Integrative genomic analysis identifies ancestry-related expression quantitative trait loci on DNA polymerase β and supports the association of genetic ancestry with survival disparities in head and neck squamous cell carcinoma

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Résumé en anglais	BACKGROUND: African Americans with head and neck squamous cell carcinoma (HNSCC) have a lower survival rate than whites. This study investigated the functional importance of ancestry-informative single-nucleotide polymorphisms (SNPs) in HNSCC and also examined the effect of functionally important genetic elements on racial disparities in HNSCC survival. METHODS: Ancestry-informative SNPs, RNA sequencing, methylation, and copy number variation data for 316 oral cavity and laryngeal cancer patients were analyzed across 178 DNA repair genes. The results of expression quantitative trait locus (eQTL) analyses were also replicated with a Gene Expression Omnibus (GEO) data set. The effects of eQTLs on overall survival (OS) and disease-free survival (DFS) were evaluated. RESULTS: Five ancestry-related SNPs were identified as cis-eQTLs in the DNA polymerase β (POLB) gene (false discovery rate [FDR] < 0.01). The homozygous/heterozygous genotypes containing the African allele showed higher POLB expression than the homozygous white allele genotype (P < .001). A replication study using a GEO data set validated all 5 eQTLs and also showed a statistically significant difference in POLB expression based on genetic ancestry (P = .002). An association was observed between these eQTLs and OS (P < .037; FDR < 0.0363) as well as DFS (P = .018 to .0629; FDR < 0.079) for oral cavity and laryngeal cancer patients treated with platinum-based chemotherapy and/or radiotherapy. Genotypes containing the African allele were associated with poor OS/DFS in comparison with homozygous genotypes harboring the white allele. CONCLUSIONS: Analyses show that ancestry-related alleles could act as eQTLs in HNSCC and support the association of ancestry-related genetic factors with survival disparities in patients diagnosed with oral cavity and laryngeal cancer. Cancer 2017;123:849-60. © 2016 American Cancer Society.
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