



## Review

# Epigenetic basis of cancer health disparities: Looking beyond genetic differences



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## ABSTRACT

Despite efforts at various levels, racial health disparities still exist in cancer patients. These inequalities in incidence and/or clinical outcome can only be explained by a multitude of factors, with genetic basis being one of them. Several investigations have provided convincing evidence to support epigenetic regulation of cancer-associated genes, which results in the differential transcriptome and proteome, and may be linked to a pre-disposition of individuals of certain race/ethnicity to early or more aggressive cancers. Recent technological advancements and the ability to quickly analyze whole genome have aided in these efforts, and owing to their relatively easy detection, methylation events are much well-characterized, than the acetylation events, across human populations. The early trend of investigating a pre-determined set of genes for differential epigenetic regulation is paving way for more unbiased screening. This review summarizes our current understanding of the epigenetic events that have been tied to the racial differences in cancer incidence and mortality. A better understanding of the epigenetics of racial diversity holds promise for the design and execution of novel strategies targeting the human epigenome for reducing the disparity gaps.

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## 1. Introduction

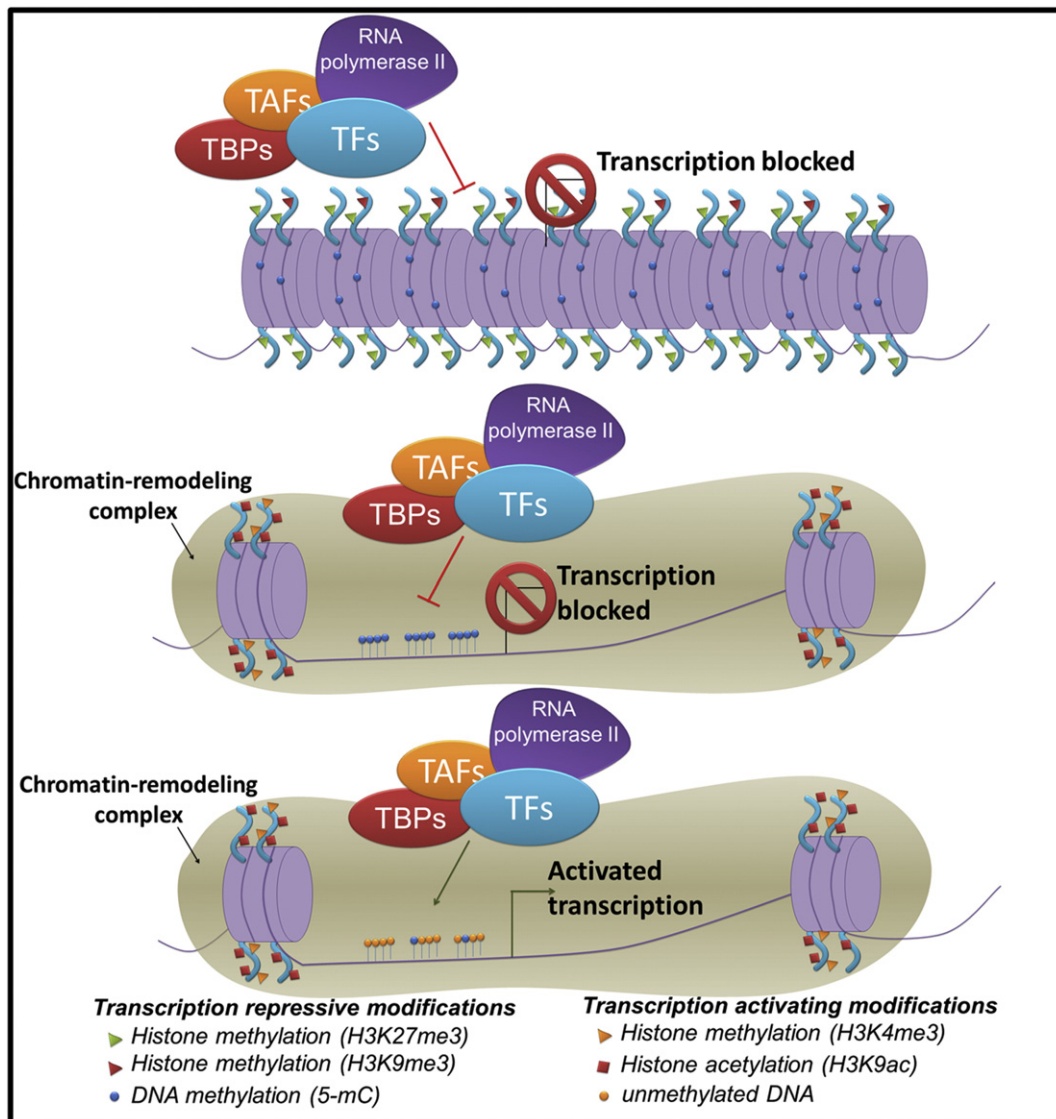
Health disparities in cancer patients of different racial and ethnic backgrounds have attracted a lot of attention in recent years. Because of the increased awareness and scrutiny, some progress has been made but there is irrefutable evidence to support that racial health disparities still exist in a vast majority of cancer patients [1–4]. When discussing racial cancer health disparities, black patients, most frequently African Americans (AA), are the most common racial group compared to the Caucasian Americans (CA) or white population of European heritage, referred as European Americans. Data on races other than AA and CA, such as Hispanics and Native Americans, is emerging, and points to existence of racial cancer health disparities in these groups as well [5]. Besides racial disparities in cancer incidence and overall clinical outcome, there is incongruence in diagnosis at the initial presentation and the time between the diagnosis and initiation of treatment as well [6,7]. Even the low participation of minorities in clinical studies is a point of concern [8]. While there are studies that suggest narrowing cancer health disparities between different populations because of concerted efforts of health and local authorities [9], there is still

overwhelming data to support existence of racial disparities across almost all human cancers [10–14].

In addition to the non-biological factors (such as socioeconomic, cultural, etc.), biological factors are also believed to play important roles in cancer health disparities [15–18]. Recent data has connected inherent genetic differences, such as those resulting in increased tumor heterogeneity in AA breast cancer patients, with more aggressive tumor biology [19]. AA breast cancer patients have substantially poorer outcomes if they present with a hormone receptor-positive, HER-2 (human epidermal growth factor receptor-2)-negative or the triple negative phenotype [20]. While the genetic basis of disparity is being actively pursued [17,21], recent findings provide strong suggestion for an epigenetic basis of racial health disparities in cancer, which is discussed in the following sections.

## 2. Epigenetics in cancer health disparities

Epigenetics is the study of changes in gene expression that are heritable and caused by events other than the change in DNA/gene sequence [22] (Fig. 1). Epigenetic events have largely been identified as



**Fig. 1.** Epigenetic events. Epigenetic events such as methylation and acetylation have profound effect on the transcription of individual genes. These events serve as 'ON'/'OFF' switches for transcription of genes and the eventual expression of gene products. While generally tightly regulated in 'normal' cells, these epigenetic changes are altered in cancer cells to favor proliferation, anti-apoptotic and pro-metastatic functions. The evidence suggesting a role of epigenetic events in cancer racial disparity is emerging, and more detailed studies are needed to fully understand the complex role of epigenetic events in cancer health disparities.

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