THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

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Molecular Profiling of Black and White Patients With Indeterminate Thyroid Nodules

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Introduction

- Black patients with thyroid cancer experience disproportionately poorer outcomes compared to White counterparts.
- While potentially linked to delayed diagnosis and systemic barriers, it remains unclear whether biologic differences contribute.
- Our aim is to explore race-associated molecular differences in indeterminate thyroid nodules (ITN) sent for molecular testing and assess whether they may contribute to observed disparities.

Methods

Study Design
- Retrospective cohort (2017–2023)
- 135 patients: Black (n=65), White (n=70)
- Thyroid nodule FNA → surgical evaluation

Data Collection
- Genomic variables: Afirma GSC classification (Benign vs. Suspicious), Xpression Atlas alterations
- Expression signatures: EMT, NIS, ERK, TDS

Study Outcomes
- Afirma GSC molecular and Genome-wide differential expression analysis by race
- Public external data: MSK-IMPACT® and AACR-GENIE®

Results

Genomic differences amongst thyroid cancer patients from two public databases

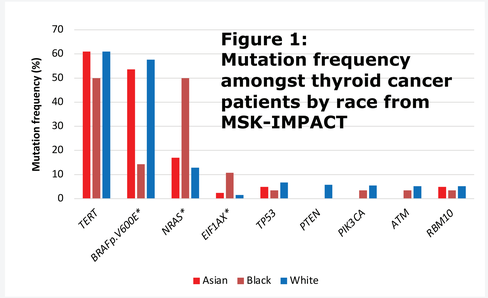


Figure 1: Mutation frequency amongst thyroid cancer patients by race from MSK-IMPACT

	Asian (n=140)	Black (n=81)	White (n=1397)	p value
NRAS variants	15%	33.30%	11%	p<0.0001
*BRAF*p.V600E	50%	15%	46%	p<0.0001
HRAS variants	6.40%	3.70%	3.90%	p=0.3

Table 1: % of *BRAF*p.V600E and *RAS* family mutations in thyroid cancer by race in AACR-GENIE®

Black patients' thyroid cancers are relatively enriched in *RAS* family mutations.

		Race	
		Black	White
Total		65	70
Cytology	B-III	56 (86%)	58 (83%)
	B-IV	9 (14%)	12 (17%)
GSC	B	26 (40%)	12 (17%)
	S	39 (60%)	58 (83%)

Table 2:
Afirma GSC ensemble classifier results by race

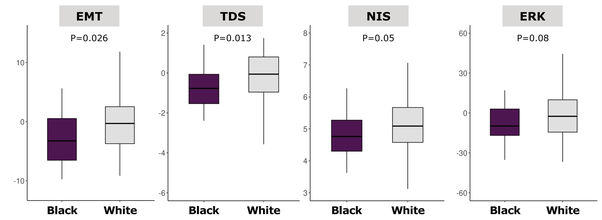
- In this cohort referred for surgery, the overall Afirma GSC-S rate is higher than the overall expected rate of ~65%.
- This appears to mainly be driven by the high rate of Afirma GSC-S results (83%) in White patients.

	Black	White	
Total	39	58	Fisher's test
Any XA variant	10 (25.6%)	24 (41.4%)	p=0.13
*BRAFp.*V600E	3 (7.7%)	8 (13.8%)	
NRAS	5 (12.8%)	8 (13.8%)	
HRAS	1 (2.5%)	6 (10.3%)	
DICER1	0	2 (3.4%)	
JAK2	1 (2.5%)	0	
Any XA fusion	3 (7.7%)	8 (13.8%)	p=0.5
PAX8::PPARG	2 (5%)	5 (8.6%)	
BRAF::HOOK3	0	1 (1.7%)	
CCDC6::RET	0	1 (1.7%)	
ETV6::NTRK3	1 (2.5%)	1 (1.7%)	
Any XA alteration	13 (33%)	32 (55%)	p=0.04

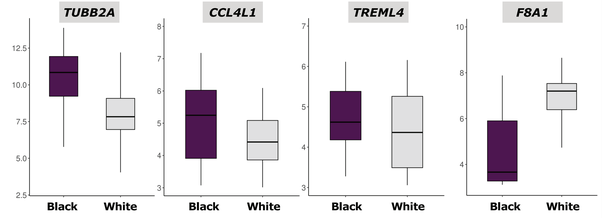
Table 3: XA alterations in Afirma GSC-S samples by race

- White patients had more expressed alterations than Black patients.
- There was trend toward higher *BRAF*p.V600E in Whites vs Blacks.

Figures 2 & 3: Molecular differences by self-reported race



Black patients had significantly lower expression of the EMT pathway, TDS, and NIS.



TUBB2A was the highest differentially expressed genes in Black patients, *F8A1* was the lowest.

Conclusion

- White patients: ↑ detectable XA variants, trend toward ↑ *BRAFp.*V600E positivity, ↑ EMT expression.
- Black patients: ↓ TDS, ↑ *NRAS*, ↓ NIS.
- This work highlights the need to further examine racial influences on tumor biology amid underrepresentation of Black patients in genomic datasets.