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Differences in the Mutation of DAXX, ATRX, and MENIN in Pancreatic Neuroendocrine Tumors from Black and White Patients

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BACKGROUND: Racial disparities in outcomes are known to exist in pancreatic neuroendocrine tumors (pNETs) but have historically been attributed to socioeconomic factors. However, recent studies of racial health disparities have uncovered numerous prognostic differences in the (epi)genetics of various cancers among ethnoracial groups. Such differences have been discovered in breast, prostate, colon, and endometrial cancer, but haven't been investigated in pNETs. The known prognostic epigenetic regulatory proteins DAXX, ATRX, and MENIN are commonly mutated in pNETs (59%, 25-85%, and 18-72% respectively). Most mutations alter the protein and are detectable by IHC. This research aimed to evaluate DAXX, ATRX, and MENIN between Black and White patients for differences in mutation frequency as determined by immunohistochemistry (IHC).

METHODS: Tissue microarrays (TMAs) containing resected primary well-differentiated pNETs from 40 White and 13 Black patients were stained with antibodies specific to DAXX, ATRX, or MENIN. Stains were evaluated by a pathologist as positive or negative based on published guidelines for each respective protein. Frequencies of positive and negative stains between Black and White patients were compared using Fisher's exact test.

RESULTS: 9/40 (23%) White and 2/13 Black patients (15%) were negative for DAXX expression (p=0.711;). 2/40 (5%) White and 1/13 (7%) Black patients were negative for ATRX expression (p=>0.999). 11/40 (28%) White and 0/13 Black patients were negative for MENIN expression (p=0.047; Table 1).

CONCLUSION: The significant difference in loss of MENIN in specimens from Black patients supports the hypothesis that differential epigenetic modulation may be occurring in pNETs arising in this population.

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Table 1.

Stain	Black (13)	White (40)	P-Value
DAXX Negative	2/13 (15%)	9/40 (23%)	0.711
ATRX Negative	1/13 (7%)	2/40 (5%)	>0.999
MENIN Negative	0/13 (0%)	11/40 (28%)	**0.047***