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Perspective

NcRNAs as Biomarkers for Predicting Glycolysis-Driven Tumor Progression

Hesami Sepideh*

Department of Biophysics, Tarbiat Modares University, Tehran, Iran

DESCRIPTION

Cancer is a complex and heterogeneous disease characterized by uncontrolled cell growth and division. One of the major symptom of cancer cells is their altered metabolism, which is characterized by a shift from oxidative phosphorylation to glycolysis, even in the presence of oxygen, a phenomenon known as the Warburg effect. This metabolic rewiring allows cancer cells to meet their increased energy demands and maintain rapid proliferation. Emerging research has highlighted the crucial role of Non-Coding RNAs (ncRNAs) in regulating glycolysis in human cancers. In this article, we delve into the molecular profile of ncRNA-mediated glycolysis control, focusing on the potential therapeutic implications of these findings.

Categories of non-coding RNAs

Non-coding RNAs are a diverse class of RNA molecules that do not code for proteins but play essential roles in the regulation of gene expression. There are two main categories of ncRNAs: microRNAs (miRNAs) and Long Non-Coding RNAs (lncRNAs).

MicroRNAs (miRNAs): These small ncRNAs, typically 19-22 nucleotides long, function as post-transcriptional regulators by binding to the 3' Untranslated Region (UTR) of target messenger RNAs (mRNAs) and promoting their degradation or inhibiting translation. MiRNAs are involved in a wide range of biological processes, including cell proliferation, differentiation, and metabolism.

Long Non-Coding RNAs (lncRNAs): LncRNAs are a heterogeneous group of ncRNAs that are longer than 200 nucleotides. They can regulate gene expression at multiple levels, including transcriptional, post-transcriptional, and epigenetic regulation. LncRNAs have gained prominence for their role in various diseases, including cancer.

NcRNAs in glycolysis regulation

Recent studies have shown that ncRNAs play a pivotal role in the regulation of glycolysis in cancer cells. Here, we discuss the molecular mechanisms through which miRNAs and lncRNAs influence glycolysis in human cancers.

miRNA-mediated glycolysis control

miRNAs that influence glycolysis in human cancers are:

miRNA regulation of glycolytic enzymes: Several miRNAs have emerged as critical regulators of key glycolytic enzymes. For instance, miR-155 exerts control over Hexokinase 2 (HK2), a rate-limiting enzyme in glycolysis. Its action results in reduced glucose uptake and diminished glycolytic activity, impeding the metabolic vigor of cancer cells.

miRNA-mediated hypoxia response: miRNAs also play an integral role in enabling cancer cells to adapt to hypoxic conditions, a prevailing feature of the tumor microenvironment. miR-210, as an illustrative example, undergoes upregulation under hypoxia, facilitating glycolysis by targeting multiple genes intricately involved in mitochondrial metabolism.

LncRNA-mediated glycolysis control

LncRNAs that influence glycolysis in human cancers are:

H19: The long non-coding RNA H19 has been ascribed the function of promoting glycolysis in cancer cells. It accomplishes this by suppressing the expression of the tumor suppressor protein p53, which exerts negative regulation over glycolysis. H19 functions as a Competing Endogenous RNA (ceRNA), sequestering miRNAs that would otherwise target p53, thereby unleashing glycolytic activity.

PVT1: Another lncRNA of note, PVT1, serves as a promoter of glycolysis across various cancers. PVT1 achieves this by engaging with the transcription factor c-Myc, a master regulator overseeing glycolytic genes. Through its interaction with c-Myc, PVT1 enhances the stability of this transcription factor, culminating in heightened expression of glycolytic enzymes.

Therapeutic implications

Understanding the role of ncRNAs in glycolysis control opens up exciting possibilities for cancer therapy. Targeting ncRNAs involved in glycolysis regulation may provide a novel approach to disrupt the metabolic advantage of cancer cells. Here are a few potential therapeutic strategies:

Correspondence to: Hesami Sepideh, Department of Biophysics, Tarbiat Modares University, Tehran, Iran, E-mail: HesamiSepideh@gmail.com

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Small molecule inhibitors: Developing small molecules that specifically target dysregulated miRNAs or lncRNAs could inhibit their function and disrupt the glycolytic pathway in cancer cells.

RNA-based therapies: Utilizing RNA-based therapeutics, such as antisense oligonucleotides or Small Interfering RNAs (siRNAs), to directly target and silence oncogenic ncRNAs involved in glycolysis promotion.

Combination therapies: Combining ncRNA-targeted therapies with existing anticancer treatments, such as chemotherapy or immunotherapy, to enhance the overall therapeutic response and reduce resistance.

The molecular profile of ncRNA-mediated glycolysis control in human cancers is a rapidly evolving field of research. It is increasingly clear that non-coding RNAs play a significant role in rewiring cancer cell metabolism, contributing to tumour progression and survival. Targeting these ncRNAs holds potential as a novel therapeutic strategy to disrupt cancer cell metabolism and improve patient outcomes.