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Integrating Clinical and Multiomics Data to Characterize Ethnic Disparities in Breast Cancer on the Gulf Coast

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Background

Breast cancer is a heterogeneous disease comprising distinct molecular subtypes with variable clinical behavior and outcomes. In the United States, significant racial disparities persist, with Black/African American women experiencing approximately 40% higher breast cancer mortality compared to Non-Hispanic White women despite similar or lower incidence rates(1, 2). These disparities are multifactorial and reflect the interplay between social determinants of health, access to care, and intrinsic tumor biology(3). Notably, Black/African American women exhibit a disproportionately higher prevalence of aggressive subtypes, particularly triple-negative breast cancer (TNBC), which accounts for 15–20% of breast cancers and is associated with poor prognosis and limited targeted therapeutic options(4). Emerging evidence suggests that, beyond socioeconomic factors, biological differences—including variations in gene expression, tumor microenvironment, and signaling pathways—may contribute to the more aggressive disease phenotype observed in this population(5, 6). However, the extent to which these disparities are reflected at the regional level and the molecular mechanisms underlying them remain incompletely understood. In this study, we integrate clinical and multiomics data to characterize racial differences in breast cancer subtype distribution and tumor biology within a Gulf Coast population.

Objective

To characterize racial differences in breast cancer subtype distribution, age at diagnosis, and tumor molecular profiles.

Study design and cohort

This retrospective study integrated clinical and multiomics data to investigate ethnic disparities in breast cancer. Clinical and demographic information from 1,229 women diagnosed with breast cancer in the University of South Alabama Medical System from 2016 to 2024 was reviewed; 1,089 women with complete datasets were included. Race/ethnicity was extracted from the electronic medical record based on patient registration data. EMR categories were Non-Hispanic White (n=615), Non-Hispanic Black/African American (n=437), Asian (n=11), Native Hawaiian or Pacific Islander (n=3), Other (n=22), and Multiple (n=1). Because the EMR-defined “Other” category lacked granular annotation, it was not reclassified post hoc. Comparative analyses focused on the two largest groups. (Table 1).

Clinical variables and stratification

Age at diagnosis was calculated from date of birth and pathology report date. Breast cancer subtypes (Luminal A, Luminal B, HER2-positive, and TNBC) were defined based on receptor status. Patients were stratified into six age groups (<40, 40–<50, 50–<60, 60–<70, 70–<80, ≥80 years). Subtype distributions were compared between groups overall and within each age stratum, with additional analyses focusing on TNBC versus non-TNBC.

Statistical analysis

Age was compared using the Mann–Whitney U test. Subtype distributions were analyzed using chi-square or Fisher’s exact tests, including 2×2 comparisons for TNBC. Age-stratified analyses were performed independently for each group. Bonferroni correction was applied for multiple comparisons ($p < 0.05$ considered significant).

Tissue selection and multiomics profiling

A subset of breast tumor samples (n = 21; including TNBC and non-TNBC cases from both NHW and NHB/AA women) and three normal breast tissue samples were selected for molecular analysis. Tissue samples were obtained through the institutional biobank and processed using standardized histopathology procedures.

nCounter multiomics analysis

Gene expression and protein profiling were performed using the nCounter platform (NanoString Technologies, Seattle, WA). Tumor and normal tissue samples were analyzed using the Breast Cancer 360 (BC360) transcriptomic panel, which measures 776 genes spanning 23 major breast cancer pathways and biologic processes, in combination with the nCounter Multiomics Protein Core, nCounter Multiomics Immune Pathways Protein, and nCounter Multiomics Tumor Signaling Protein panels, encompassing a total of 545 protein-related analytes. This platform provides direct digital quantification of RNA transcripts and proteins without the need for amplification, enabling integrated assessment of oncogenic pathways, immune signatures, and the tumor microenvironment.

Results

The distribution of breast cancer molecular subtypes differed significantly between Non-Hispanic White and Non-Hispanic Black/African American women ($\chi^2 = 32.8$, df = 3, $p < 0.001$; Cramér’s V = 0.18). Non-Hispanic Black/African American women exhibited a higher proportion of TNBC (26.9% vs 13.5%), whereas Non-Hispanic White women had a higher proportion of luminal A tumors (73.0% vs 60.3%) (Table 2). Non-Hispanic Black/African American women were diagnosed at a younger age than Non-Hispanic White women (median 59 vs 64 years, $p < 0.001$). Subtype-specific analysis showed that this difference was significant for luminal A tumors (median 61 vs 64 years, $p < 0.001$) and TNBC (median 55 vs 62 years, $p = 0.0025$), while no significant differences were observed for HER2-positive tumors. Age-stratified analysis showed that the disparity in TNBC was age-dependent, with the greatest difference observed between 40 and 60 years of age, while no significant difference was detected among women younger than 40 years. Multiomics analysis further demonstrated distinct gene and protein expression profiles between tumors from both groups, supporting the presence of underlying biological differences. These findings suggest that racial disparities in breast cancer are shaped by age-dependent biological and epidemiological mechanisms, with potential implications for risk stratification and targeted therapeutic approaches.

Table 1. Distribution of race/ethnicity in the study cohort. Race/ethnicity categories were extracted from the electronic medical record based on patient-reported information at the time of registration. Data are presented as counts (n) and percentages (%). The “Other” and “Multiple” categories reflect EMR-defined groupings and were not further reclassified.

Race/ethnicity	n	%
Non-Hispanic White	615	56.5
Non-Hispanic Black/African American	437	40.1
Asian	11	1.0
Native, Hawaiian, or Pacific Islanders	3	0.3
Others	22	2.0
Multiple	1	0.1
Total	1089	100

Table 2. Distribution of breast cancer molecular subtypes by race/ethnicity in the study cohort. Breast cancer subtypes (luminal A, luminal B, triple-negative, and HER2-positive) are presented as counts and percentages for Non-Hispanic White and Non-Hispanic Black/African American women. Group differences were evaluated using a chi-square test of independence.

BC subtype*	All patients		Non-Hispanic White		Non-Hispanic Black/African American	
	n	%	n	%	n	%
Luminal A	743	68.2	449	73.0	264	60.3
Luminal B	93	8.5	58	9.4	32	7.3
TNBC	204	18.7	83	13.5	118	26.9
HER2-positive	49	4.5	25	4.1	24	5.5
Total	1089	100	615	100	438	100

* Breast cancer subtypes were defined using immunohistochemical surrogates based on estrogen receptor (ER), progesterone receptor (PR), and HER2 status, as follows:

•Luminal A: ER-positive and/or PR-positive, HER2-negative.

•Luminal B: ER-positive and/or PR-positive, HER2-positive.

•Triple-negative breast cancer (TNBC): ER-negative, PR-negative, and HER2-negative.

•HER2-positive (non-luminal): ER-negative, PR-negative, and HER2-positive.

Table 3. Age at diagnosis by race and breast cancer molecular subtype. Age at diagnosis is reported as mean ± standard deviation and median for Non-Hispanic White (NHW) and Non-Hispanic Black/African American (NHB/AA) women within each subtype (Luminal A, Luminal B, HER2-enriched, and triple-negative breast cancer). Group comparisons were performed using the Mann–Whitney U test. Adjusted p-values were obtained using Bonferroni correction for multiple comparisons.

BC Subtype	NHW (n)	NHW mean ± SD	NHW median	NHB/AA (n)	NHB/AA mean ± SD	NHB/AA median	p-value	p-value†
Luminal A	449	63.1 ± 11.9	64	264	59.3 ± 12.6	61	0.0001	0.00039
Luminal B	58	62.9 ± 11.7	64.5	32	58.1 ± 12.2	58.5	0.043	0.173
HER2-positive	25	62.7 ± 13.6	61	23	59.8 ± 11.8	61	0.536	1.000
TNBC	83	61.9 ± 14.3	62	118	56.1 ± 13.2	55	0.0025	0.0101

† Bonferroni-adjusted p-values for multiple comparisons across subtypes.

Sample ID	Race/Ethnicity	Age at diagnosis	ER	PR	HER2	KI67 (%)	Subtype	Response to neoadjuvant therapy	Histological grade	Pathologic stage (pTNM)	Number of positive lymph nodes	Lymphovascular invasion	Distant metastasis/Recurrence status	Vital status
12	NHB/AA	58	Negative	Negative	Negative	42.1	TNBC	NA	3	pT1c pN0(sn)-i	0	No determined	No	Alive
14	NHB/AA	54	Negative	Negative	Negative	19.6	TNBC	NA	3	NA	NA	No determined	NA	Alive
15	NHB/AA	56	Negative	Negative	Negative	47.0	TNBC	No response	3	ypT2 ypN0	0	Present	No	Deceased
17	NHB/AA	49	Negative	Negative	Negative	76.9	TNBC	No response	3	ypT3 ypN1a	1	Present	NA	Alive
18	NHB/AA	45	Negative	Negative	Negative	47.9	TNBC	No response	3	ypT2 ypN0	0	No identified	No	Alive
20	NHB/AA	61	Negative	Negative	Negative	63.7	TNBC	NA	3	NA	NA	No determined	NA	Deceased
21	NHB/AA	31	Negative	Negative	Negative	60.2	TNBC	No known presurgical therapy	3	pT2 pN0	0	Present	No	Alive
10	NHB/AA	33	Negative	Negative	Negative	66.0	TNBC	Probable response	3	pyT3 ypN0	0	No identified	No	Alive
2	NHB/AA	54	Positive (99%)	Positive (7%)	Negative	21.0	Luminal A	NA	3	pT1c pN1a	1	No identified	No	Alive
3	NHB/AA	54	Positive	Positive	Negative	21.0	Luminal A	NA	3	pT1c pN1a	1	No determined	No	Alive
7	NHB/AA	71	Positive (96%)	Positive (15%)	Negative	9.0	Luminal A	NA	2	pT3 pN1a	1	No identified	No	Deceased
1	NHW	56	Positive (68%)	Negative	Negative	28.0	Luminal A	NA	3	pT2(3) pN1a	1	Present	No	Alive
8	NHW	85	Negative	Negative	Negative	43.5	TNBC	NA	NA	NA	NA	No determined	Metastatic unknown primary	Alive
9	NHW	43	Negative	Negative	Negative	75.5	TNBC	Minimal response	3	ypT2 ypN1a	2	Present	No	Alive
13	NHW	62	Positive (95%)	Positive (93%)	Negative	17.0	Luminal A	NA	3	pT2(m) pN0	0	No determined	No	Deceased
19	NHW	60	Positive (100%)	Positive (23%)	Negative	30.0	Luminal A	NA	2	pT4b pN2a	4	Present	Ulceration of skin	Deceased
11	NHW	58	Negative	Negative	Negative	76.8	TNBC	No response	3	ypT3(m) ypN1a	2	Present	No	Deceased
16	NHW	35	Negative	Negative	Negative	77.2	TNBC	NA	3	NA	NA	No determined	Axillary LN	Deceased
4	NHW	58	Positive (90%)	Positive (94%)	Negative	5.9	Luminal A	NA	2	pT1c pN1a	1	No identified	NA	Alive
5	NHW	65	Negative	Negative	Negative	69.0	TNBC	NA	3	pT1 pN0	0	Present	Recurrence	Deceased
6	Other	47	Positive (87%)	Positive (89%)	Negative	5.0	Luminal A	NA	1	pT1c pN1a	1	Present	No	Alive

Table 4. Clinical and pathologic characteristics of breast cancer cases included in the nCounter multiomics analysis. Data were obtained from the electronic medical record for each patient whose tumor was analyzed using the nCounter platform. Variables include age at diagnosis, race/ethnicity, receptor status (ER, PR, HER2), Ki-67 proliferation index, molecular subtype, histologic grade, pathologic stage (pTNM), lymph node status, lymphovascular invasion, response to neoadjuvant therapy, metastatic status, and vital status.

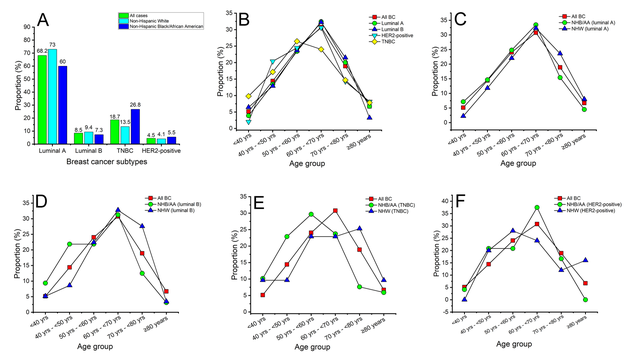

Figure 1. Distribution of breast cancer subtypes by race and age at diagnosis. (A) Proportion of breast cancer subtypes among all cases and by race (Non-Hispanic White [NHW] and Non-Hispanic Black/African American [NHB/AA]). (B) Distribution of subtypes across age groups. (C–F) Age-stratified distribution of Luminal A (C), Luminal B (D), triple-negative breast cancer (TNBC) (E), and HER2-positive tumors (F) in NHW and NHB/AA women. Values represent the proportion (%) of cases within each age group.

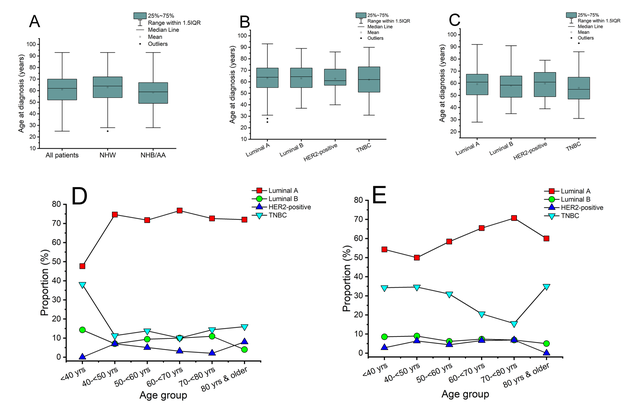

Figure 2. Age at diagnosis and age-dependent distribution of breast cancer subtypes by race. (A) Distribution of age at diagnosis in the overall cohort and stratified by Non-Hispanic White (NHW) and Non-Hispanic Black/African American (NHB/AA) women. (B–C) Distribution of age at diagnosis by breast cancer subtype among NHW (B) and NHB/AA (C) women.(D–E) Age-stratified distribution of breast cancer subtypes in NHW (D) and NHB/AA (E) women. Boxplots display median, interquartile range, and outliers. Line plots represent the proportion (%) of each subtype within age groups

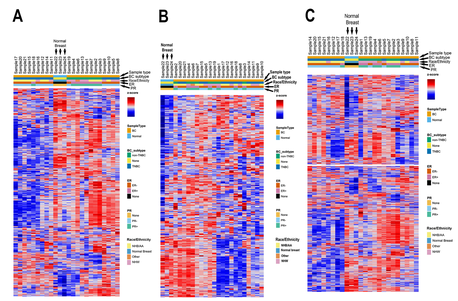

Figure 3. Heatmaps of transcriptomic (A), proteomic (B), and integrated multiomic (C) profiles in 21 breast cancers and 3 normal breast tissues analyzed by nCounter. Columns represent samples, rows represent features, and values are shown as z-scores; annotation tracks indicate sample type, subtype, race/ethnicity, ER, and PR status.

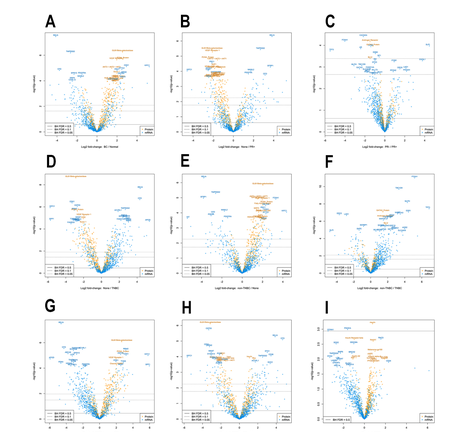

Figure 4. Transcriptomic and proteomic volcano plots showing differential features by tissue type, receptor status, subtype, and race/ethnicity. mRNA and protein changes are plotted as log2 fold-change versus −log10(p-value); horizontal lines indicate BH FDR thresholds. Panels compare BC vs normal, PR-positive BC vs normal, PR-negative vs PR-positive BC, TNBC vs normal, non-TNBC vs normal, non-TNBC vs TNBC, NHB/AA BC vs normal, NHW BC vs normal, and NHB/AA vs NHW BC.

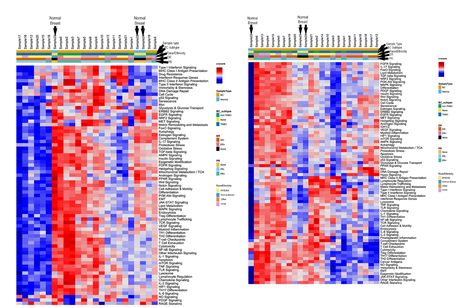

Figure 5. Figure 5. Heatmaps of transcriptomic (A) and proteomic (B) signaling pathway profiles in 21 breast cancers and 3 normal breast tissues. Columns represent samples, rows represent pathways, and values are shown as z-scores; annotation tracks indicate sample type, subtype, race/ethnicity, ER, and PR status.

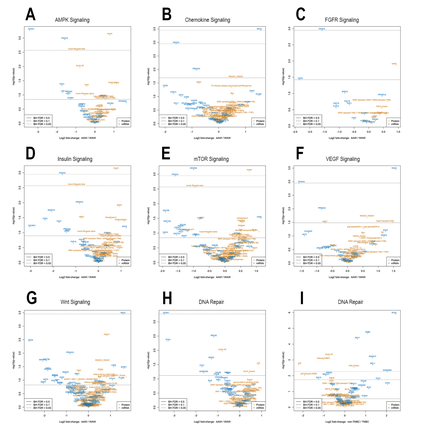

Figure 6. Pathway-focused volcano plots of transcriptomic and proteomic differences by race/ethnicity and subtype. Features are plotted as log2 fold-change versus −log10(p-value), with BH FDR thresholds indicated. Panels A–H compare NHB/AA and NHW tumors across AMPK, chemokine, FGFR, insulin, mTOR, VEGF, Wnt, and DNA repair pathways; panel I compares non-TNBC and TNBC tumors in the DNA repair pathway.

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Acknowledgements

We thank the USA Health Biobank and Histology Core Facility team: Dr. Elba Turbat-Herrera, Dr. Veronica Ramirez-Alcantara, and Terry Pierse—for their technical assistance with immunohistochemistry. We are grateful to Adrian Hoff for his kind assistance in preparing the poster. This study was funded by a grant from the Breast Cancer Research Foundation of Alabama (BCRFA) to LPY.