the methanolic extract of *P. longifolia* leaves (PLME, 1 mg/mL) possesses anti-aging properties in *Saccharomyces cerevisiae* BY611 yeast cells. Building on these findings, this study delves deeper into the potential antiaging mechanism of PLME, by analyzing the transcriptional responses of BY611 cells treated with PLME using RNA-sequencing (RNA-seq) technology. The RNA-seq analysis results identified 1691 significantly ($\text{padj} < 0.05$) differentially expressed genes, with 947 upregulated and 744 downregulated genes. Notably, the expression of three important aging-related genes, *SIR2*, *SOD1*, and *SOD2*, showed a significant difference following PLME treatment. The subsequent integration of these targeted genes with GO and KEGG pathway analysis revealed the multifaceted nature of PLME's anti-aging effects in BY611 yeast cells. Enriched GO and KEGG analysis showed that PLME treatment promotes the upregulation of *SIR2*, *SOD1*, and *SOD2* genes, leading to a boosted cellular antioxidant defense system, reduced oxidative stress, regulated cell metabolism, and maintain genome stability. These collectively increased longevities in PLME-treated BY611 yeast cells and indicate the potential anti-aging action of PLME through the modulation of *SIR2* and *SOD* genes. The present study provided novel insights into the roles of *SIR2*, *SOD1*, and *SOD2* genes in the anti-aging effects of PLME treatment, offering promising interventions for promoting healthy aging.

Keywords: *Polyalthia longifolia*; Anti-aging; Methanolic Leaf Extract (PLME); *Saccharomyces cerevisiae* BY611; RNA-Sequencing (RNA-seq);

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