World Academy of Science, Engineering and Technology
International Journal of Health and Medical Engineering
Vol:19, No:01, 2025

Targeting Methionine Metabolism In Gastric Cancer; Promising To Improve Chemosensetivity With Non-hetrogeneity

Authors : Nigatu Tadesse, Li Juan, Liuhong Ming

Abstract : Gastric cancer (GC) is the fifth most common and fourth deadly cancer in the world with limited treatment options at late advanced stage in which surgical therapy is not recommended with chemotherapy remain as the mainstay of treatment. However, the occurrence of chemoresistance as well as intera-tumoral and inter-tumoral heterogeneity of response to targeted and immunotherapy underlined a clear unmet treatment need in gastroenterology. Several molecular and cellular alterations ascribed for chemo resistance in GC including cancer stem cells (CSC) and tumor microenvironment (TME) remodeling. Cancer cells including CSC bears higher metabolic demand and major changes in TME involves alterations of gut microbiota interacting with nutrients metabolism. Metabolic upregulation in lipids, carbohydrates, amino acids, fatty acids biosynthesis pathways identified as a common hall mark in GC. Metabolic addiction to methionine metabolism occurs in many cancer cells to promote the biosynthesis of S-Adenosylmethionine (SAM), a universal methyl donor molecule for high rate of transmethylation in GC and promote cell proliferation. Targeting methionine metabolism found to promotes chemo-sensitivity with treatment non-heterogeneity. Methionine restriction (MR) promoted the arrest of cell cycle at S/G2 phase and enhanced downregulation of GC cells resistance to apoptosis (including ferroptosis), which suggests the potential of synergy with chemotherapies acting at S-phase of the cell cycle as well as inducing cell apoptosis. Accumulated evidences showed both the biogenesis as well as intracellular metabolism of exogenous methionine could be safe and effective target for therapy either alone or in combination with chemotherapies. This review article provides an over view of the upregulation in methionine biosynthesis pathway and the molecular signaling through the PI3K/Akt/mTOR-c-MYC axis to promote metabolic reprograming through activating the expression of L-type aminoacid-1 (LAT1) transporter and overexpression of Methionine adenosyltransferase 2A(MAT2A) for intercellular metabolic conversion of exogenous methionine to SAM in GC, and the potential of targeting with novel therapeutic agents such as methioninase (METase), Methionine adenosyltransferase 2A (MAT2A), c-MYC, methyl like transferase 16 (METTL16) inhibitors that are currently under clinical trial development stages and future perspectives.

Keywords : gastric cancer, methionine metabolism, pi3k/akt/mtorc1-c-myc axis, gut microbiota, MAT2A, c-MYC, METTL16, methioninase
Conference Title : ICGEC 2025 : International Conference on Gastroenterology, Endoscopy and Colonoscopy
Conference Location : Vancouver, Canada
Conference Dates : January 11-12, 2025