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Transcriptomic Influences of Racial Disparities in Black Patients with Pancreatic Neuroendocrine Tumors

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BACKGROUND

There are known outcome disparities between Black and White patients with pancreatic neuroendocrine tumors (pNETs). Recently, Black patients were shown to have higher rates of lymph node metastasis in smaller tumors than White patients, indicating possible differences in tumor biology. Numerous prognostic gene expression differences between racial groups have been reported in other cancers, but no such analysis has been conducted in pNETs. This study evaluated pNET transcriptomes for differential expression that may be influencing racially disparate outcomes.

METHODS

Quality control of formalin-fixed, paraffin-embedded pNETs specimens and demarcation of cancer cells were performed by a board-certified pathologist before laser microdissection and RNA isolation. Sequencing was performed on an Illumina NextSeq550 at 30 million reads/sample. GRCh38 transcriptome alignments were performed using Salmon and differentially expressed genes (DEG's) determined using DESeq2. Significance was determined by FDR-adjusted p-value (q-value; qv) < 0.05 and log2 fold-change (log2FC) ≥ ±2. Gene set enrichment analysis was then performed using clusterProfiler and the Gene Ontology (GO) consortium gene sets. Ingenuity Pathway Analysis (IPA) was then conducted to determine regulator effect networks.

RESULTS

RNA sequencing was conducted on 14 and 16 grade and sex-matched primary pNETs from self-identified Black and White patients, respectively. Mean age was 51 for Black and 56 for White patients. 11/16 (69%) of White and 9/14 (64%) of Black patients were female. 8 Black patients and 8 White patients had grade 1 tumors, while 6 Black patients and 8 White patients had grade 2 tumors. Metastatic disease was present in 4 Black and 5 White patients. Using White patients as the reference level, 372 genes and 179 gene sets were significantly differentially expressed. Notably, among the top 10 differentially expressed biological processes were: angiogenesis/blood vessel and vasculature development (qv=1.34e-07, normalized enrichment score [NES]=1.89), positive regulation of cell migration and locomotion (qv=1.34e-07, NES=1.91), and humoral immune response (qv=9.8e-07, NES=-2.06). Among the top 5 regulator effect networks identified by IPA were: angiogenesis of lesion/cell movement of monocytes (consistency score [CS]=19.3), activation of blood cells (CS=18.9), and activation of cells (CS=17.9).

CONCLUSIONS

Numerous pathways related to blood vessel development and cellular migration, key elements of metastatic development, are significantly enriched in pNETs from Black patients. Additionally, pathways related to the immune response are downregulated in Black patients. These data indicate differences in tumor biology that may influence disparate outcomes reported in Black patients with pNETS. Additional samples and incorporation of genetic ancestry are necessary to validate these findings.

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