DNA methylation signatures linked to different grades of prostate tumors from African American and European American patients

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Background: Prostate cancer is the second leading cause of cancer-related deaths among men in the United States. Health disparities in men diagnosed with prostate cancer are observed between patients of African and those of European ancestry. To develop biomarkers and elucidate the molecular mechanisms behind prostate tumorigenesis and racial disparities, we collected prostate tumor tissues from African American (AA) and European American (EA) patients.

Methods: By comparing global DNA methylation profiles among normal samples and different grades of tumor samples from AA and EA, we revealed distinct prostate cancer subgroups with variable DNA methylated regions.

Results: We identified thousands of differentially methylated regions between normal and tumor samples, defining hypermethylated and hypomethylated regions. When we examined the frequency of differentially methylated regions among different grades of tumor samples. We found that low-grade tumor samples exhibited fewer hypermethylated regions while high-grade tumors exhibited numerous hypermethylated regions across AA and EA samples. On the contrary, we found that a subset of low-grade tumors exhibited more hypomethylated regions like high-grade tumors. By clustering prostate tumor samples with the identified differentially methylated regions, we revealed distinct prostate cancer subgroups with unique DNA methylation patterns. By integrating immunohistochemistry data with DNA methylation profiles, we found that the identified subgroups are tightly linked to the overexpression status of ERG, surpassing the ethnicity-related variations. Associating DNA methylation patterns with clinicopathological features and integrating this data with other molecular features, we are characterizing the molecular mechanisms underlying prostate tumorigenesis and health disparities.

Conclusions: This study will pave the way to identify novel DNA methylation biomarkers and therapeutic targets linked to different prostate cancer subgroups.

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