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Knockdown of RPS3, a DNA repair endonuclease, impedes colon cancer growth and progression by decreasing lactate dehydrogenase activity

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Statement of the Problem: In addition to their role in ribosome biogenesis, ribosomal proteins (RPs) play important roles in DNA repair, proliferation, apoptosis and resistance to drugs and chemotherapy. Ribosomal protein S3 (RPS3), a DNA repair endonuclease, is known to be overexpressed in colon adenocarcinoma. In order to ensure their survival, cancer cells rely on aerobic glycolysis catalyzed by the enzyme lactate dehydrogenase (LDH). Our aim is to identify the role of RPS3 in colon cancer growth and metabolism.

Methodology & Theoretical Orientation: Human colon adenocarcinoma Caco-2 and normal colon NCM-640 cells were tested for the expression of RPS3 by Western blot. In order to inhibit RPS3 expression, cells were transfected with siRNA against RPS3 or a non-targeting siRNA (siNT) as a negative control. Upon RPS3 knockdown, cell behaviors were tested including proliferation and survival by trypan blue and WST-1 assays and cell migration and invasion by the Boyden chamber assays. The glycolysis state of colon cancer cells was assessed by measuring LDH activity upon RPS3 knockdown using the LDH assay.

Findings: RPS3 was shown to be expressed in both Caco-2 and NCM-640 cells. RPS3 knockdown in Caco-2 significantly reduced cell proliferation, survival, migration and invasion compared to siNT-transfected cells. In NCM-640, RPS3 knockdown did not significantly affect cell proliferation and survival implying that RPS3 expression is selectively crucial for colon cancer cell growth. Interestingly, LDH activity was suppressed upon RPS3 knockdown, suggesting a decrease in glycolysis which explains in part the decrease in proliferation.

Conclusion & Significance: This is the first report that shows a role of RPS3 in regulating LDH activity therefore affecting the glycolytic state, the survival and proliferation of cancer cells. Our results also demonstrate that RPS3 is a selective molecular marker in colon cancer and a potential attractive target for colon cancer therapy.

Biography

Zeina Nasr is Assistant Professor, at the Department of Biology in the University of Balamand, Lebanon. She did her PhD from McGill University in the Department of Biochemistry. She has her interest in understanding the molecular aspect of tumor initiation and progression. Her research focuses on studying the effect of translation initiation dysregulation on cancer behavior. She has worked with several cell lines and transgenic mouse models and deciphered important pathways that contribute to cancer initiation and progression to metastasis. She has experience in conducting research and teaching at various institutions. Currently, her work focuses on the extra-ribosomal functions of ribosomal proteins and their effects on tumorigenesis.

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