Glycerol-3-Phosphate Dehydrogenase 1-Like Serves as a Tumor Suppressor in Colorectal Cancer Through ATF3-Mediated Ferroptosis

Changjiang Yang[1, 2], Long Zhao[1, 2], Zhanlong Shen[1, 2], Yingjiang Ye[1, 2], Zhidong Gao[1, 2], Lin Gan[1, 2, *]

[1]Department of Gastroenterological Surgery, Peking University People's Hospital, Beijing, China

[2]Beijing Key Laboratory of Colorectal Cancer Diagnosis and Treatment Research, Laboratory of Surgical Oncology, Peking University People's Hospital, Beijing, China

Email address:

yangchangjiang1115@163.com (Changjiang Yang), ganxiunan1995@163.com (Lin Gan)

[*]Corresponding author

Abstract

Colorectal cancer (CRC) continues to be a prevalent malignancy, posing a significant risk to human health. The involvement of Glycerol-3-phosphate dehydrogenase 1-like (GPD1L) in CRC development was suggested by our analysis of clinical samples. However, the role of GPD1L in CRC remains unclear. This study seeks to elucidate the clinical relevance, biological function, and potential molecular mechanisms of GPD1L in CRC. Our results demonstrated that GPD1L expression in CRC tissues was notably lower compared to adjacent normal tissues. This low expression correlated with a poorer prognosis for CRC patients. GPD1L overexpression impeded CRC cell proliferation and migration while inducing G0/G1 cell cycle arrest and apoptosis. Moreover, knockdown of GPD1L could reduce the iron content and lipid oxidation level, increase the antioxidant capacity of cells, and weaken the ferroptosis of CRC cells. Mechanistically, GPD1L affected ferroptosis by affecting the expression level of ATF3, and finally led to the change of the biological behavior of CRC cells. In summary, GPD1L functions as a tumor suppressor, primarily by promoting ferroptosis through ATF3 and affects the malignant phenotype and biological behavior of CRC. This role established GPD1L as a promising prognostic biomarker and a potential therapeutic target for CRC patients.

Keywords

Glycerol-3-Phosphate Dehydrogenase 1-Like, Colorectal Cancer, Ferroptosis