Conference Abstracts

Methylome-Wide Profiling of Early-Onset Colorectal Cancer in Underrepresented Populations

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Background

Early onset colorectal cancer (EOCRC) or colorectal cancer in patients under the age of 50 is now the second most common cancer and the third leading cause of cancer mortality in people <50 years of age in the USA. Notably, Blacks and Hispanics are disproportionately affected. It has been proposed that environmental exposures including westernized diet, metabolic factors, and the microbiome might be responsible for the rise in incidence of EOCRC. Epigenetic modifications including DNA methylation are well-known mechanisms by which the environment can modulate gene expression without changing the DNA sequence. Unfortunately, little is known about the role of DNA methylation in EOCRC and much less is understood of EOCRC in minority populations.

Methods

Therefore, we identified a unique cohort of Hispanic and Black patients with sporadic EOCRC within the Harris Health System. Using whole-genome bisulfite sequencing, we comprehensively characterized the DNA methylome at single-base resolution in our EOCRC patient samples.

Results

Our analyses revealed distinct EOCRC methylation patterns, including both global hypomethylation and promoter-specific hypermethylation, which were not previously captured in The Cancer Genome Atlas (TCGA) Analyses. Furthermore, we identify epigenetic alterations in metabolic genes that are specific to our racial minority EOCRC cohort but not Caucasian patients from TCGA. Top genes differentially methylated between these cohorts included the obesity-protective MFAP2 gene as well as cancer risk susceptibility genes APOL3 and RNASEL. We show the epigenetic landscape of our EOCRC patients differs from that of late-onset colorectal cancer patients, and methylation canyons in EOCRC tumor tissue preferentially overlapped genes in cancer-related pathways.

Conclusion

We are the first group to take this comprehensive unbiased approach to analyze the methylome in an underrepresented EOCRC cohort of patients. Our exploratory findings highlight epigenetic mechanisms underlying the pathogenesis of EOCRC and nominate novel biomarkers for EOCRC in underrepresented populations.