**ALDOA contributes to colorectal tumorigenesis and metastasis by targeting YAP**

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**Background:**Metabolic reprogramming is considered one of the hallmarks of cancer in which cancer cells reprogram their metabolic cascades, mostly driven by the specific chemical microenvironment in cancer tissues. Cancer cells can generate ATP without oxygen, a process described as the Warburg effect , which was thought to be at the basis of carcinogenesis. Therefore, high-throughput biochemical techniques have discovered various glycolytic enzymes or metabolic pathways as prospective therapeutic targets for cancer therapy. Fructose-bisphosphate aldolase catalyzes the reversible conversion of fructose-1,6-bisphosphate (FBP) to glyceraldehyde-3-phosphate (G3P) and dihydroxyacetone phosphate (DHAP) in the glycolytic pathway. Aldolase A (ALDOA) is one of three aldolase isozymes (A, B, and C) involved in cellular functions, such as ATP generation. ALDOA has been revealed to be highly expressed in numerous malignancies, including human pancreatic , prostate, hepatocellular, cervical, bladder, gastric, and lung cancer. In CRC, relative to healthy glandular epithelium tissues, ALDOA was found to be substantially expressed in tumor tissues and liver metastatic CRC, and an elevated level of ALDOA contributed to the poor survival outcomes in CRC patients. However, the exact role and mechanism of ALDOA in CRC have not been fully explored.

**Objective/Hypothesis:** This could suggest a novel avenue for treating CRC by inhibiting both ALDOA and YAP signaling.

**Results:** In this study, ALDOA expression was substantially elevated in CRC tissues and was correlated with prognosis of CRC patients. The loss and gain of function investigations revealed that ALDOA elevated the proliferative and migratory potential of CRC cells in vitro and in vivo. High ALDOA expression leads to AMPK inhibition and YAP unphosphorylation. Unphophorylated YAP translocates into the nucleus and triggers its target genes expression that promotes CRC cell proliferation and migration. Our findings reveal that ALDOA can function as a crucial regulator of YAP and may become a novel therapeutic target for CRC.

**Conclusion:** In the current study, author demonstrated that ALDOA expression was increased in human CRC tissues. Additionally, clinical evaluation demonstrated a positive correlation between high ALDOA expression and tumor size, invasion depth, LNM, and TNM stage. K-M analysis revealed that elevated ALDOA levels correlated with a poor prognosis in CRC patients with stage I-III, whereas the prognosis tends to be favorable in patients with advanced CRC. Furthermore, the loss and gain of function assay suggested that ALDOA depletion inhibited CRC cell proliferation and migration while ectopic ALDOA showed the opposing results, indicating the oncogenic roles of ALDOA in CRC.