Comprehensive spatial profiling of the tumor immune microenvironment in triple negative breast cancer from Black women

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BACKGROUND

- Breast cancer is more common among US Black women, and the most common non-viral driven cancer in African and Caribbean countries
- US Black (USB) women are 40% more likely to die from breast cancer despite being diagnosed at similar rates as US White (USW) women (Figure 1)
- USBwomen are more frequently diagnosed at younger ages and later stages of the disease and with aggressive breast cancer subtypes (such as triple-negative) compared to women of other races. (Figure 2).

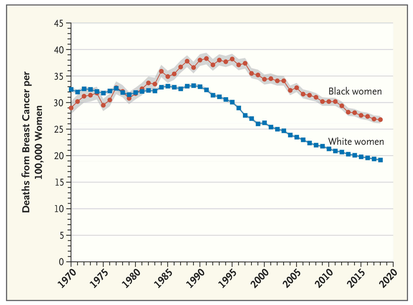


Figure 1. Trends in Breast-Cancer Mortality among Black Women and White Women in the United States, 1970 through 2018. *(Jatoi et al. NEJM,2022)*

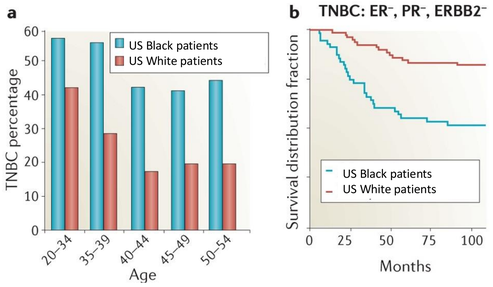
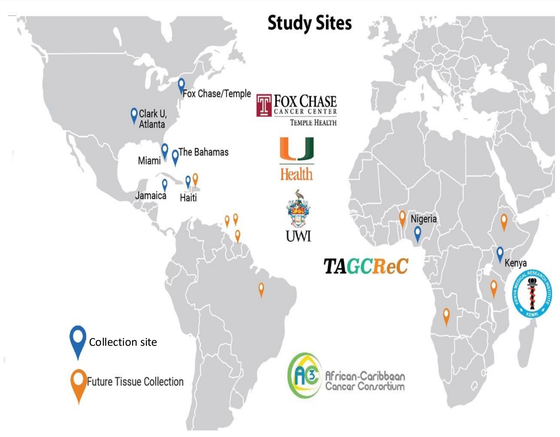
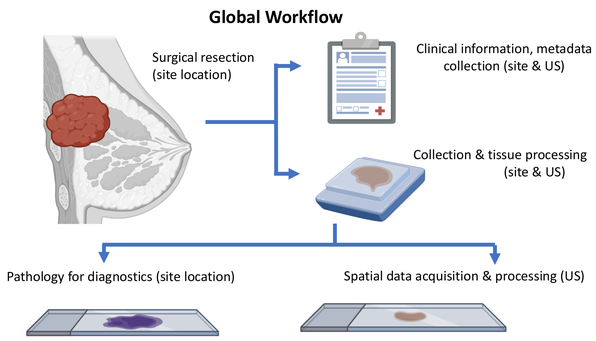


Figure 2. a) US Black women age related incidence is lower than US White women b) TNBC survival in US White Women vs US Black women (*Dietze et al, Nat. Rev. Canc, 2015*)

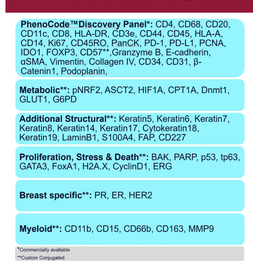
STUDY DESIGN

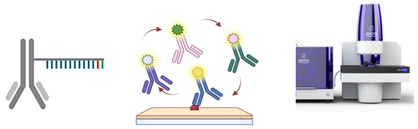


With the African-Caribbean Cancer Consortium (AC3) & Transatlantic Gynecologic Cancer Research Consortium (TaGCReC), we have created a multi-omic spatial atlas of triple-negative and other breast cancers across Africa, the Caribbean, and among USB individuals.



METHODS





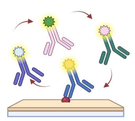
Antibody conjugation

65 IF TNBC panel

Spatial data acquisition



Proximity Ligation Assay



IO cyclical IF panel



Spatial data acquisition

- 65 plex antibody panel developed with Akoya for triple negative breast cancer (TNBC) curated by pathologists and clinical diagnostic laboratories
- TNBC panel applied to USW and USB women with age and stage matched
- PDL1 proximity ligation assay (PLA) and IO cyclical IF panel developed with Navinci and Bruker spatial biology
- A multi-omic approach to complement the existing TNBC panel with RNA targets was also utilized

RESULTS

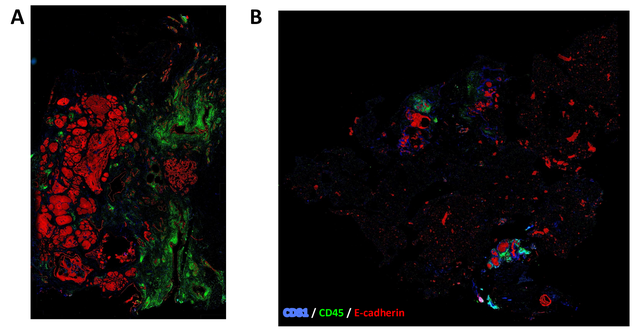


Figure 3. Examples of whole slide tissue and biopsy samples processed for CD31 (endothelial) , CD45 (immune), E-cadherin (cancer epithelial) cell markers from the TNBC panel in A) USB & B) USW patients. C) Cell type specific populations for both normal & tumor associated markers seen across all samples using the TNBC panel.

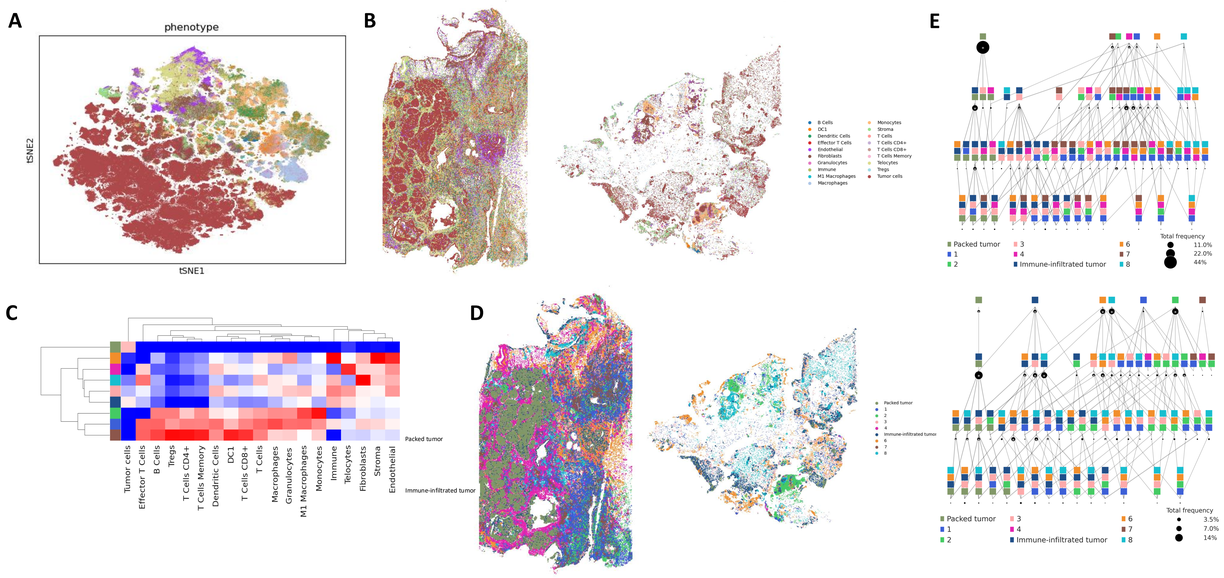


Figure 4. A) tSNE plot across ~4 million cells shows canonical cell typing seen in tumors & their microenvironment across both USB and USW patient samples. B) Spatial mapping of cell typing for the USB patient (left) and the USW patient (right). C) Cellular neighborhood heatmap defining the different microenvironments. D) Spatial mapping of cellular neighborhoods for the USB patient (left) and the US White patient (right). E) Interaction between different cellular neighborhoods in USB patients (upper) and USW patients (lower).

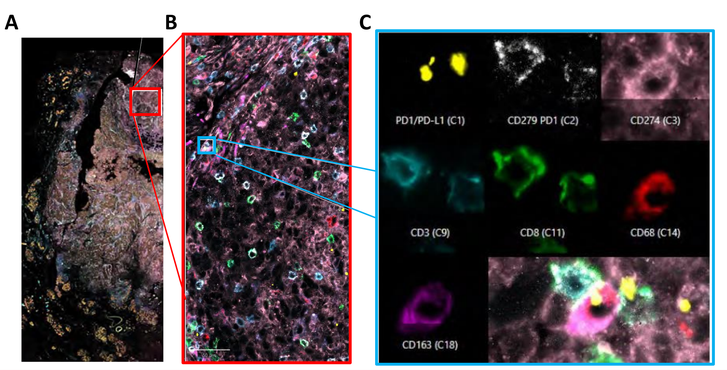


Figure 5. PLA of PD1 interaction with PD-L1 . A) IO panel across tissue section B) Magnified view of CD3 (T cells teal) , CD8 (cytotoxic T cells), CD274 (PDL1 pink) , CD279 (white PD1), CD68 (red, macrophage), CD163 (purple, M2 type macrophage) C) PLA signal between two cytotoxic T cells and CD68+ CD163+ macrophage

- USB patient breast tissue showed elevated levels of solitary packed tumor behavior as compared to that of USW patient samples.
- Meanwhile, in USW patient breast tissue, we observe higher immune penetration in the tumors and higher interaction levels between tumor microenvironments and other immune microenvironments.

CONCLUSIONS

- We aim to develop a benchmark that confidently measures and interprets ancestral genomic differences at the cellular level to deciphering the relationship between African ancestry, aggressive disease biology, and early onset.