San Antonio Breast Cancer Symposium – December 6-10, 2016

Racial differences in the molecular landscape of breast cancer

Filipa Lynce[1], Joanne Xiu[2], Maria Raquel Nunes[3], Sandra M Swain[1], Zoran Gatalica[2], Claudine Isaacs[1], Paula R Pohlmann[1]

[1]Lombardi Comprehensive Cancer Center, MedStar Georgetown University Hospital; [2]Caris Life Sciences; [3]Sibley Hospital at Johns Hopkins

Background

African Americans (AA) have a higher mortality associated with breast cancer when compared to Caucasians (C).This has been attributed to diverse factors that include access to care, reproductive factors and different somatic genomic profiles. We aimed to compare the racial mutational landscape of 565 breast cancer samples.

Objectives and Methods

• Hypothesis: there are differences in the mutational landscape of breast cancer based on race

• Cross-sectional retrospective study of biomarker data obtained from de-identified 565 breast cancer samples

• Sample testing: Multiplatform profiling at Caris Life Sciences:

- IHC: Immunohistochemistry using FFPE samples - 20 protein panel
- ISH: Fluorescence/Chromogenic *in situ hybridization* (FISH/CISH) - 4 gene panel
- DNA Sequencing (NGS or Sanger) for somatic mutations: Illumina MiSeq platform (Illumina TruSeq Amplicon Cancer Hotspot panel, 47 gene) and NextSeq (Agilent SureSelect XT, 592 gene selected based on COSMIC database

Results

Table 1. Prevalence of breast cancer subtypes

	AA (%)	C (%)
Total	118	447
HR+ HER2-	38 (32.2)	168 (37.5)
HER2+	9 (7.6)	36 (8.1)
TNBC	38 (32.2)*	76 (17.0)*
Unknown	33 (28.0)	167 (37.4)

*** Difference in prevalence was statistically significant**

Results

Table 2. Protein expression by IHC in AA and C patients

		BC			TNBC		
		AA %	C %	p	AA %	C %	p
IHC	HER2	9	12	ns	0	0	ns
	AR	40	60	0.00	5	18	0.07
	ER	44	62	0.00	0	0	ns
	PR	35	46	0.09	0	0	ns
	EGFR	30	16	0.03	60	50	ns
	ERCC1	33	46	0.06	36	26	ns
	MGMT	61	63	ns	65	71	ns
	PD-1	50	34	0.06	65	48	ns
	PD-L1	0	6	ns	0	11	ns
	PGP	7	6	ns	10	15	ns
	PTEN	56	58	ns	42	47	ns
	RRM1	39	27	0.04	59	27	0.01
	TLE3	50	59	0.10	43	57	ns
	TOP2A	71	64	ns	86	47	0.08
	TOPO1	63	58	ns	69	46	0.03
	TS	44	30	0.01	63	49	ns
	TUBB3	55	41	0.06	77	51	0.03

Figure 1. AR expression by subtypes

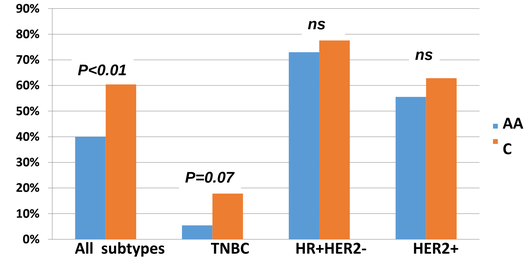
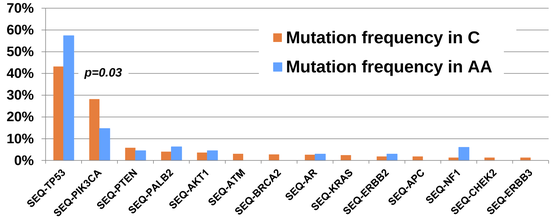
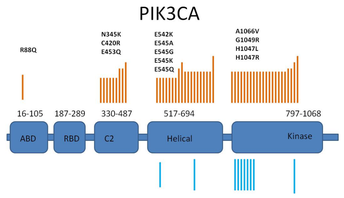


Figure 2. Mutation frequency of selected genes (frequency of ≥1%)



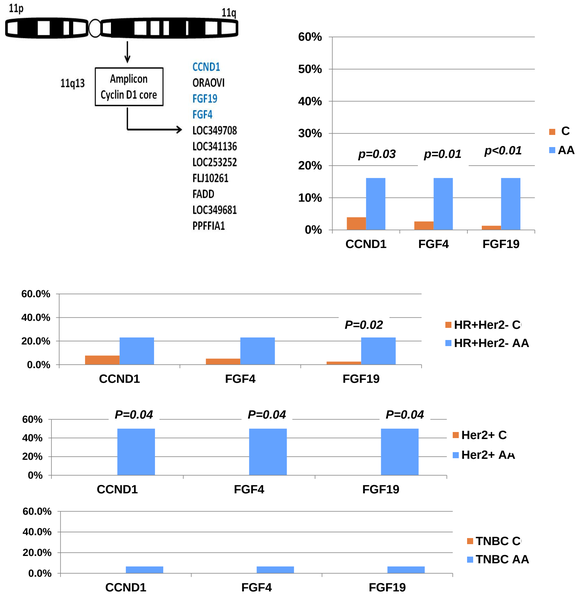
Results

Table 3. PIK3CA mutations by race



	Exon	AA	C
R88Q	2		1
N345K	4		6
C420R	7		2
E453Q	8		1
E542K	9	1	7
E545A	9		1
E545G	9		1
E545K	9	1	9
E545Q	9		1
A1066V	20		1
G1049R	20		1
H1047L	20	1	2
H1047R	20	7	18
Total		10	51

Figure 3. Schematic view of 11q13 and Copy Number Variation (CNV) of CCND1, FGF4 and FGF19



Conclusions

1. **Racial differences were found in the molecular landscape of breast cancer, including PIK3CA mutations, AR expression and CNV**
2. **Protein expression by IHC revealed lower expression of AR in AA**
3. **PIK3CA mutations were overall less prevalent in AA; there were also differences on the location of PIK3CA mutations when comparing AA to C**
4. **CCND1, FGF4 and FGF19 excess of copies in AA suggest 11q13 region abnormality**
5. **Our data support racial molecular differences in breast cancer that can be explored in future studies**

References

1. Keenam T, Moy B, et al. Comparison of the Genomic Landscape Between Primary Breast Cancer in African American Versus White Women and the Association of Racial Differences With Tumor Recurrence. J Clin Oncol 2015;33(31);3621-3627
2. DeSantis C, et al. Breast Cancer Statistics, 2015: Convergence of Incidence Rates Between Black and White Women. CA Cancer J Clin 2015
3. Hughes-Davies L, et al. *EMSY* Links the BRCA2 Pathway to Sporadic Breast and Ovarian Cancer. Cell 2003;115, 523–535
4. Silvestri V, Rizollo P, et al. Novel and known genetic variants for male breast cancer risk at 8q24.21, 9p21.3, 11q13.3 and 14q24.1: Results from a multicenter study in Italy. European Journal of Cancer 2015;51,2289-2295