TOPIC

CANCER METABOLISM

Regulation of AURKA, BIRC5 and PLK1 protein expression in colorectal cancer

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Introduction

The study of proteins implicated in radiation resistance is important to understand the mechanisms of regulation and expression in order to improve new therapies. In this way, the proteins AURKA, BIRC5 and PLK1 are related to resistance in colorectal cancer. The identification of multiple transcription factors that regulate the expression of these key genes, as well as the higher level of expression observed in tumors, suggests their high potential as possible biomarkers.

Objectives

The study and analysis of the transcription factors that regulate the expression of AURKA, BIRC5 and PLK1 proteins in patients affected by colorectal cancer are the main objectives of this work in order to know how to improve new therapies.

Methods

The genes AURKA, BIRC5 and PLK1 were identified, as the core genes implicated in radiation resistance in colorectal cancer, after data mining and in-silico analysis. Then, a transcription factors regulatory network study was made with ChIP-X Enrichment Analysis v.3 (CHEA3), and the description and function of each transcription factor was obtained from Harmonizome 3.0.

Results

AURKA, BIRC5 and PLK1 proteins showed a regulatory network with multiple transcription factors implicated in their expression. The greatest co-expression and co-occurrence is represented by the thickness of the edges in the network. It should be noted that the regulators E2F7, DRAP1 and ZNF511 were those with the highest integrated scaled rank (>0.999). The complete description of the most prominent transcription factors is included, noting that most of them are involved in some phenomenon related to the regulation of the cell cycle or cell proliferation.

AURKA is overexpressed in a wide cancer types including colorectal, where aberrant expression has been observed, linked to cell resistance to drugs. BIRC5 plays a key role in cell division, interacting with caspases, and contributes to the regulation of apoptosis and mitosis cycle. This protein is highly expressed in colorectal cancer promoting cell proliferation migration and invasion. The down-regulation could suppress the promotion of colorectal cancer cells, through the regulation of immune cells. This protein plays a crucial role in the regulation of apoptosis and cell survival. Its overexpression has been associated with tumor progression, resistance to apoptosis and worse patient survival. PLK1 was found to be overexpressed in different tumors. Its inhibition reduces cell proliferation and increases apoptosis. This protein is involved in cell cycle regulation, especially in the progression of mitosis. Its overexpression is associated with tumor progression, invasion and metastasis; as well as resistance to radiotherapy and worse patient prognosis.

Conclusions

AURKA, BIRC5 and PLK1 proteins show multiple regulatory transcription factors, highlighting E2F7, DRAP1 and ZNF511. The regulation of these protein is important to modulate the progression of cell cycle, cell proliferation, apoptosis and resistance to treatment.