

## Cross-Link Axis, Levels of IL-6/TGF and MicroRNA 146a/215 Indicate a Link between Obesity and Colorectal Cancer

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### Abstract

Obese people are more likely to develop a variety of cancers, including colorectal and liver cancers, and chronic inflammatory conditions have been linked to this association. In a cross-link axis between obesity and colorectal cancer (CRC), we are attempting to determine the clinical relevance of the mechanisms controlling the expression of microRNAs (miR-215 and miR-146a) and transforming growth factor (TGF)/interleukin-6 (IL-6). The participants in the study were split into four groups: wholesome controls; without colorectal cancer, obese; non-obese colorectal cancer; and overweight with colon cancer. Cancer biomarkers like carcinoembryonic antigen (CEA), carbohydrate antigen 19.9 (CA19.9), and alpha-fetoprotein (AFP) levels were significantly higher in obese and CRC patients. In obese colorectal cancer patients, the relative expression of the microRNAs miR-215 and miR-146a was significantly lower. The correlation between BMI and the microRNAs miR-215 and miR-146a was significant and negative. TGF- had a positive effect on IL-6, cholesterol, triglyceride levels, and body mass index (BMI). High blood levels of TGF- and IL-6 indicate how intensely obesity-related inflammation develops, which may raise the risk of colorectal cancer.

**Keywords:** Obesity; Colorectal cancer; TGF- $\beta$

### Introduction

Obesity and overweight which are now public health issues and nutritional disorders are two conditions that can be exacerbated by a diet that is high in energy and low in nutrients as well as a lack of physical activity. A chronic inflammatory state has been linked to obesity, which is a key characteristic of metabolic syndrome. Obesity is considered an independent risk factor for cancer in general and CRC in particular, contributing to a higher mortality rate for these diseases [1]. Obesity promotes CRC carcinogenesis through complex pathways. In obese individuals, excessive macronutrients increase the release of inflammatory adipokines and transforming growth factor (TGF-  $\beta$ ), which leads to chronic inflammation. The cytokine IL-6, which is pro-inflammatory, both controls inflammatory responses and promotes inflammation [2]. Higher IL-6 serum levels were found in obese patients with chronic inflammatory diseases and abnormal blood lipid concentrations, which may increase their risk of cardiovascular disease and cancer.

TGF- is a cytokine that is present in high concentrations at the site of an ongoing inflammatory response and regulates tissue growth and homeostasis. TGF- levels that are high in the initial colorectal tumor are linked to advanced CRC stages. These stages encourage tumor growth in the later stages of colorectal carcinogenesis. Despite significant advancements in CRC diagnosis and treatment, individuals with distant metastases beginning with metastasis still have poor prognoses [3,4]. As a result, the identification of CRC cancer growth and metastasis necessitates the development of novel biomarkers.

### Literature Review

Among the many miRNAs that have the potential to regulate the immune system, miR-146a and miR-215 have emerged as significant immune response regulators. MiR-146a/215 is multifunctional miRNAs whose absence causes inflammatory adipokines to be produced excessively and inflammatory diseases. The significance of microRNA 146a/215 and IL-6/TGF- levels in relation to obesity and colorectal cancer is the focus of this investigation. In addition, the study tries to figure out if the expression of miR-146a and miR-215 in the serum of obese and CRC patients suggest that they could be used to

diagnose CRC earlier in obese patients [5,6].

Obesity is thought to be a global health problem because obesity causes inflammation during certain stages of colorectal cancer development. It is important to note that effective preventative measures and intervention tools that can lower the disease's rising incidence and co-morbidities require an understanding of the pathophysiology of obesity. The purpose of this study was to investigate the cross-link axis between obesity and colorectal cancer and the levels of IL-6/TGF- $\beta$ .

Concerning the relative expression of miR-146a, recent research has shown that miR-146a plays a crucial role in the prognosis of cancer (prostate, colorectal, lung, hepatocellular carcinoma, and breast cancer). This suggests that miR-146a is a therapeutic target and a potential biomarker.

### Discussion

IL-6 and TGF-  $\beta$  levels were strongly correlated with BMI, cholesterol, and triglyceride levels. In addition, significant increases in IL-6 expression levels have been observed in obese and CRC patients in previous studies. Chronic inflammation and release from adipose tissue may be associated with elevated IL-6 expression. Ovarian cancer patients had significantly higher plasma levels of IL6 and TGF-1. In addition, our findings were consistent with those of who assert that TGF-  $\beta$  is a fundamental regulator of all stages of disease progression, including early liver injury, cirrhosis, and hepatocellular carcinoma via inflammation and fibrosis [7]. According to recent studies, sustained

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TGF-  $\beta$  expression in obesity is mostly linked to the advanced stages of inflammation and is considered to be a risk factor for significant disorders. In addition, the high expression of tumor markers (CEA and CA19.9) in CRC patients confirmed the role of elevated IL-6 protein levels in CRC. Additionally, elevated IL-6 serum levels significantly increase the likelihood of developing CRC. In addition, it has been demonstrated that IL-6 promotes the development of numerous cancers, including CRC, by supporting chronic inflammation. Due to elevated levels of circulating proinflammatory cytokines like IL-6, obese individuals may ultimately be more likely to develop and advance CRC. Hepatocellular cancer also had significant IL-6 and TGF-  $\beta$  expression. The adaptable substances IL-6 and TGF-  $\beta$  can be utilized to fine-tune transcriptional epigenetic regulation processes. It was discovered that these cytokines associated with inflammation interact strongly and have a positive correlation with cellular invasion, EMT and resistance [8].

## Conclusion

The investigation study found that miR-146a and miR-215 have the potential to be used as diagnostic biomarkers. The study also emphasized the significant relationship between TGF-/IL-6 expression and miR146a/miR215 expression in CRC and obesity.

## Acknowledgement

None

## Conflict of Interest

None

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