ISSN 2582-788X REVIEW ARTICLE

INTERNATIONAL JOURNAL OF
APPLIED CHEMICAL AND BIOLOGICAL SCIENCES

# Interlinkage among DNA methylation, obesity and colorectal cancer

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**ABSTRACT**

Many kinds of epigenetic methods like DNA methylation affect the weight and cause obesity, which is a high risk factor of colorectal cancer. To find the association between obesity and CRC and DNA methylation we studied CRC patients and obese, concentrating on genome-wide DNA methylation changes. Consequences exhibited unequal distributions of overlapping distinct methylated regions like hyper methylated CpG islands that can be responsible for epigenetic instability causing cancer to start in obese patients. In addition, functional investigation proposes that DNA methylation alterations of extracellular components like o-glycan processing and intracellular components play a role for activation of cancer causing genes like KRAS and SCL2A1 and repression of tumor suppressors like ARHGEF4, EPHB2 and SOCS3 causing an increase in ability of oncogenes to cause cancer. Our study suggests that how in obesity DNA methylation occurs and takes part in development of colorectal cancer, giving direct evidence of relationship between CRC and obesity. It also shows using DNA methylation as diagnostic marker and early risk evaluation to detect patients with high risk for CRC.

**Keywords:** DNA Methylation, Colorectal Cancer, Obesity.

## 1. INTRODUCTION

Colorectal cancer is the most common type of cancer of alimentary canal [1]. Obesity is one of the risk factors for colorectal cancer [2]. When abnormal fat is accumulated in body, it leads to development of many disorders such as diabetes, liver diseases and hypertension [3]. The incidence of colorectal cancer is increasing day by day and it is most common third type of cancer that affects males. In females it is second most common type of cancer [4]. Diet, gender, immune system of host, exposure to microbes and environment are the main factors that can influence colorectal cancer [5]. Recent studies have shown that obesity has an association with the risk of colorectal cancer [6-7]. It is proved from recent studies that body mass index has a direct relation with the increased risk of colorectal cancer [8-9]. According to statistical studies, risk of colorectal cancer increases up to three folds with one fold increase in BMI [10-11]. Another major risk for colorectal cancer is type 2 diabetes [12].

In particular, CRC-related mortality is expanding quickly in some low and center pay nations. Moreover, the rate of CRC is anticipated to keep on expanding, particularly in creating areas because of changing socioeconomics and maturing populaces. When looking at the CRC rate rates somewhere in the range of 1988 and 2007 of every eight areas around the world, it is clear that this increment is wonderful in both creating and created nations besides in America [13-14].

## 2. OBESITY & COLORECTAL CANCER

According to Rudolf Virchow there is a link between colorectal cancer and inflammation [15]. People with inflammatory diseases are at more risk for developing colorectal cancer [16]. Obese patients have adipose tissues that are chronically impaired and release inflammatory mediators that contribute to tumor growth [17]. Among all contemplated epigenetic biomarkers, DNA methylation is the most often inspected in different malignancies, counting Colorectal cancer [18]

Obesity is identified with energy unevenness and metabolic dysfunction. Administrative related protein of mTOR (RPTOR) is engaged with the control of mTORC1 action, which assumes a significant part in lipogenesis and in directing the endothelial cell multiplication [19-20].

In spite of the solid epidemiological information on the association among corpulence and the expanded danger of CRC, fundamental systems interfacing corpulence to CRC pre-fundamental is unclear. Corpulence and metabolic condition are interrelated conditions that share a few pathophysiological components that seem to go with each other. Hence, the significance of obesity in essence as an free supporter of cardiometabolic messes, irrespective of weight actuated metabolic unsettling influences, is still questionable. A subset of corpulent people doesn't display corpulence related metabolic disturbances like insulin obstruction, hyperglycemia, dyslipidemia, and high blood pressure (BP), regardless of inordinate muscle to fat ratio accumulation. This populace is alluded to as having MHO). Thus far, significant proof has shown that patients with MHO have a lower mortality and lower danger of CVD than those with "metabolically unfortunate obesity (MUO)," and they don't have a higher danger of CVD than those with typical weight [21].

Many cohort studies [22-23] and case control studies [24] have shown a direct link of obesity and colon cancer risk. A case control study in Canada showed that there is 60 percent higher risk of colorectal cancer in men who gain 21kg weight after the age of 20 years than those who gain only 1 to 5 kg weight [25].

The prognostic estimation of MHO faces a considerable test, and the worth may depend on the pre-owned wellbeing outcomes. Studies have detailed clashing outcomes regarding the danger of CRC in patients with MHO; nonetheless, expanded danger of CRC has been altogether related with MUO. Hence, it is muddled whether heftiness plays a job in the improvement of CRC, autonomous of obesity related metabolic aggravations [26-27].

## 3. WEIGHT REDUCTION IN PATIENTS WITH OBESITY & COLORECTAL CANCER

Fewer studies have shown association of weight reduction with lower risk of colorectal cancer. These studies proved that weight loss through bariatric surgery leads to 29 to 60 % reduction of cancer related mortality risk [28]

## 4. METHYLATION & COLORECTAL CANCER

Genome-wide planning of differentially methylated CpG destinations or differentially methylated locales is a significant way to uncover the effect of epigenetic modifications on inheritable phenotypic variety in both weight and CRC and to comprehend their relationship [29]. As of now, a huge effort is aimed at giving better knowledge into tissue-specific epigenetic variations and their parts in illness advancement [30].

CRC stays the subsequent driving reason for disease related passing in the United States. The 5-year relative endurance rate for beginning phase CRC is 90%; for cutting edge stage IV CRC, the rate drops to about 11%. Be that as it may, just around 4 out of 10 CRCs are found at the early stages, in part because of the helpless patient acknowledgment or potentially affectability of accessible screening modalities [31]. Blood-based DNA methylation has incredible potential as an early, precise, non-intrusive biomarker for hazard assessment and early discovery to improve the endurance rate for CRC patients. Stoutness is a complex jumble that adds to numerous human infections [32].

Being obese is viewed as a significant danger factor for some malignant growths, specifically colorectal cancer. Epidemiological information proposes that obesity is related with a 1.2–2.0 crease expanded risk of colorectal cancer [33]. Despite these facts, the nearby connection among corpulence and the danger of CRC has been proposed by an enormous number of studies [34].

## 5. POTENTIAL MECHANISM FOR ASSOCIATION BETWEEN OBESITY AND COLORECTAL CANCER

5.1. *Elevated levels of insulin*:

Weight, especially stomach corpulence is related with insulin opposition, a state when insulin is less viable than ordinary in bringing down blood glucose levels. As an outcome, more insulin is delivered to the blood, bringing about constantly expanded insulin levels, which has been conjectured to be a logical connection among corpulence and colorectal disease hazard. Insulin may increment colorectal malignancy hazard by either direct mitogenic impacts or by expanding the bioavailability of the powerful mitogen insulin-like growth factor 1 [35].

5.2. *Constant inflammation*:

Inflammation has been speculated to play a significant job in carcinogenesis, especially for colorectal disease [36]. This is upheld by considers which have shown that people with ongoing incendiary entrail infection have a higher danger of colorectal malignant growth contrasted with the typical populace [37].

5.3. *Hypoadiponectinemia:*

Adiponectin is a hormone that is derived from adipose tissue [38]. This hormone has an inverse relation with body weight and other diseases like insulin resistance and cardiovascular diseases [39]. Studies have shown that this hormone is inversely related with cancer growth especially colorectal cancer. This hormone does so by the use of direct mechanisms for example inhibiting cancer cell growth [40] and promoting apoptosis [41]. It inhibits cancer proliferation indirectly through glucose metabolism pathways and insulin resistance [42-43]. Risk of colorectal cancer is 60 percent reduced in the individuals of highest adiponectin quantile independent of body mass index [44].

## 6. FUTURE PERSPECTIVE

A few expansive conclusions rise up out of the present status of information with regard to obesity and colorectal malignant growth. The first Is that an

assortment of individual dietary segments over which consumers have a few proportion of control do appear to impact the danger of colon malignant growth, yet to a moderately unassuming degree. Numerous of the examinations checked on here contained discoveries that suggest that huge danger factors for colon disease do not have any significant bearing to rectal disease; this overall perception is by all accounts affirmed by the couple of studies that have tended to the issue straightforwardly.

## 7. CONCLUSION

Our investigation illustrates how DNA methylation changes in corpulence add to CRC advancement, giving direct proof of a relationship among obesity, DNA methylation and CRC. It additionally uncovers the symptomatic capability of utilizing DNA methylation as an early danger assessment to identify patients with high danger for CRC.

## 8. ACKNOWLEDGEMENT

NA.

## 9. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

## 10. SOURCE/S OF FUNDING

No source of funding.

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