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Association between gene and repair pathways activated often related to response of a neoadjuvant treatment in rectal cancer: a literary review using Cbio Portal and PubMed

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Resumo

Rectal cancer is defined as cancer located in the rectal tissue. The main treatment of this disease is based on combination of radiation treatment with 5-FU generates insults to the cancerous cells of the rectum. To survive this damage, such cells need to activate specific repair mechanisms. This study tries to demonstrate the relationship of these most commonly activated pathways with tumor resistance to treatment, identifying what are the most common ways of repair and the most frequently genes activated. A literature review was made consulting the database: Scielo, PubMed, LiLACS. In these sites, the following descriptors was used: "oncogenes", "rectal cancer", "neoadjuvant treatment" and "clinical outcome". Such terms were searched with the conjunction's "AND" and "OR" in both English and Portuguese with regards to the language of the works. we have arrived at results involving approximately 20 main genes involved in damage repair tissue of rectum adenocarcinoma cells, as we can mention APLF, APTX, ASCC3, DNTT, LIG1 amongst others, being the lives most often activated in relation of 20 genes analyzed to Missense Mutation , Deep Deletion and Amplification. In ending, such study demonstrates the relationship of these most commonly activated pathways with tumor resistance to treatment, relating these activated DNA trajectories with the clinical outcome of the patient, thus contributing to the relevance for future studies, therapies more specific and understanding of patients' prognosis in relation to rectal cancer.

1. Introduction

Rectal cancer is defined as cancer located in the rectal tissue. The diagnosis of rectal adenocarcinoma is made through the biopsy anatomopathological examination of the tumor lesion, which can be requested[1,2,3]. Surgical resection is the most effective therapy for rectal cancer. However, there are

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several surgical and pharmacological (non-surgical) approaches available that vary depending on the location, locoregional growth and presence of metastatic rectal tumor disease[2,3]. In this aspect, neoadjuvant therapy is one of the more relevant alternatives in terms of pharmacological therapy being 5-FU (5 - Fluorouracil) which is one of the commonly used drugs together with radiotherapy[3,4]. This combination of radiation treatment with 5-FU generates insults to the cancerous cells of the rectum[4,5]. To survive this damage, such cells need to activate specific repair mechanisms. This is done through genes associated with tissue repair and through known routes[4,5]. In this sense, when these mechanisms work properly without interference, malignant cells can survive causing the tumor to persist in the patient in the final analysis[4,5]. Furthermore, other oncological cells that cannot repair the damage end up dying generating a better prognosis and more chances of survival of the patient[6]. In this article , our purpose was identify what are the most common routes associated with this process of repair and what are the most genes associated too.

2. Methods

A literature review was made consulting the database: Scielo, PubMed, LiLACS. In these sites, the following descriptors was used: "oncogenes", "rectal cancer", "neoadjuvant treatment" and "clinical outcome". Such terms were searched with the conjunction's "AND" and "OR" in both English and Portuguese with regards to the language of the works. The selection of 15 works used as theoretical reference for the development of this article taking into account the following inclusion criteria: works published in the last 5 years, works with more than 50 citations and with direct link to the theme, works with research methodology with a high level of evidence as meta-analysis and systematic review. As an addendum, works that did not meet the inclusion criteria of description, addressed other topics not related to this project or other types of cancer that were not the adenocarcinoma of the rectum were rejected. These 15 articles was detailed with CbioPortal, a platform that shows with more details the results of this studies such as graphics , tables, and frequency of genes activation.

3. Results

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The most relevant results can be summarized in the following tables which the data was extracted in these 15 works:

Table 1: Qualitative description of the main oncogenes and the most frequently routes activated.

Main genes involved in repairing tissue cells of adenocarcinoma cells	
APLF	PARG
APTX	PARP1
ASCC3	PARP3
DNTT	PARPBP
LIG1	PNKP
LIG3	POLB

Table 2: Description of the main pathways related to tissue repair studied in this work.

12 main routes related to tissue repair studied in this work	
Inframe mutation	Truncating mutation
Putative driver	Truncating mutation unknown
Missense mutation	Structural variant
Missense mutation unknown	Structural variant unknown
Splice mutation	Amplification
Splice mutation unknown	Deep deletion

Afterwards, we have arrived at results involving approximately 20 main genes involved in damage repair tissue of rectum adenocarcinoma cells, as we can mention APLF, APTX, ASCC3, DNTT, LIG1 amongst others, being the lives most often activated in relation of 20 genes analyzed to Missense Mutation, Deep Deletion and Amplification. Nevertheless, there is no pattern of pathway activation sequence, and it has been shown in all the oncogenes found there are regions that do not activate the repair pathways

4. Discussion

Rectal cervical cancer is a cancer with location in the rectal tissue, which rectal adenocarcinoma is diagnosed by anatomopathological examination with biopsy of the tumor lesion, making surgical resection the most effective therapy for this type of cancer[1,2,3,4,5,6,7]. Furthermore, there are still numerous existing surgical and pharmacological approaches depending on the type of cancer, location and the presence

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of metastases. In this case, therapy neoadjuvant with 5-FU (5-fluoroucacil) becomes widely used in combination with radiotherapy, which in this form, corroborates the aggression to the cancer cells of the rectum, making them activate specific repair mechanisms, through the repair gene tissue, and if working properly such cells become persistent to treatment[7,8,9,10]. Otherwise, when cancer cells are unable to repair the damage suffered, such cells suffer from cell death, resulting in better prognosis of the patient's survival, demonstrating the responsiveness to damage caused by the combination of pharmacological therapy and radiotherapy[11,12,13,14]. Therefore, such an article used secure sources such as the platform CbioPortal and PubMed to inquire about the protein synthesis of carcinogenic DNA repair genes more constantly related to the genes activated in rectal cancers, such as rectal adenocarcinoma, in which has the most incident[15,16].

5. **Final Considerations**:

In ending, such study demonstrates the relationship of these most commonly activated pathways with tumor resistance to treatment, relating these activated DNA trajectories with the clinical outcome of the patient, thus contributing to the relevance for future studies, therapies more specific and understanding of patients' prognosis in relation to rectal cancer.

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