# Evaluation of tumor immune microenvironment in Hispanic and African American breast cancer

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## BACKGROUND

- Hispanics or Latinos (HL) and Non-Hispanic African Americans or Black (NHB) have a higher prevalence of advanced-stage breast cancer (BC) at diagnosis compared to Non-Hispanic Whites (NHW).
- To understand the role of immune system, we evaluated the tumor immune microenvironment (TIME) by race/ethnicity among HL, AA, and NHW BC patients.

## METHODS

- 15544 BC samples were tested by NGS (592, NextSeq; WES, NovaSeq) and WTS(NovaSeq; Caris Life Sciences, Phoenix, AZ).
- Race/ethnicity data is self-reported.
- Immune cell fractions were calculated by deconvolution of WTS: Quantiseq.
- Gene expression profiles were analyzed for T-cell inflammation score (TIS) and interferon-gamma (IFNγ) score.
- Real-world median overall survival (mOS) was obtained from insurance claims and calculated from date of tumor biopsy to last contact using Kaplan-Meier estimates.
- Statistical significance was assessed using chi-square, Mann-Whitney U tests with multiple comparison adjustments (q<0.05).

**Table 1: BC primary and metastatic demographic information**

| | | NHW | NHB | HL |
|---|---|---|---|---|
| **All** | **Count (N)** | 7170 | 1508 | 1754 |
| | **Median age [range]** | 67 [23 ->89] | 60 [22- 86] | 60 [22 ->89] |
| **Primary** | **Count (N)** | 2528 | 592 | 774 |
| | **Median age [range]** | 67 [24 ->89] | 59 [22- 86] | 59 [22 ->89] |
| **Metastatic** | **Count (N)** | 4642 | 916 | 980 |
| | **Median age [range]** | 67 [23 ->89] | 61 [24-> 89] | 60 [23 ->89] |

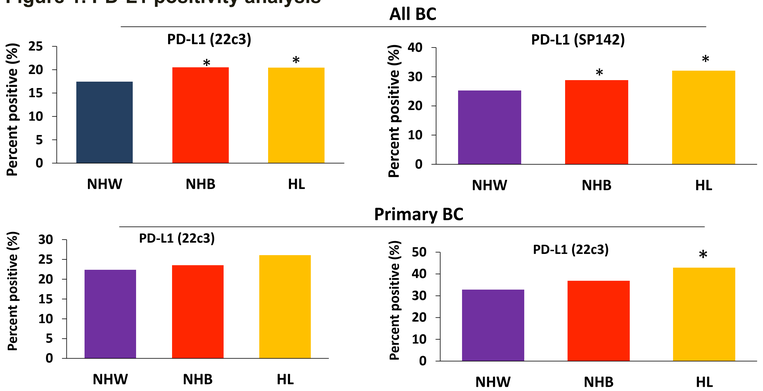
**Table 2: BC subtypes demographic information**

| | | NHW | NHB | HL |
|---|---|---|---|---|
| **HER2+** | **Count (N)** | 448 | 109 | 137 |
| | **Median age [range]** | 64 [26 ->89] | 57 [26 - 86] | 55 [23 ->89] |
| **HR+HER2-** | **Count (N)** | 2485 | 407 | 533 |
| | **Median age [range]** | 67 [26 ->89] | 62 [25 ->89] | 60 [26 ->89] |
| **TNBC** | **Count (N)** | 1182 | 404 | 370 |
| | **Median age [range]** | 68 [24 ->89] | 59 [22 ->89] | 59 [22 ->89] |

NHW: Non-Hispanic White
NHB: Non-Hispanic Black/African American (AA)
HL: Hispanic or Latino

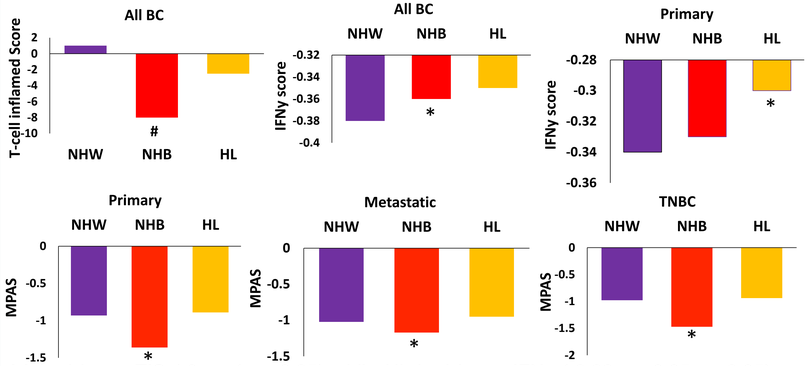
## RESULTS

**Figure 1. PD-L1 positivity analysis**




Across all cases, AA (20.5%) and HL (20.4%) had greater incidence (%) of PD-L1+ cases versus (vs)NHW (17.4%), all q<0.05. Hispanics tumors biopsied in breast (primary) had greater PD-L1+ in SP142 (42.8% vs 32.8%) compared to NHW q<0.05.

**Figure 2. Gene signature analysis**




AA had lower TIS (-8 vs 1, p<0.05) while HL had lower IFNγ (-0.38vs. -0.35, q<0.05) vs NHW in all BC. NHW had lower IFNγ score (-0.34 vs -0.30) compared to HL, while NHB had lower (-1.36 vs -0.93) MAPK activation score compared to NHW primary BC. NHB had lower MAPK activation score (-1.17 vs -1.02) compared to NHW metastatic BC. NHB had lower MAPK activation score (-1.47 vs -0.98) compared to NHW TNBC. #p<0.05, *q<0.05

**Figure 3. Immune cell infiltration**

| All BC | Median % | | |
|---|---|---|---|
| | NHW | NHB | HL |
| B cell | 5.21 | 4.89 | 5.04 |
| Mϕ M1 | 2.5 | 2.49 | 2.44 |
| **Mϕ M2** | **4.63** | **3.71*** | **4.23*** |
| DC | 2.63 | 2.76 | 2.69 |
| **Neutrophil** | **3.71** | **3.53*** | **3.4*** |
| NK cell | 2.96 | 2.92 | 2.92 |
| **T cell CD8+** | **0.14** | **0.15** | **0.26*** |
| Tregs | 1.58 | 1.57 | 1.66 |

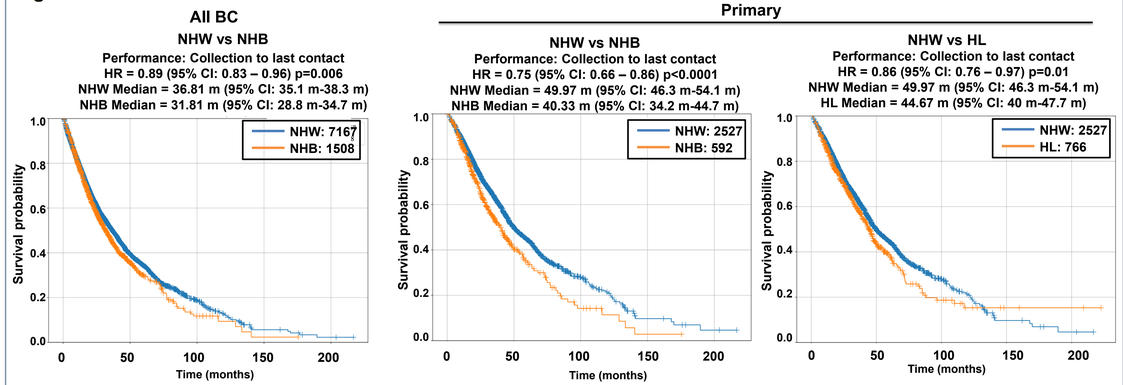
| Primary | Median % | | |
|---|---|---|---|
| | NHW | NHB | HL |
| B cell | 5.27 | 4.64 | 4.96 |
| Mϕ M1 | 2.79 | 2.95 | 2.68 |
| **Mϕ M2** | **4.44** | **3.32*** | **3.93*** |
| **DC** | **2.62** | **2.82** | **2.75** |
| Neutrophil | 3.69 | 3.52 | 3.54 |
| NK cell | 2.99 | 2.92 | 2.96 |
| **T cell CD8+** | **0.28** | **0.24** | **0.44*** |
| Tregs | 1.73 | 1.74 | 1.8 |

| TNBC | Median % | | |
|---|---|---|---|
| | NHW | NHB | HL |
| B cell | 3.91 | 3.88 | 3.94 |
| Mϕ M1 | 3.12 | 2.91 | 2.88 |
| **Mϕ M2** | **3.28** | **2.5*** | **3.18** |
| **DC** | **2.84** | **3.14** | **3.07** |
| **Neutrophil** | **4.39** | **4.06*** | **4.33** |
| NK cell | 2.81 | 2.95 | 2.91 |
| T cell CD8+ | 0.49 | 0.29 | 0.5 |
| Tregs | 1.75 | 1.68 | 1.66 |

High median %
Low median %

In all BC, AA had lower median % cell infiltration of M2 Mφ, and neutrophils vs NHW. HL had a lower fraction of M2 Mφ and higher CD8+ T cells vs NHW. In primary BC AA and HL had lower cell infiltration of M2Mφ compared to NHW. HL had higher CD8+ T cells compared to NHW. In TNBC, AA had lower M2 Mφ and neutrophil infiltration compared to NHW. *q<0.05

**Figure 4. Patient survival**




AA had worse mOS than NHW overall (31.8 vs 36.8 m, HR 0.89, 95% CI 0.83 –0.96, p <0.01), in pBC (40.3 vs 49.9 mo, HR 0.75, 95% CI 0.6 – 0.8, p<0.01). HL had worse mOS than NHW overall (44.6 vs 49.9 mo, HR 0.8, 95% CI 0.76 –0.97, p <0.01).

## CONCLUSIONS

**Our study shows worse mOS in NHB and HL primary BC cases vs NHW, possibly from a less inflamed TIME in NHB and HL and lower fraction of neutrophils and M2 Mφ despite higher %of PD-L1+. Targeting Mφ and CD8+ T cells and converting cold to hot TIME may lessen race/ethnic disparities, especially in early-stage BC.**