MYG1 drives glycolysis and colorectal cancer development through nuclear mitochondrial collaboration

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Background:

Metabolic remodeling is a hallmark of cancer and plays a crucial role in helping colorectal cancer (CRC) cells to survive in complex stress conditions. A central feature of this remodeling is the Warburg effect, where cancer cells preferentially use aerobic glycolysis over oxidative phosphorylation (OXPHOS), even when oxygen is sufficient. This metabolic shift supports rapid proliferation and evasion of apoptosis, forming a favorable environment for tumor growth. While several oncogenes have been implicated in this shift, the precise molecular mechanisms particularly those involving coordination between nuclear and mitochondrial functions remain incompletely understood. MYG1 (Melanocyte Proliferating Gene 1), known for its dual nuclear and mitochondrial localization and RNA exonuclease activity, has recently emerged as a candidate gene potentially involved in cancer metabolism.

Objective:

To investigate the role of MYG1 in colorectal cancer (CRC) progression and its potential involvement in tumor metabolic reprogramming.

Results:

Through analysis of public colorectal cancer (CRC) datasets, the authors identified MYG1 as a differentially expressed gene associated with CRC progression and metabolic reprogramming. Subsequent experiments confirmed that MYG1 is significantly upregulated in CRC tissues and correlates with poor clinical outcomes. The study then elucidated distinct roles of MYG1 in the nucleus and mitochondria. In the nucleus, MYG1 recruits the HSP90/GSK3β complex to phosphorylate and stabilize PKM2, promoting MYC-driven glycolytic gene expression. In the mitochondria, MYG1 inhibits oxidative phosphorylation and prevents apoptosis by blocking cytochrome c release. Ultimately, the findings demonstrate that both nuclear and mitochondrial functions of MYG1 cooperatively drive CRC progression, contributing to a metabolic environment that supports tumor growth and survival.

Conclusion:

These findings demonstrate that both nuclear and mitochondrial functions of MYG1 independently and synergistically facilitate CRC progression, highlighting MYG1 might as a promising therapeutic target in CRC.