

TOPIC

CANCER METABOLISM

AURKA, BIRC5 and PLK1 as potential biomarkers of response in radiation-resistant colorectal cancer

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Introduction

Today, there is a wide variety of treatment modalities available to combat colorectal cancer, in some cases depending on the molecular target they address. Focusing on radiotherapy treated tumors, patients are not free from recurrences where the cells that repopulate the tumor are more resistant to treatment. In fact, cells that increase the DNA repair mechanisms have a higher rate of radioresistance. Numerous mechanisms have been described that induce resistance to ionizing radiation in multiple tumor types. In colorectal cancer the mechanisms are related to: apoptosis, cell cycle, DNA damage repair, and the epithelial-mesenchymal transition.

Objectives

The objective of this study is the evaluation of the expression levels of the central genes AURKA, BIRC5 and PLK1 in patients with radiation resistant colorectal cancer, with the purpose of assessing their potential use as response markers.

Methods

Genes implicated in radiation resistance obtained after data mining in Pubmed were subjected to an In-Silico analysis to study the level of expression in multitude of patients. GEPIA website (<http://gepia.cancer-pku.cn/>) was used to analyze RNA sequencing expression data in tumor and normal tissue, based on thousands of patients from the GTEx projects and TCGA database. The hypergeometric statistical test was used with a p value adjusted to obtain the most enriched annotations.

Results

Data mining and the in-silico study showed that radiation resistant colorectal cancer hyper-expresses AURKA, BIRC5 and PLK1 proteins. To validate whether these core genes could be considered as potential biomarkers, the GEPIA website was used to analyse the expression levels in 1034 patients from the GTEx projects and TCGA database. The analysis of tumor samples from colon and rectum adenocarcinoma affected patients showed an overexpression of AURKA, BIRC5 and PLK1 proteins in relation to the expression level of normal tissues (p -value Cutoff: 0.01). Furthermore, the study of the expression levels of these genes in tumors in the different stages (I–IV) showed that the average levels observed were similar for the three genes in all stages, with no statistically significant differences being observed. These results highlight the importance of these genes/proteins in the object of study of this work. The results suggest that AURKA, BIRC5 and PLK1 could be considered as predictive biomarkers.

Conclusions

The study demonstrated that AURKA, BIRC5 and PLK1 proteins are over-expressed in patients affected by colon and rectum adenocarcinoma resistant to radiotherapy. The validation of the expression levels in patient samples shows that they are conserved in tumor stages I-IV, suggesting their potential as possible biomarkers.