Journal of Clinical Oncology and Therapeutics

Short Communication

DOI: https://doi.org/10.47275/2690-5663-137
Volume 6 Issue 2

The Role of Leukocyte Immunoglobulin Receptor B2 Overexpression as a Novel Biomarker and Potential Therapeutic Agent for Colorectal Cancer

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Abstract

There is an urgent need to identify screening markers and precise therapeutic targets for colorectal cancer (CRC), which has become the third most deadly malignancy in the world. In the past few decades, the medical field has implemented multiple levels of CRC screening tests, including fecal tests, endoscopic examinations, radiological examinations, and blood tests. Acute myeloid leukemia and non-small cell lung cancer have previously been shown to exhibit leukocyte immunoglobulin-like receptor B2 (LILRB2)-mediated immune evasion and tumor progression. CRC was identified as a characteristic protein by several researchers upon their research by LILRB2, but there is no clear relationship between LILRB2 expression and clinicopathological characteristics, internal mechanisms underlying CRC progression, or screening diagnostic effectiveness. Our hypothesis was that LILRB2 is highly expressed in CRC tissues, correlates with advanced stages and poor prognoses, and could be used as a screening biomarker and a therapeutic target. Despite this, there is still room for discussion regarding this research's data processing and analysis.

Keywords: Biomarker, Colorectal cancer, Leukocyte immunoglobulin receptor B2, Angiopoietin-like protein 2, Therapeutic agent, Biomarker

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Citation: Satwika C, Shetty A, Ravela GC (2024) The Role of Leukocyte Immunoglobulin Receptor B2 Overexpression as a Novel Biomarker and Potential Therapeutic Agent for Colorectal Cancer. J Clin Oncol Ther, Volume 6:2. 137. DOI: https://doi.org/10.47275/2690-5663-137

Received: September 06, 2024; **Accepted:** December 02, 2024; **Published:** December 04, 2024

Introduction

According to the most recent global cancer statistics, CRC has become the third most common malignant tumor in the world. The disease has a high incidence rate, a poor prognosis at advanced stages, and ranks second in cancer-related deaths. The implementation of population-based CRC screening, such as fecal occult blood tests and endoscopy, has, however, significantly improved overall survival rates and enhanced prospects for cures. Several researchers like Mani et al. [1] have written an excellent case-control study that we have carefully read [1]. To begin with, this study discusses the worldwide incidence of CRC, its prognosis, and the challenges associated with currently available treatments. As a result of previous proteomic investigations, the team discovered the LILRB2 protein. It is proposed that LILRB2 could be used as a biomarker for CRC as well as a therapeutic agent. A substantial number of patients with CRC who had undergone curative surgery were collected as part of the experimental section [2]. Serological tests, immunohistochemistry, enzyme-linked immunosorbent assays, and other experimental approaches were used to compare LILRB2 expression levels across different populations. A comparison was also made between this tumor marker and traditional tumor markers in terms of detection [3]. Finally, the study summarizes the results of the experiments and makes recommendations for future research. For mutual validation, flow cytometry analysis was used in conjunction with traditional immunohistochemical staining methods. In this way, the findings of the experiment are effectively confirmed [4]. In addition, the researchers used gene platforms for online analysis of differentially expressed genes and mRNAs between normal and cancer tissues, which added to the protein-level experiments. Using tissue from the CRC and tissues adjacent to the CRC, the researchers compared the levels of expression of the LILRB2 protein [5]. Additionally, they examined the correlation between LILRB2 mRNA expression and angiopoietin-like protein 2 (ANGPTL2) mRNA expression in CRC tissues, as well as the correlation between LILRB2 protein expression and ANGPTL2 protein expression. A comparison was also made between LILRB2 and traditional tumor markers using serum samples. Congratulations on the compelling findings of the research team [6]. LILRB2 and its ligand ANGPTL2 were examined in detail for their role in the occurrence and development of CRC. In terms of this article, there are a few questions that require further consideration. Between 2021 and 2023,in a study the researchers collected 324 serum samples. CRC patients provided 132 preoperative serum samples, 91 postoperative serum samples, 87 adenoma patients provided 87 serum samples, and 14 healthy controls provided 14 serum samples. Following this, the researchers compared serum LILRB2 concentrations among patients with CRC, patients with adenoma, and healthy controls. They found statistically significant differences in LILRB2 concentrations between these three groups. Although the number of serum samples from CRC patients (197 samples) and health controls (15 samples) differ significantly, we would like to draw your attention to this disparity. The results of this research may be biased due to potential data bias [7]. Furthermore, patients with normal colonoscopy may be included in the health control group

based on too broad criteria. To establish detailed inclusion criteria for healthy controls, we believe it is necessary to define detailed criteria. Research findings in this article suggest that LILRB2 mRNA expression in CRC patients is not correlated with overall survival or progression-free survival. However, overexpression of the LILRB2 protein is significantly associated with reduced overall survival in CRC patients, suggesting that the LILRB2 protein plays a pro-cancer role [8]. A deeper understanding of the mechanisms behind these findings would be gained by further in-depth studies. We noticed that no mention is made in the article regarding baseline data processing for the participants. The omission raises concerns about the potential introduction of bias into the research results, which may impact on the truthfulness and validity of the findings [9-11].

LILRB2 has primarily been studied in relation to hematopoietic stem cells and bone marrow immune cells. CRC has received less attention in previous studies. In these cells, LILRB2 is associated with inflammatory responses and cell proliferation processed. AML, CLL, esophageal cancer, pancreatic cancer, non-small cell lung cancer, and breast cancer are also enriched for LILRB2. Since elevated serum levels of LILRB2 can be found in various solid tumor types, LILRB2 cannot be considered a specific tumor marker for CRC. Therefore, we understand that LILRB2 protein was significantly overexpressed in cancer tissues compared to paracancerous tissues [12]. As the ligand of LILRB2, ANGPTL2 was synergistically overexpressed in CRC tissues, and the overexpression of these proteins was related to poor differentiation, vascular involvement, lymph node metastasis, distant metastasis, advanced tumor-node-metastasis stage and poor prognosis, suggesting that LILRB2 and ANGPTL2 are closely linked to the progression of CRC [13].

LILRB2

CRC is the third most common malignant tumor in the world, according to the latest global cancer statistics. CRC screening tests have evolved in recent decades to include fecal tests, endoscopic examinations, radiological examinations, and blood tests. There is evidence that LILRB2 suppresses immune cell function and immune evasion, as well as promotes tumor progression in acute myeloid leukemia and non-small cell lung cancer [14]. The interaction between this compound and CRC is, however, unknown. ANGPTL2 and LILRB2 are markedly overexpressed in CRC, according to a study published in the World Journal of Gastroenterology. An overexpression of this gene is closely linked to tumor progression and is associated with poor prognoses. A promising biomarker for tumors could be derived from the level of LILRB2 in serum, according to the study [15]. However, there is still room for discussion regarding this research's data processing and analysis (Figure 1).

Flow cytometry analysis was combined with immunohistochemical staining methods in this study to validate the results obtained from both approaches. Experimental findings are effectively confirmed by this approach. Additionally, the researchers used gene platforms to identify genes or mRNAs that were differentially expressed between normal and cancer tissues to complement protein-level experiments [2, 16]. A comparison was made between LILRB2 expression levels in CRC tissues and adjacent tissues. The researchers also examined the correlation between LILRB2 mRNA expression and ANGPTL2 mRNA expression in CRC tissues, as well as the correlation between LILRB2 protein expression and ANGPTL2 protein expression. LILRB2 was also compared to traditional tumor markers (carcinoembryonic antigen and carbohydrate antigen 199) using serum samples.

Our congratulations go out to the research team and several authors for their compelling findings. Their study investigated the expression changes of the LILRB2 protein and its ligand ANGPTL2 in colorectal tumor occurrence and development. There are, however, some questions about this article that need further consideration by the researchers [17].

During the period of 2021 to 2023, 346 serum samples were collected by the researchers. Serum samples from CRC patients were 126, postoperative serum samples were 97, adenoma patients were 99, and healthy controls were 24. The researchers compared the serum LILRB2 concentrations of CRC patients, adenomas, and health controls, and found statistically significant differences among these groups [18]. CRC patients and health controls have significantly different numbers of serum samples, which we would like to point out. The results of the research are therefore likely to be skewed by potential data bias. Furthermore, patients with normal colonoscopy findings may be included in the healthy control group with too broad criteria [3, 19]. The health control group should have detailed inclusion criteria. According to the findings in this article, LILRB2 mRNA expression does not appear to be associated with overall survival or progression-free survival in patients with CRC. LILRB2 overexpression is significantly associated with a reduced overall survival, suggesting that the LILRB2 protein plays a pro-cancer role in CRC progression and indicates a poor prognosis for CRC patients [4, 20]. A deeper understanding of these intriguing findings requires further in-depth studies. Based on our review of the research results in the article, we found no mention of baseline data processing for participants' data. Due to this omission, bias may be introduced into the research results, diminishing the reliability and validity of the results and the accuracy of the assessment. Previously, LILRB2 has mainly been studied in relation to hematopoietic stem cells and bone marrow immune cells, with little focus on CRC. Cell proliferation and inflammation are regulated by LILRB2 in these cells. The enrichment of LILRB2 has also been observed in several malignant tumors, such as acute myeloid leukemia, chronic lymphocytic leukemia, esophageal cancer, pancreatic cancer, non-small cell lung cancer, and breast cancer [21]. Because elevated serum levels of LILRB2 can occur in various solid tumors, it is premature to consider LILRB2 as a specific CRC tumor marker. LILRB2 mRNA and protein expression differentially affect CRC prognosis. A phase I clinical trial for LILRB2 inhibitors is currently underway, and further studies are needed to determine their efficacy [22]. The results of this study provide preliminary evidence supporting the potential of LILRB2 as a new Therapeutic agent as well as a biomarker for noninvasive screening in CRC. The implications of this discovery are particularly beneficial for clinical practitioners, as it will enable them to screen for CRC early, to treat it precisely, and to estimate its prognosis accurately [23].

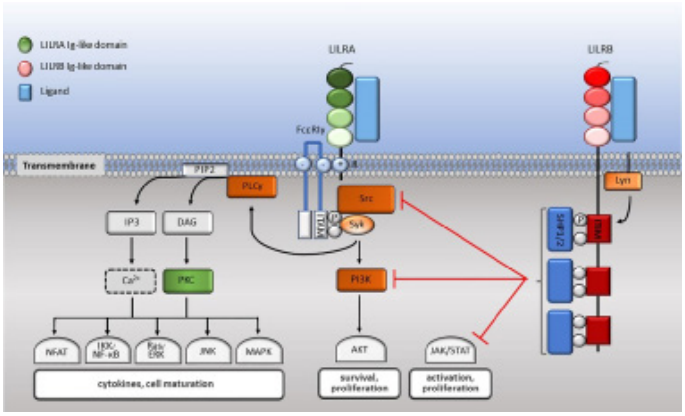

Figure 1: LILR signalling pathways [15].

Conclusion

CRC tissues express high levels of the LILRB2 protein, and high levels of LILRB2 protein expression are significantly associated with tumor progression and poor outcome. There is a synergistic interaction between the LILRB2 receptor and the ANGPTL2 ligand that is related to the development of CRC. LILRB2 concentrations in serum demonstrated greater diagnostic efficacy than traditional markers, suggesting that it could be used as an innovative screening tool for CRC. As a potential therapeutic target and noninvasive screening biomarker, LILRB2 protein could be helpful for early screening and precise treatment, as well as for the development of new therapeutic strategies against CRC.

Acknowledgements

None.

Conflict of Interest

None.

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