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# **Supplementary Materials: Low-frequency mutational heterogeneity of invasive ductal carcinoma subtypes: information to direct precision oncology**

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**Table S1A** PIK3CA, KRAS, HRAS, and BRAF mutant fraction measurements in HR+/HER2+ ductal carcinomas

ID	Age/Race	Dim.	Max. Tumor	T Stage   N Stage		Smoker	MP	Mutant Fraction					
				Hist. Grade	Clinical Stage			PIK3CA H1047R	PIK3CA E545K	KRAS G12D	KRAS G12V	HRAS G12D	BRAF V600E
1	40/C	1.8	T1   N1   II   II	N	Pre	1.99 × 10 <sup>-6</sup>	6.99 × 10 <sup>-6</sup>	3.37 × 10 <sup>-6</sup>	5.88 × 10 <sup>-7</sup>	4.94 × 10 <sup>-5</sup>	1.72 × 10 <sup>-5</sup>		
2	85/C	3.2	T4   N0   III   III	-	Post	1.16 × 10 <sup>-7</sup>	4.37 × 10 <sup>-6</sup>	3.22 × 10 <sup>-5</sup>	2.29 × 10 <sup>-6</sup>	7.26 × 10 <sup>-6</sup>	5.71 × 10 <sup>-6</sup>		
3	56/C	4.2	T4   N2   II   III	-	Post	1.11 × 10 <sup>-7</sup>	4.06 × 10 <sup>-6</sup>	4.23 × 10 <sup>-5</sup>	2.57 × 10 <sup>-7</sup>	1.14 × 10 <sup>-5</sup>	8.62 × 10 <sup>-6</sup>		
4	69/C	1.2	T1   N-   II   -	N	Post	9.21 × 10 <sup>-3</sup>	1.32 × 10 <sup>-1</sup>	1.56 × 10 <sup>-5</sup>	1.06 × 10 <sup>-4</sup>	1.44 × 10 <sup>-6</sup>	2.07 × 10 <sup>-5</sup>		
5	43/C	1.9	T1   N0   II   I	-	Pre	9.87 × 10 <sup>-5</sup>	6.10 × 10 <sup>-6</sup>	9.09 × 10 <sup>-6</sup>	1.48 × 10 <sup>-6</sup>	6.02 × 10 <sup>-6</sup>	1.74 × 10 <sup>-5</sup>		
6	42/C	1.5	T1   N0   II   I	-	-	1.08 × 10 <sup>-7</sup>	1.36 × 10 <sup>-5</sup>	1.91 × 10 <sup>-5</sup>	3.65 × 10 <sup>-7</sup>	3.00 × 10 <sup>-5</sup>	4.99 × 10 <sup>-6</sup>		
7	47/C	1.2	T1   N0   II   I	-	Pre	9.58 × 10 <sup>-6</sup>	1.08 × 10 <sup>-5</sup>	7.13 × 10 <sup>-6</sup>	1.98 × 10 <sup>-7</sup>	3.24 × 10 <sup>-5</sup>	5.71 × 10 <sup>-6</sup>		
8	56/C	1.5	T1   N2   II   III	-	Pre	1.14 × 10 <sup>-7</sup>	9.75 × 10 <sup>-6</sup>	1.27 × 10 <sup>-5</sup>	1.65 × 10 <sup>-6</sup>	9.73 × 10 <sup>-6</sup>	1.09 × 10 <sup>-5</sup>		
9	60/C	2.5	T2   N0   II   II	N	Post	4.50 × 10 <sup>-8</sup>	1.61 × 10 <sup>-5</sup>	1.51 × 10 <sup>-5</sup>	1.81 × 10 <sup>-6</sup>	1.38 × 10 <sup>-6</sup>	8.57 × 10 <sup>-6</sup>		
10	66/C	1.2	T1   N1   III   II	-	Post	3.64 × 10 <sup>-4</sup>	7.40 × 10 <sup>-6</sup>	1.06 × 10 <sup>-5</sup>	4.13 × 10 <sup>-7</sup>	9.00 × 10 <sup>-7</sup>	4.72 × 10 <sup>-6</sup>		
11	54/C	1.2	T1   N0   III   I	-	-	2.69 × 10 <sup>-5</sup>	2.79 × 10 <sup>-5</sup>	2.39 × 10 <sup>-5</sup>	8.12 × 10 <sup>-6</sup>	7.95 × 10 <sup>-5</sup>	3.73 × 10 <sup>-5</sup>		
12	60/C	2.0	T1   N1   II   II	N	Post	1.01 × 10 <sup>-3</sup>	3.67 × 10 <sup>-6</sup>	6.96 × 10 <sup>-6</sup>	8.89 × 10 <sup>-7</sup>	1.31 × 10 <sup>-4</sup>	7.35 × 10 <sup>-6</sup>		
13	58/C	1.5	T1   N0   II   I	-	Post	4.72 × 10 <sup>-6</sup>	3.03 × 10 <sup>-5</sup>	1.46 × 10 <sup>-5</sup>	1.98 × 10 <sup>-6</sup>	8.53 × 10 <sup>-5</sup>	7.36 × 10 <sup>-6</sup>		
14	27/C	1.5	T1   N0   III   I	-	Pre	2.15 × 10 <sup>-4</sup>	1.27 × 10 <sup>-1</sup>	1.10 × 10 <sup>-5</sup>	3.05 × 10 <sup>-6</sup>	7.28 × 10 <sup>-5</sup>	1.62 × 10 <sup>-5</sup>		
15	60/C	2.5	T2   N0   II   II	N	Post	4.15 × 10 <sup>-2</sup>	7.34 × 10 <sup>-6</sup>	1.26 × 10 <sup>-5</sup>	1.97 × 10 <sup>-6</sup>	8.51 × 10 <sup>-5</sup>	8.83 × 10 <sup>-5</sup>		
16	77/C	2.5	T2   N1   III   II	N	Post	2.55 × 10 <sup>-7</sup>	7.56 × 10 <sup>-6</sup>	1.59 × 10 <sup>-6</sup>	1.81 × 10 <sup>-5</sup>	4.14 × 10 <sup>-5</sup>	4.36 × 10 <sup>-5</sup>		
17	50/C	2.7	T2   N0   II   II	N	Post	1.14 × 10 <sup>-3</sup>	4.72 × 10 <sup>-6</sup>	1.78 × 10 <sup>-5</sup>	2.13 × 10 <sup>-6</sup>	8.57 × 10 <sup>-5</sup>	9.79 × 10 <sup>-6</sup>		
18	50/C	1.4	T1   N0   II   I	-	Pre	2.58 × 10 <sup>-5</sup>	1.09 × 10 <sup>-5</sup>	1.72 × 10 <sup>-5</sup>	1.67 × 10 <sup>-6</sup>	1.67 × 10 <sup>-5</sup>	7.38 × 10 <sup>-6</sup>		
19	66/C	5.0	T2   N0   II   II	N	Post	2.17 × 10 <sup>-8</sup>	2.04 × 10 <sup>-1</sup>	1.10 × 10 <sup>-5</sup>	1.54 × 10 <sup>-6</sup>	8.86 × 10 <sup>-6</sup>	8.17 × 10 <sup>-6</sup>		
20	49/C	4.7	T2   N2   II   III	Y	Pre	2.88 × 10 <sup>-3</sup>	4.68 × 10 <sup>-6</sup>	3.57 × 10 <sup>-5</sup>	2.96 × 10 <sup>-6</sup>	2.19 × 10 <sup>-4</sup>	1.17 × 10 <sup>-5</sup>		
<b>Mean ± SD</b>								<b>Geometric Mean MF</b>					
55.8 ± 13.3								1.32 × 10 <sup>-5</sup>	3.66 × 10 <sup>-5</sup>	1.79 × 10 <sup>-5</sup>	1.80 × 10 <sup>-6</sup>	2.09 × 10 <sup>-5</sup>	1.19 × 10 <sup>-5</sup>

**Table S1B.** *PIK3CA*, *KRAS*, *HRAS*, and *BRAF* mutant fraction measurements in HR+/HER2- ductal carcinomas

ID	Age/Race	Tumor Dim.	Hist. Grade   Clinical Stage	Smoker	MP	Mutant Fraction					
						<i>PIK3CA</i>	<i>PIK3CA</i>	<i>KRAS</i>	<i>KRAS</i>	<i>HRAS</i>	<i>BRAF</i>
						H1047R	E545K	G12D	G12V	G12D	V600E
21	58/AA	15.7	T3   N3   II   III	Y	-	1.55 × 10 <sup>-7</sup>	4.91 × 10 <sup>-6</sup>	8.32 × 10 <sup>-6</sup>	2.76 × 10 <sup>-7</sup>	3.66 × 10 <sup>-5</sup>	7.46 × 10 <sup>-4</sup>
22	63/C	1.9	T1   N2   II   III	N	Post	9.45 × 10 <sup>-8</sup>	1.92 × 10 <sup>-6</sup>	3.55 × 10 <sup>-6</sup>	2.29 × 10 <sup>-7</sup>	3.16 × 10 <sup>-5</sup>	5.01 × 10 <sup>-5</sup>
23	65/C	5.8	T3   N2   II   III	Y	Post	6.92 × 10 <sup>-3</sup>	6.71 × 10 <sup>-5</sup>	3.50 × 10 <sup>-6</sup>	1.19 × 10 <sup>-7</sup>	4.15 × 10 <sup>-5</sup>	1.67 × 10 <sup>-4</sup>
24	56/C	3.9	T2   N1   II   II	Y	-	3.88 × 10 <sup>-3</sup>	7.09 × 10 <sup>-6</sup>	6.62 × 10 <sup>-5</sup>	2.36 × 10 <sup>-6</sup>	4.21 × 10 <sup>-5</sup>	1.85 × 10 <sup>-5</sup>
25	61/C	2.7	T2   N0   III   II	N	Post	2.80 × 10 <sup>-7</sup>	1.14 × 10 <sup>-5</sup>	8.17 × 10 <sup>-6</sup>	6.53 × 10 <sup>-7</sup>	4.11 × 10 <sup>-5</sup>	8.19 × 10 <sup>-5</sup>
26	67/C	4.0	T2   N3   III   III	N	Post	8.74 × 10 <sup>-5</sup>	5.79 × 10 <sup>-6</sup>	4.71 × 10 <sup>-6</sup>	1.45 × 10 <sup>-7</sup>	6.03 × 10 <sup>-5</sup>	5.32 × 10 <sup>-5</sup>
27	70/C	2.5	T2   N1   III   II	N	-	2.53 × 10 <sup>-5</sup>	3.00 × 10 <sup>-3</sup>	1.31 × 10 <sup>-5</sup>	1.48 × 10 <sup>-7</sup>	2.26 × 10 <sup>-5</sup>	1.85 × 10 <sup>-5</sup>
28	30/C	2.2	T2   N1   I   II	Y	Pre	3.85 × 10 <sup>-8</sup>	3.61 × 10 <sup>-3</sup>	5.31 × 10 <sup>-6</sup>	3.43 × 10 <sup>-7</sup>	5.68 × 10 <sup>-5</sup>	3.49 × 10 <sup>-5</sup>
29	57/AA	3.5	T2   N0   III   II	N	Post	2.06 × 10 <sup>-7</sup>	1.87 × 10 <sup>-5</sup>	9.07 × 10 <sup>-6</sup>	5.50 × 10 <sup>-7</sup>	1.29 × 10 <sup>-5</sup>	9.20 × 10 <sup>-5</sup>
30	68/C	3.2	T2   N0   III   II	Y	Post	2.29 × 10 <sup>-6</sup>	1.56 × 10 <sup>-6</sup>	1.66 × 10 <sup>-6</sup>	1.02 × 10 <sup>-7</sup>	2.32 × 10 <sup>-5</sup>	4.45 × 10 <sup>-5</sup>
31	69/S.Am.	4.5	T2   N2   II   III	N	Post	1.38 × 10 <sup>-6</sup>	6.60 × 10 <sup>-6</sup>	3.01 × 10 <sup>-6</sup>	3.28 × 10 <sup>-5</sup>	3.87 × 10 <sup>-5</sup>	7.41 × 10 <sup>-5</sup>
32	49/?	4.5	T2   N3   I   III	Y	Pre	2.06 × 10 <sup>-7</sup>	4.52 × 10 <sup>-7</sup>	2.01 × 10 <sup>-5</sup>	5.28 × 10 <sup>-7</sup>	6.15 × 10 <sup>-4</sup>	2.46 × 10 <sup>-5</sup>
33	55/C	3.5	T2   N0   III   II	N	Post	6.65 × 10 <sup>-2</sup>	5.07 × 10 <sup>-6</sup>	2.57 × 10 <sup>-6</sup>	4.68 × 10 <sup>-8</sup>	1.69 × 10 <sup>-5</sup>	1.90 × 10 <sup>-5</sup>
34	53/C	4.8	T2   N0   I   II	N	Post	3.17 × 10 <sup>-2</sup>	2.48 × 10 <sup>-3</sup>	1.29 × 10 <sup>-5</sup>	2.95 × 10 <sup>-8</sup>	1.68 × 10 <sup>-5</sup>	2.32 × 10 <sup>-5</sup>
35	42/C	3.2	T2   N2   III   III	N	-	1.82 × 10 <sup>-4</sup>	4.95 × 10 <sup>-7</sup>	4.70 × 10 <sup>-6</sup>	1.26 × 10 <sup>-7</sup>	8.27 × 10 <sup>-5</sup>	3.18 × 10 <sup>-5</sup>
36	28/AA	2.7	T2   N0   I   II	N	Pre	5.11 × 10 <sup>-8</sup>	6.82 × 10 <sup>-6</sup>	6.04 × 10 <sup>-6</sup>	6.21 × 10 <sup>-7</sup>	1.10 × 10 <sup>-5</sup>	1.80 × 10 <sup>-5</sup>
37	65/C	2.5	T2   N0   II   II	N	Post	7.43 × 10 <sup>-4</sup>	5.35 × 10 <sup>-6</sup>	7.22 × 10 <sup>-6</sup>	6.39 × 10 <sup>-8</sup>	1.25 × 10 <sup>-5</sup>	2.58 × 10 <sup>-4</sup>
38	86/AA	10.5	T3   N2   -   III	-	Post	6.20 × 10 <sup>-8</sup>	4.66 × 10 <sup>-6</sup>	9.06 × 10 <sup>-6</sup>	3.96 × 10 <sup>-8</sup>	1.29 × 10 <sup>-5</sup>	5.33 × 10 <sup>-5</sup>
39	49/C	4.2	T2   N0   II   II	N	Pre	2.40 × 10 <sup>-4</sup>	1.56 × 10 <sup>-1</sup>	3.30 × 10 <sup>-5</sup>	5.59 × 10 <sup>-7</sup>	6.10 × 10 <sup>-5</sup>	7.36 × 10 <sup>-5</sup>
40	38/C	1.4	T3   N3   II   III	Y	-	1.42 × 10 <sup>-5</sup>	3.35 × 10 <sup>-5</sup>	7.81 × 10 <sup>-6</sup>	3.89 × 10 <sup>-6</sup>	1.11 × 10 <sup>-4</sup>	7.91 × 10 <sup>-6</sup>

Mean ± SD	Geometric Mean MF					
56.5 ± 14.2	$1.20 \times 10^{-5}$					

**Table S1C.** *PIK3CA*, *KRAS*, *HRAS*, and *BRAF* mutant fraction measurements in HR-/HER2+ ductal carcinomas

ID	Age/Race	Dim.	Max. Tumor	T Stage   N Stage		Smoker	MP	Mutant Fraction					
				Hist. Grade	Clinical Stage			<i>PIK3CA</i>	<i>PIK3CA</i>	<i>KRAS</i>	<i>KRAS</i>	<i>HRAS</i>	<i>BRAF</i>
								H1047R	E545K	G12D	G12V	G12D	V600E
41	48/C	3.4	T2   N1   III   II	N	Pre	1.54 × 10 <sup>-7</sup>	4.08 × 10 <sup>-6</sup>	5.33 × 10 <sup>-6</sup>	1.90 × 10 <sup>-7</sup>	3.18 × 10 <sup>-5</sup>	9.95 × 10 <sup>-5</sup>		
42	48/C	1.9	T1   N0   III   I	-	Pre	9.67 × 10 <sup>-9</sup>	2.98 × 10 <sup>-6</sup>	3.10 × 10 <sup>-6</sup>	5.51 × 10 <sup>-8</sup>	1.08 × 10 <sup>-5</sup>	1.73 × 10 <sup>-5</sup>		
43	85/AA	1.8	T1   N1   III   I	Y	Post	1.67 × 10 <sup>-4</sup>	3.37 × 10 <sup>-6</sup>	7.30 × 10 <sup>-6</sup>	2.08 × 10 <sup>-5</sup>	2.83 × 10 <sup>-5</sup>	3.80 × 10 <sup>-5</sup>		
44	53/C	3.5	T2   N0   III   II	Y	Post	6.84 × 10 <sup>-2</sup>	1.50 × 10 <sup>-5</sup>	2.56 × 10 <sup>-5</sup>	7.72 × 10 <sup>-7</sup>	5.36 × 10 <sup>-5</sup>	5.42 × 10 <sup>-6</sup>		
45	60/C	1.5	T1   N1   -   II	N	Post	4.29 × 10 <sup>-6</sup>	4.58 × 10 <sup>-6</sup>	8.27 × 10 <sup>-5</sup>	2.44 × 10 <sup>-6</sup>	4.44 × 10 <sup>-5</sup>	4.94 × 10 <sup>-6</sup>		
46	54/C	1.6	T1   N-   III   I	N	Post	1.19 × 10 <sup>-7</sup>	3.54 × 10 <sup>-6</sup>	1.51 × 10 <sup>-1</sup>	2.58 × 10 <sup>-4</sup>	2.14 × 10 <sup>-5</sup>	5.45 × 10 <sup>-6</sup>		
47	55/C	0.6	T1   N0   III   I	-	Post	8.60 × 10 <sup>-5</sup>	2.93 × 10 <sup>-6</sup>	4.04 × 10 <sup>-5</sup>	1.81 × 10 <sup>-4</sup>	1.66 × 10 <sup>-5</sup>	8.16 × 10 <sup>-6</sup>		
48	53/C	1.2	T1   N2   II   III	-	Post	7.92 × 10 <sup>-7</sup>	5.83 × 10 <sup>-6</sup>	1.77 × 10 <sup>-5</sup>	2.75 × 10 <sup>-6</sup>	2.04 × 10 <sup>-5</sup>	5.42 × 10 <sup>-6</sup>		
49	57/C	2.4	T2   N0   III   II	-	Post	5.71 × 10 <sup>-8</sup>	7.77 × 10 <sup>-6</sup>	5.12 × 10 <sup>-5</sup>	1.48 × 10 <sup>-7</sup>	1.29 × 10 <sup>-5</sup>	5.93 × 10 <sup>-6</sup>		
50	43/C	1.2	T1   N0   -   I	-	Post	2.28 × 10 <sup>-6</sup>	4.19 × 10 <sup>-6</sup>	5.05 × 10 <sup>-4</sup>	2.78 × 10 <sup>-6</sup>	1.17 × 10 <sup>-5</sup>	5.26 × 10 <sup>-6</sup>		
51	62/C	2.5	T2   N1   III   II	N	Post	5.94 × 10 <sup>-8</sup>	3.92 × 10 <sup>-6</sup>	2.36 × 10 <sup>-5</sup>	4.56 × 10 <sup>-5</sup>	2.46 × 10 <sup>-5</sup>	6.34 × 10 <sup>-6</sup>		
52	55/C	1.7	T1   N0   II   I	Y	Post	8.32 × 10 <sup>-4</sup>	7.23 × 10 <sup>-6</sup>	6.80 × 10 <sup>-5</sup>	3.93 × 10 <sup>-6</sup>	1.48 × 10 <sup>-5</sup>	1.54 × 10 <sup>-5</sup>		
53	50/C	2.5	T2   N1   III   II	-	Post	7.60 × 10 <sup>-8</sup>	4.46 × 10 <sup>-6</sup>	5.17 × 10 <sup>-5</sup>	1.98 × 10 <sup>-6</sup>	9.17 × 10 <sup>-5</sup>	1.56 × 10 <sup>-5</sup>		
54	51/C	2.2	T2   N0   III   II	N	Post	3.80 × 10 <sup>-5</sup>	7.02 × 10 <sup>-6</sup>	1.68 × 10 <sup>-5</sup>	1.27 × 10 <sup>-6</sup>	6.24 × 10 <sup>-5</sup>	8.00 × 10 <sup>-5</sup>		
55	44/C	2.5	T2   N2   III   III	N	Pre	2.37 × 10 <sup>-6</sup>	1.34 × 10 <sup>-1</sup>	1.07 × 10 <sup>-5</sup>	3.89 × 10 <sup>-7</sup>	4.11 × 10 <sup>-6</sup>	8.63 × 10 <sup>-6</sup>		
56	72/C	1.7	T1   N0   II   I	N	Post	3.80 × 10 <sup>-2</sup>	1.66 × 10 <sup>-7</sup>	4.36 × 10 <sup>-5</sup>	5.02 × 10 <sup>-6</sup>	2.38 × 10 <sup>-6</sup>	1.16 × 10 <sup>-5</sup>		
57	71/C	3.0	T2   N2   III   III	N	Post	2.36 × 10 <sup>-6</sup>	5.52 × 10 <sup>-6</sup>	1.68 × 10 <sup>-5</sup>	3.19 × 10 <sup>-5</sup>	7.84 × 10 <sup>-5</sup>	7.62 × 10 <sup>-6</sup>		
58	67/C	2.2	T2   N2   III   III	N	Post	6.75 × 10 <sup>-2</sup>	6.45 × 10 <sup>-6</sup>	1.57 × 10 <sup>-5</sup>	1.04 × 10 <sup>-4</sup>	8.54 × 10 <sup>-5</sup>	7.51 × 10 <sup>-6</sup>		
59	78/C	8.0	T4   N0   III   III	-	Post	7.98 × 10 <sup>-2</sup>	3.87 × 10 <sup>-5</sup>	1.73 × 10 <sup>-5</sup>	2.25 × 10 <sup>-6</sup>	7.50 × 10 <sup>-5</sup>	7.01 × 10 <sup>-5</sup>		
60	48/C	3.2	T2   N1   -   II	-	Pre	1.75 × 10 <sup>-5</sup>	6.00 × 10 <sup>-6</sup>	1.19 × 10 <sup>-5</sup>	1.58 × 10 <sup>-6</sup>	1.67 × 10 <sup>-4</sup>	7.78 × 10 <sup>-6</sup>		
61	69/C	4.0	T2   N0   III   II	Y	Post	4.20 × 10 <sup>-2</sup>	8.60 × 10 <sup>-6</sup>	8.74 × 10 <sup>-6</sup>	1.76 × 10 <sup>-6</sup>	7.15 × 10 <sup>-5</sup>	8.12 × 10 <sup>-6</sup>		

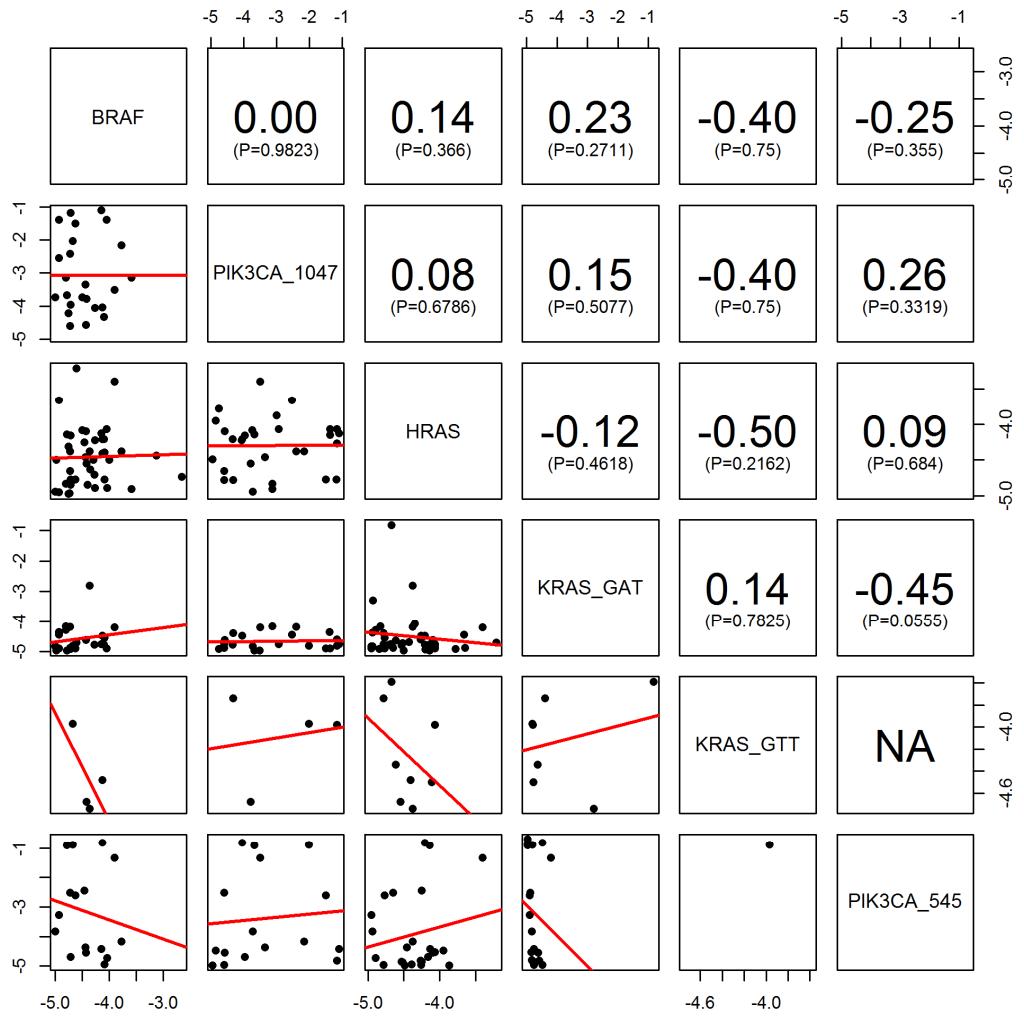
Mean ± SD	Geometric Mean MF					
55.2 ± 11.5	$2.15 \times 10^{-5}$ $7.94 \times 10^{-6}$ $3.47 \times 10^{-5}$ $3.57 \times 10^{-6}$ $2.54 \times 10^{-5}$ $1.19 \times 10^{-5}$					

**Table S1D.** PIK3CA, KRAS, HRAS, and BRAF mutant fraction measurements in HR+/HER2- (TNBC) ductal carcinomas

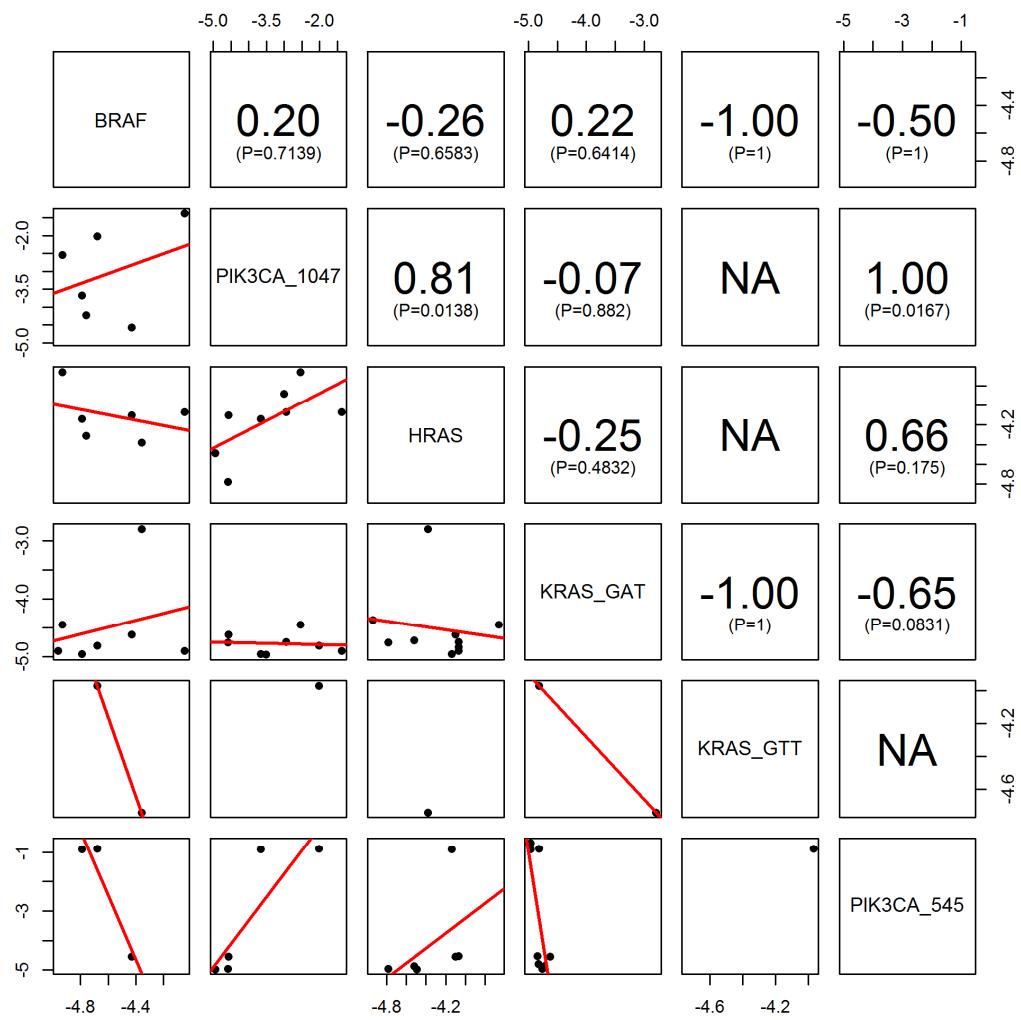
ID	Age/Race	Dim.	Max. Tumor	T Stage   N Stage		Smoker	MP	Mutant Fraction					
				Hist. Grade	Clinical Stage			PIK3CA	PIK3CA	KRAS	KRAS	HRAS	BRAF
								H1047R	E545K	G12D	G12V	G12D	V600E
62	64/C	1.8	T1   N2   III   III	-	Post			$4.44 \times 10^{-4}$	$4.25 \times 10^{-5}$	$3.63 \times 10^{-6}$	$2.75 \times 10^{-6}$	$3.48 \times 10^{-5}$	$3.64 \times 10^{-5}$
63	38/C	2.2	T2   N0   III   II	Y	Pre			$1.17 \times 10^{-8}$	$7.89 \times 10^{-6}$	$3.26 \times 10^{-6}$	$1.86 \times 10^{-7}$	$1.85 \times 10^{-5}$	$2.18 \times 10^{-3}$
64	45/C	1.8	T1   N0   III   I	-	-			$4.31 \times 10^{-8}$	$6.01 \times 10^{-6}$	$3.86 \times 10^{-6}$	$1.41 \times 10^{-6}$	$7.83 \times 10^{-6}$	$1.66 \times 10^{-5}$
65	80/?	4.2	T2   N1   II   II	Y	Post			$3.15 \times 10^{-4}$	$4.58 \times 10^{-2}$	$6.28 \times 10^{-5}$	$1.31 \times 10^{-7}$	$4.01 \times 10^{-4}$	$1.25 \times 10^{-4}$
66	54/C	2.2	T2   N0   III   II	Y	Post			$7.66 \times 10^{-8}$	$7.11 \times 10^{-6}$	$2.90 \times 10^{-5}$	$3.25 \times 10^{-8}$	$1.72 \times 10^{-5}$	$8.07 \times 10^{-5}$
67	70/C	2.7	T2   N1   III   II	-	-			$4.67 \times 10^{-8}$	$9.42 \times 10^{-6}$	$1.19 \times 10^{-5}$	$1.30 \times 10^{-6}$	$1.44 \times 10^{-5}$	$1.90 \times 10^{-5}$
68	52/C	3.0	T2   N0   III   II	Y	Post			$1.05 \times 10^{-6}$	$6.49 \times 10^{-6}$	$8.33 \times 10^{-6}$	$1.70 \times 10^{-7}$	$1.45 \times 10^{-5}$	$3.96 \times 10^{-5}$
69	52/C	1.7	T1   N0   I   I	N	Post			$9.28 \times 10^{-7}$	$1.13 \times 10^{-5}$	$3.32 \times 10^{-5}$	$1.19 \times 10^{-6}$	$5.56 \times 10^{-5}$	$6.10 \times 10^{-6}$
70	48/C	1.8	T1   N0   II   I	N	Pre			$7.94 \times 10^{-8}$	$3.63 \times 10^{-6}$	$1.47 \times 10^{-5}$	$1.23 \times 10^{-7}$	$1.12 \times 10^{-5}$	$5.03 \times 10^{-6}$
71	55/C	3.0	T2   N-   II   II	N	Post			$3.23 \times 10^{-8}$	$8.05 \times 10^{-7}$	$1.07 \times 10^{-5}$	$5.09 \times 10^{-8}$	$3.18 \times 10^{-5}$	$1.05 \times 10^{-5}$
72	45/C	1.8	T1   N0   III   I	-	Pre			$2.40 \times 10^{-8}$	$2.95 \times 10^{-6}$	$1.72 \times 10^{-5}$	$1.59 \times 10^{-6}$	$1.98 \times 10^{-5}$	$5.25 \times 10^{-5}$
73	67/C	1.5	T1   N2   III   III	-	Post			$1.60 \times 10^{-4}$	$2.02 \times 10^{-5}$	$6.37 \times 10^{-6}$	$4.85 \times 10^{-6}$	$6.89 \times 10^{-5}$	$1.91 \times 10^{-5}$
74	40/C	1.1	T2   N0   III   II	-	Pre			$2.57 \times 10^{-4}$	$1.52 \times 10^{-4}$	$1.49 \times 10^{-5}$	$4.25 \times 10^{-6}$	$1.15 \times 10^{-5}$	$1.01 \times 10^{-5}$
75	54/C	1.3	T1   N1   III   II	-	Post			$1.54 \times 10^{-6}$	$5.33 \times 10^{-4}$	$1.27 \times 10^{-5}$	$3.25 \times 10^{-6}$	$1.11 \times 10^{-5}$	$1.16 \times 10^{-5}$
76	67/C	3.5	T2   N0   III   II	Y	Post			$1.04 \times 10^{-7}$	$5.89 \times 10^{-6}$	$2.03 \times 10^{-5}$	$1.62 \times 10^{-6}$	$3.73 \times 10^{-5}$	$7.46 \times 10^{-6}$
77	74/C	2.2	T2   N0   III   II	-	Post			$1.29 \times 10^{-7}$	$5.15 \times 10^{-6}$	$1.16 \times 10^{-5}$	$1.42 \times 10^{-6}$	$6.33 \times 10^{-5}$	$6.86 \times 10^{-6}$
78	59/His.	-	T-   N-   -   -	-	-			$1.46 \times 10^{-6}$	$1.43 \times 10^{-5}$	$1.60 \times 10^{-5}$	$3.03 \times 10^{-6}$	$2.94 \times 10^{-5}$	$7.53 \times 10^{-6}$
79	49/C	3.4	T2   N0   III   II	Y	-			$4.16 \times 10^{-6}$	$1.08 \times 10^{-5}$	$7.44 \times 10^{-6}$	$9.67 \times 10^{-7}$	$1.35 \times 10^{-4}$	$7.88 \times 10^{-6}$
80	62/C	3.8	T2   N0   III   II	Y	-			$6.07 \times 10^{-7}$	$1.43 \times 10^{-5}$	$8.95 \times 10^{-6}$	$1.70 \times 10^{-6}$	$5.66 \times 10^{-5}$	$7.87 \times 10^{-6}$
81	43/C	4.0	T2   N0   III   II	-	-			$9.53 \times 10^{-8}$	$7.54 \times 10^{-6}$	$1.32 \times 10^{-5}$	$7.51 \times 10^{-6}$	$2.23 \times 10^{-4}$	$7.50 \times 10^{-6}$

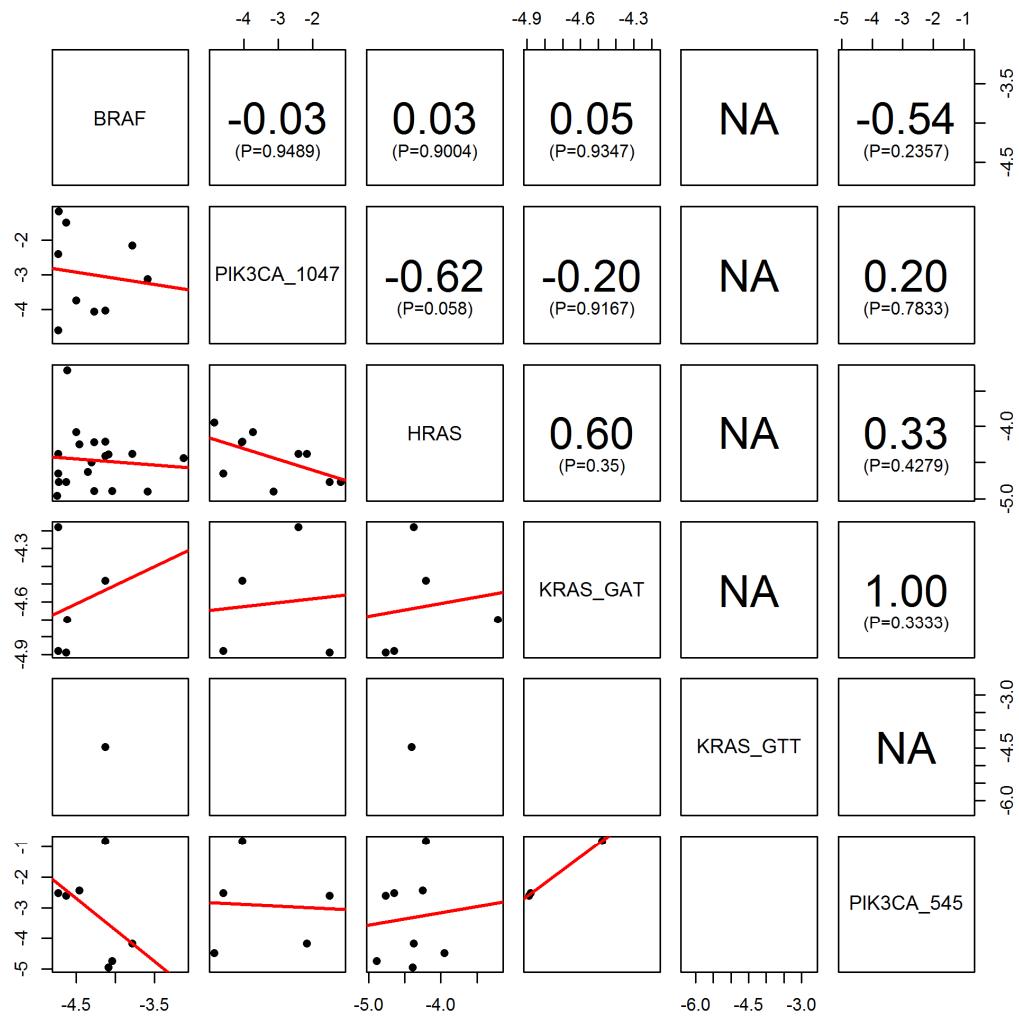
Mean ± SD				Geometric Mean MF							
$55.90 \pm 11.6$				$7.64 \times 10^{-7}$							



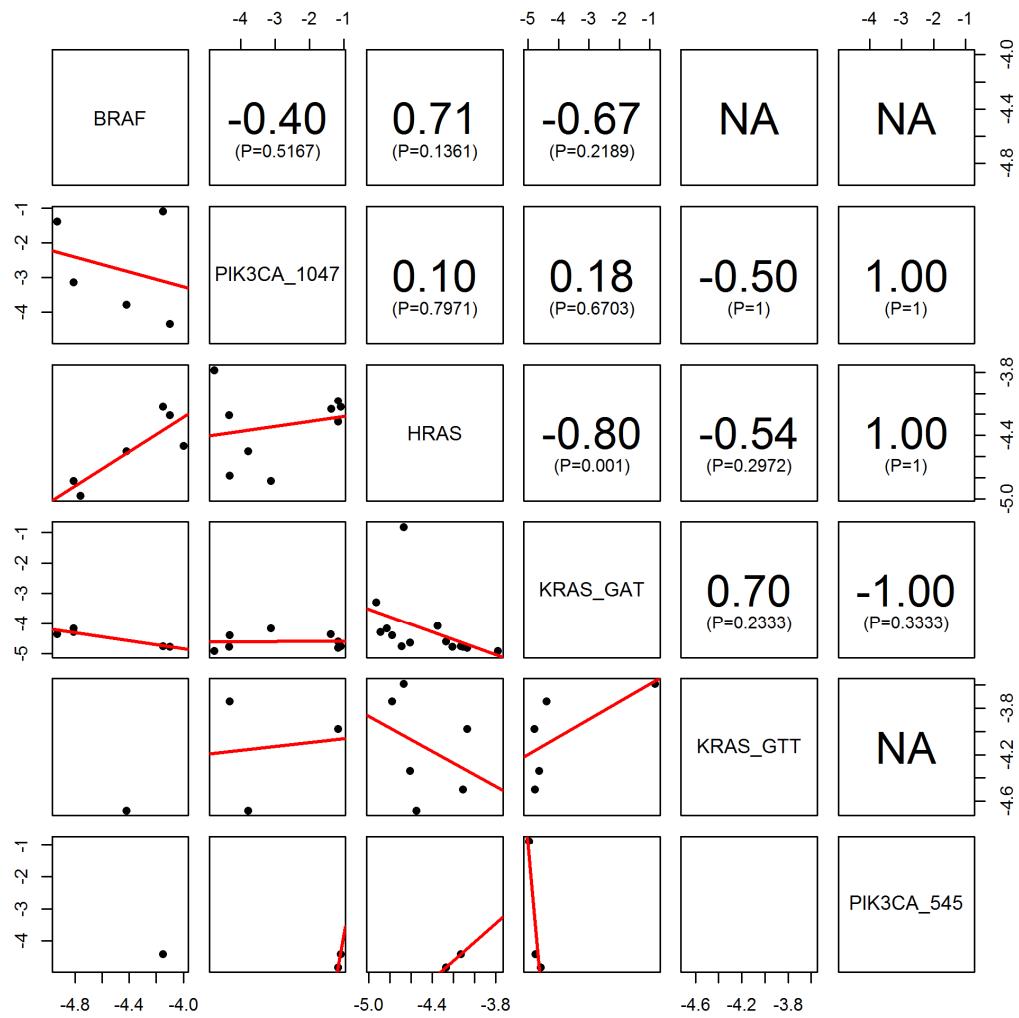
**Figure S1A.** Correlation matrix of MFs in ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



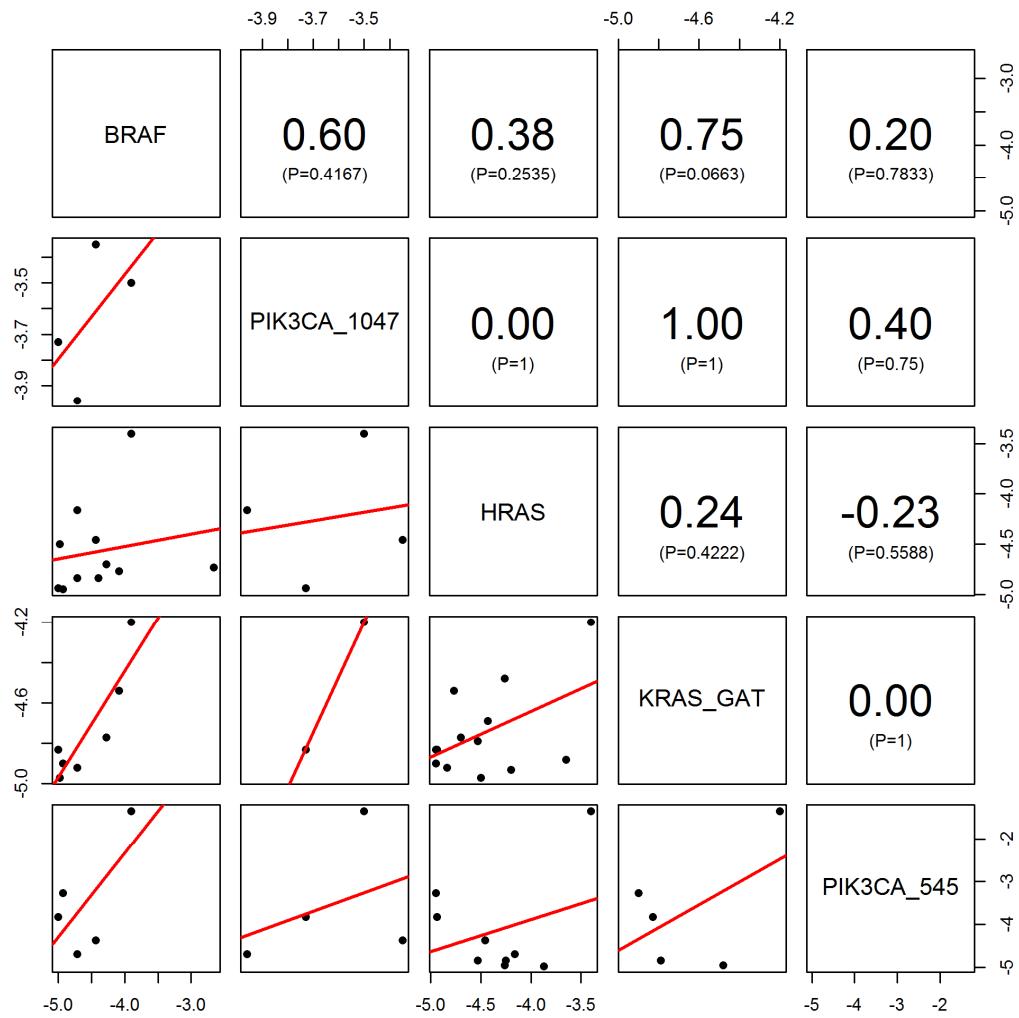
**Figure S1B.** Correlation matrix of MFs in HR+/HER2+ ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



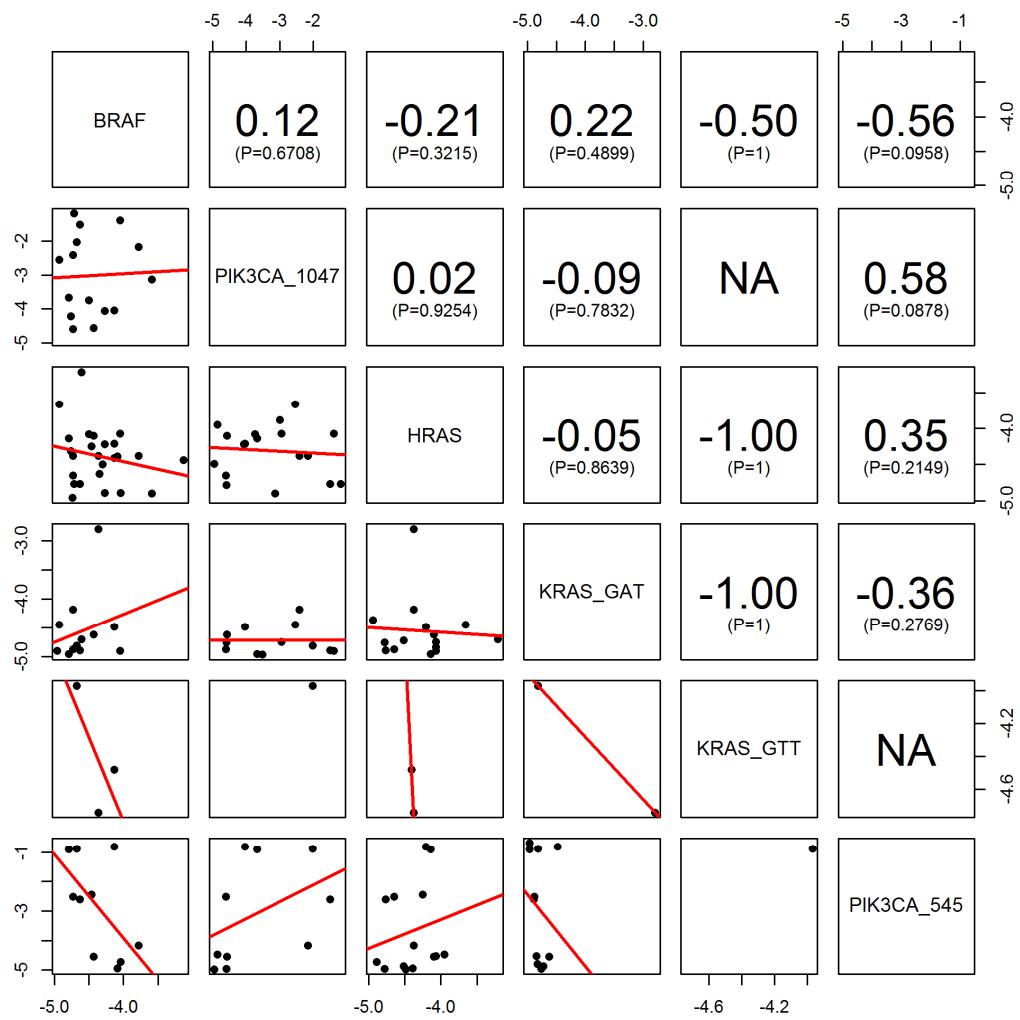
**Figure S1C.** Correlation matrix of MFs in HR+/HER2- ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



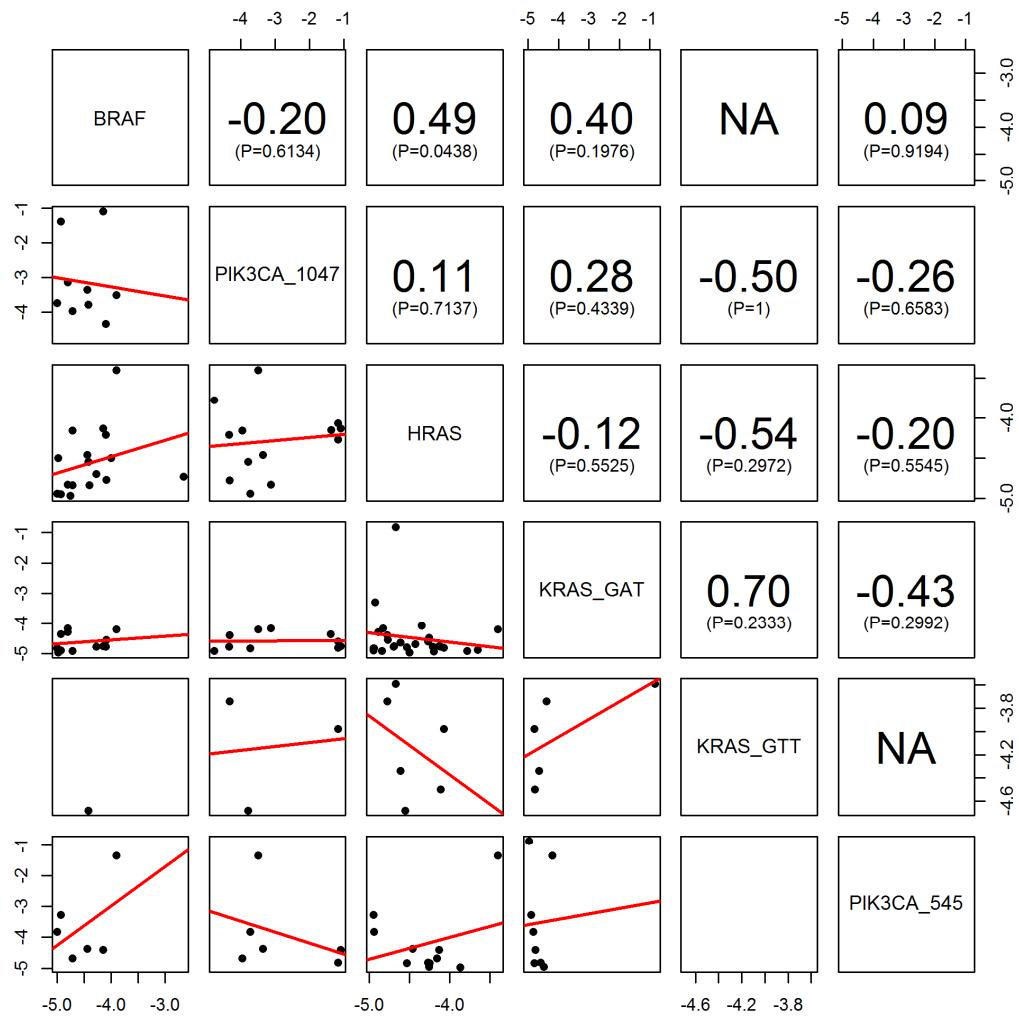
**Figure S1D.** Correlation matrix of MFs in HR-/HER2+ ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



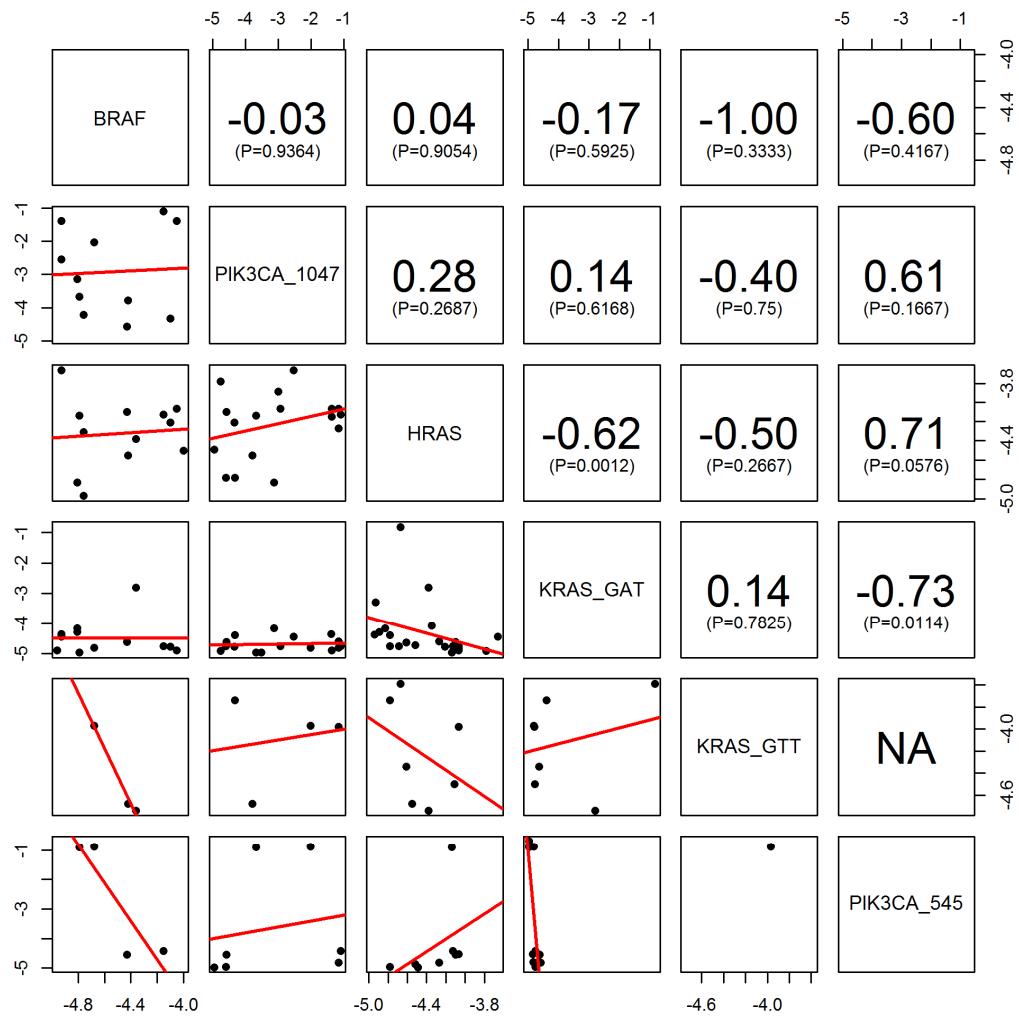
**Figure S1E.** Correlation matrix of MFs in HR-/HER2- (TNBC) ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



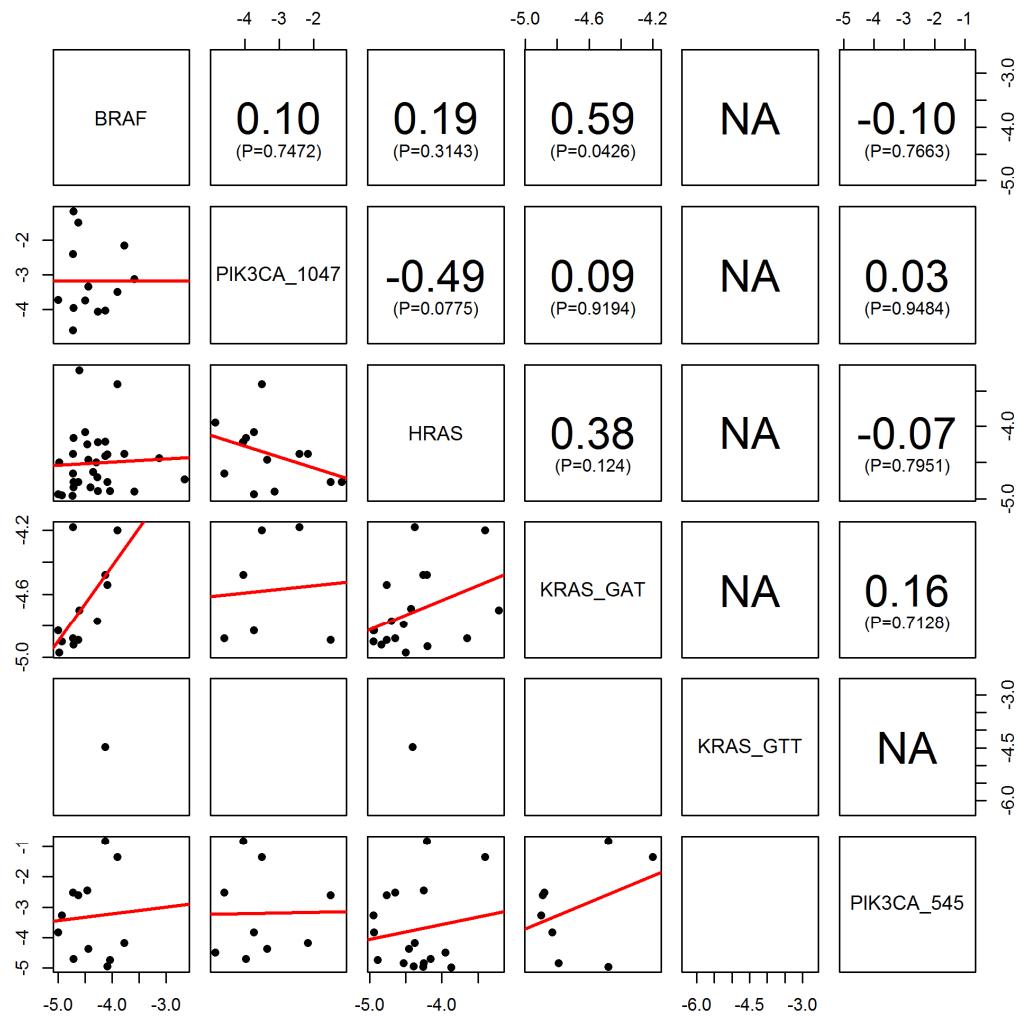
**Figure S1F.** Correlation matrix of MFs in ER+ ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



**Figure S1G.** Correlation matrix of MFs in ER- ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



**Figure S1H.** Correlation matrix of MFs in HER2+ ductal carcinomas: *PIK3CA* H1047R (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS* G12D (KRAS\_GAT) and G12V (GTT), *HRAS* G12D (HRAS), and *BRAF* V600E (BRAF).



**Figure S1I.** Correlation matrix of MFs in HER2- ductal carcinomas: *PIK3CA H1047R* (PIK3CA\_1047) and E545K (PIK3CA\_545), *KRAS G12D* (KRAS\_GAT) and G12V (GTT), *HRAS G12D* (HRAS), and *BRAF V600E* (BRAF).