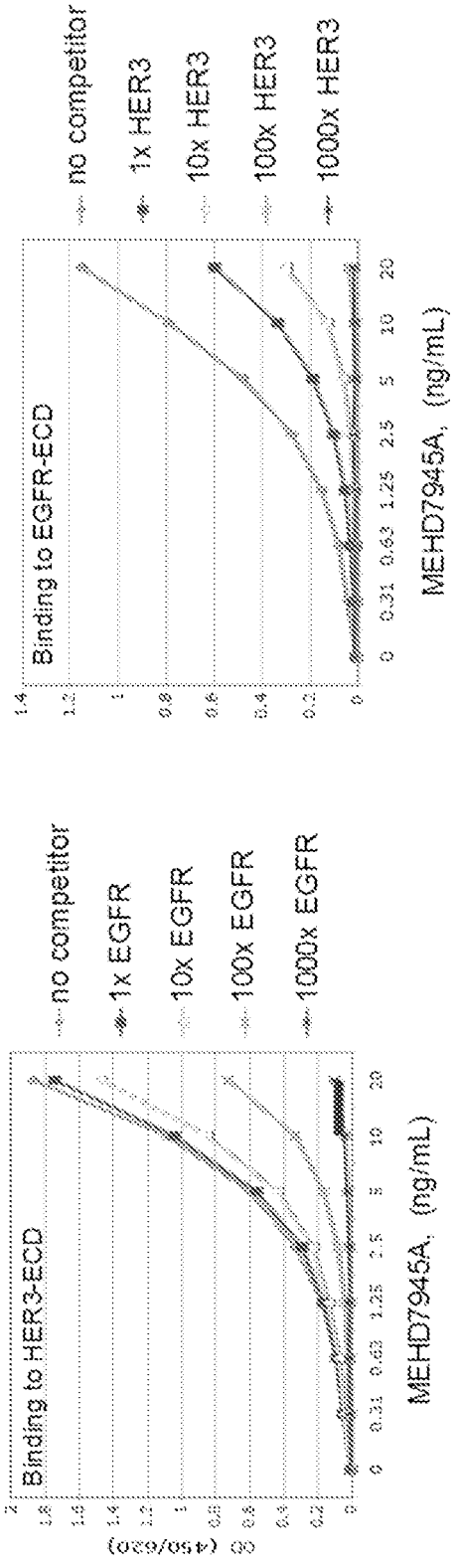

Binding to HER3-ECD
OD (450/620)
MEHD7945A, (ng/mL)
no competitor
1x EGFR
10x EGFR
100x EGFR
1000x EGFR
Binding to EGFR-ECD
MEHD7945A, (ng/mL)
no competitor
1x HER3
10x HER3
100x HER3
1000x HER3

FIG. 1

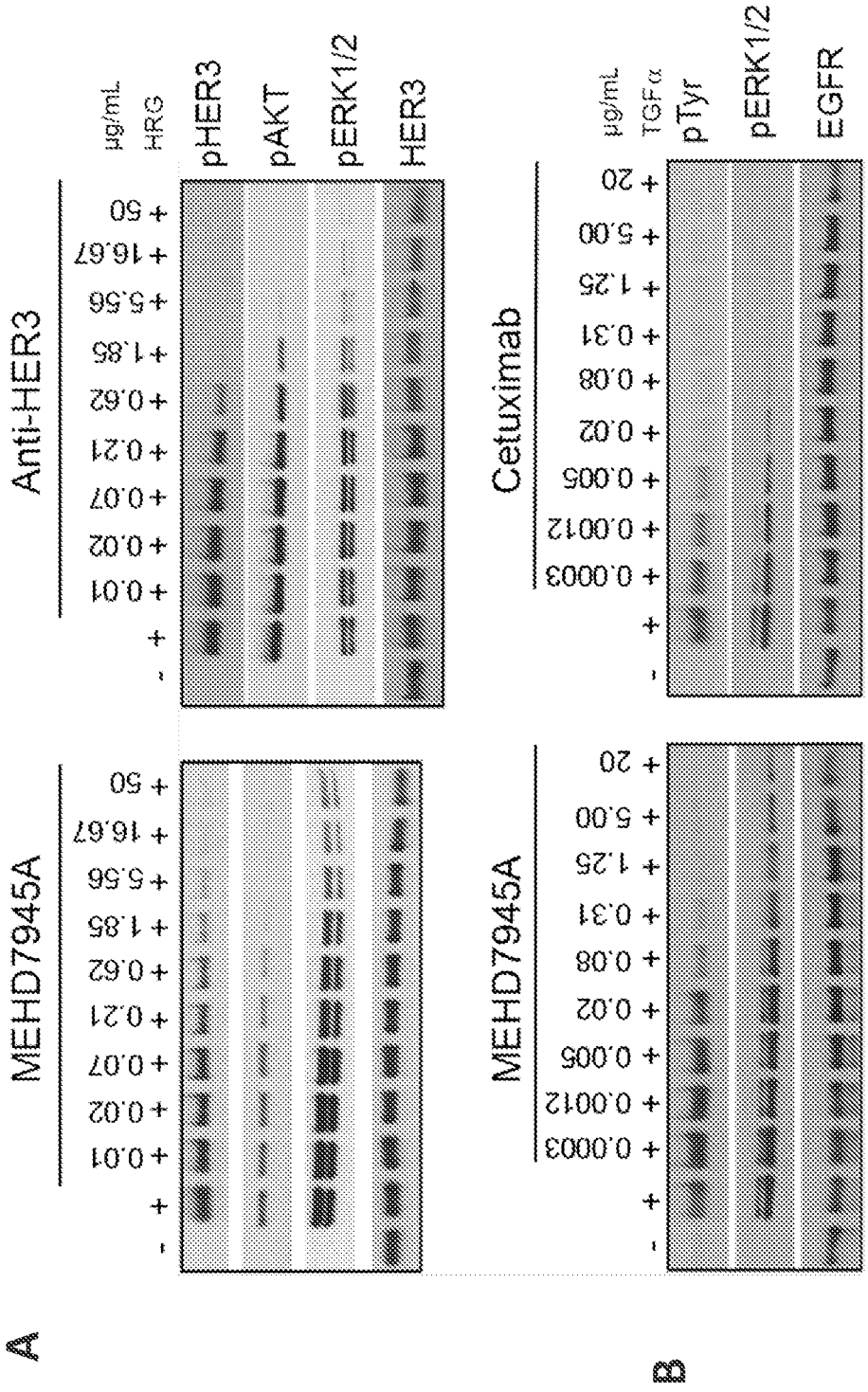

A
Anti-HER3
MEHD7945A
HRG
µg/mL
-
+
+ 0.01
+ 0.02
+ 0.07
+ 0.21
+ 0.62
+ 1.85
+ 5.56
+ 16.67
+ 50
pHER3
pAKT
pERK1/2
HER3
B
Cetuximab
MEHD7945A
TGFα
µg/mL
-
+
+ 0.0003
+ 0.0012
+ 0.005
+ 0.02
+ 0.08
+ 0.31
+ 1.25
+ 5.00
+ 20
pTyr
pERK1/2
EGFR

FIG. 2

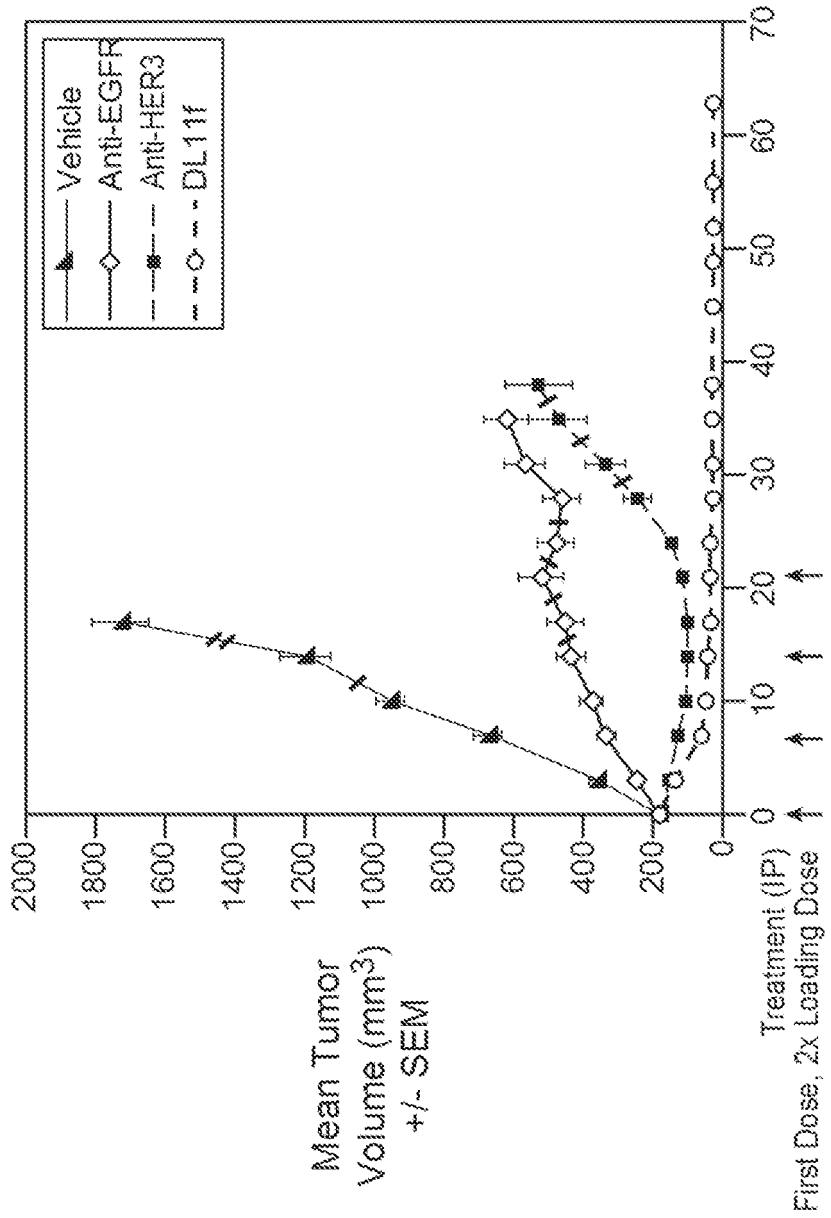

Vehicle
Anti-EGFR
Anti-HER3
DL11f
Mean Tumor Volume (mm^3) +/- SEM
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
70
Time (Days)
Treatment (IP)
First Dose, 2x Loading Dose

FIG. 3

Model	phenotype	Cetuximab	MEHD7945A	anti-HER3	Cetuximab + anti-HER3
NCI-H292	NSCLC	+++	+++	-	n/a
NCI-H1975	NSCLC	+++	+++	-	n/a
SW948	CRC	++	++	+	n/a
OVXF550	ovarian	++	++	++	++
A431	epidermoid	+++	+++	++	n/a
Cal27	HNSCC	+++	+++	++	n/a
FaDu	HNSCC	++	+++	+++	n/a
LXF983	NSCLC	++	+++	++	+++
MAXF449	breast	-	+++	+++	+++
A549	NSCLC	-	++	+	+++
Calu-3	NSCLC	-	++	+	++
BxPC3	pancreas	-	++	+	n/a

FIG. 4

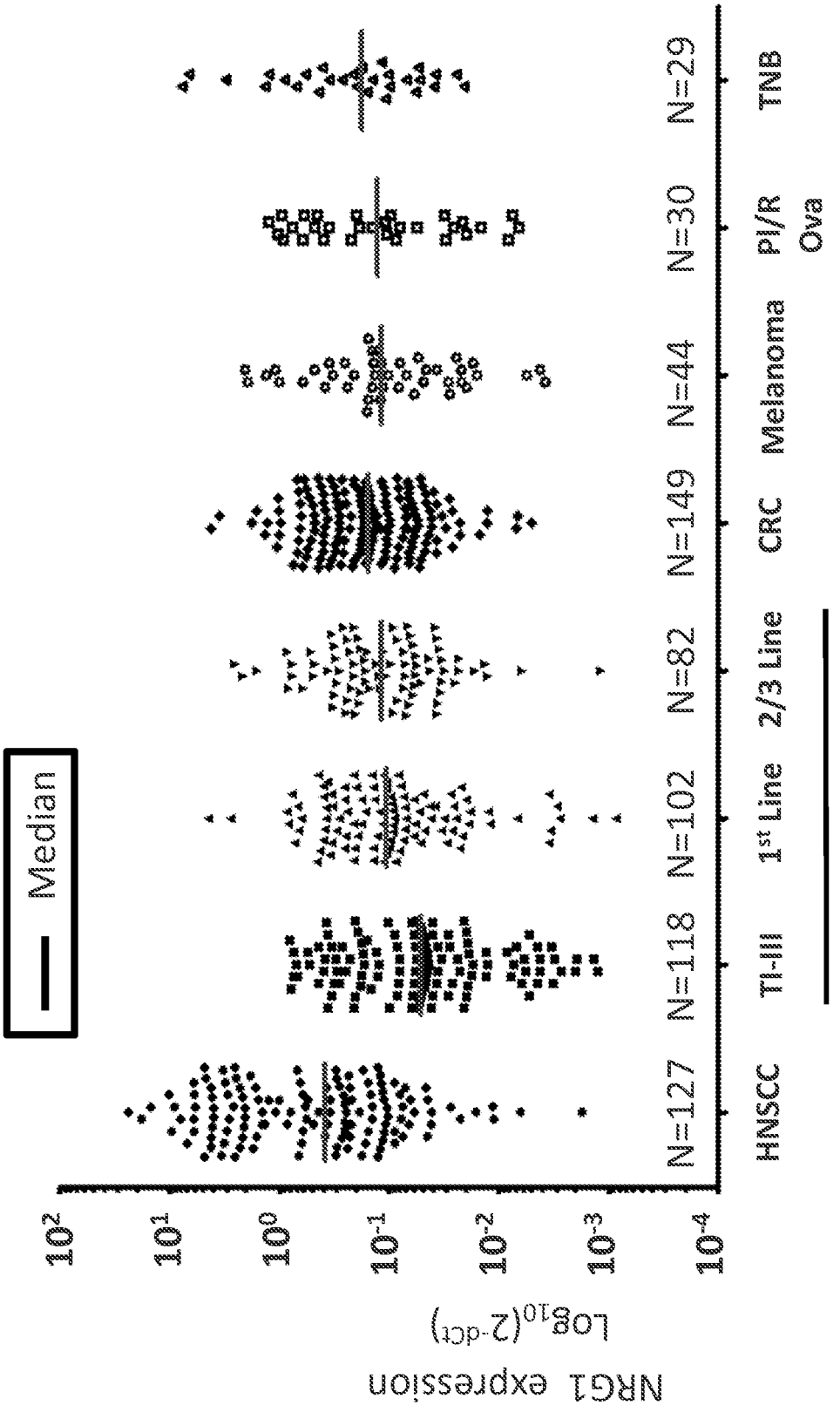

NRG1 expression
$Log_{10}(2^{-dCt})$
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}
10^{-4}
Median
N=127
N=118
N=102
N=82
N=149
N=44
N=30
N=29
HNSCC
TI-IIII
1st Line
2/3 Line
CRC
Melanoma
PI/R Ova
TNB
NSCLC

FIG. 5A

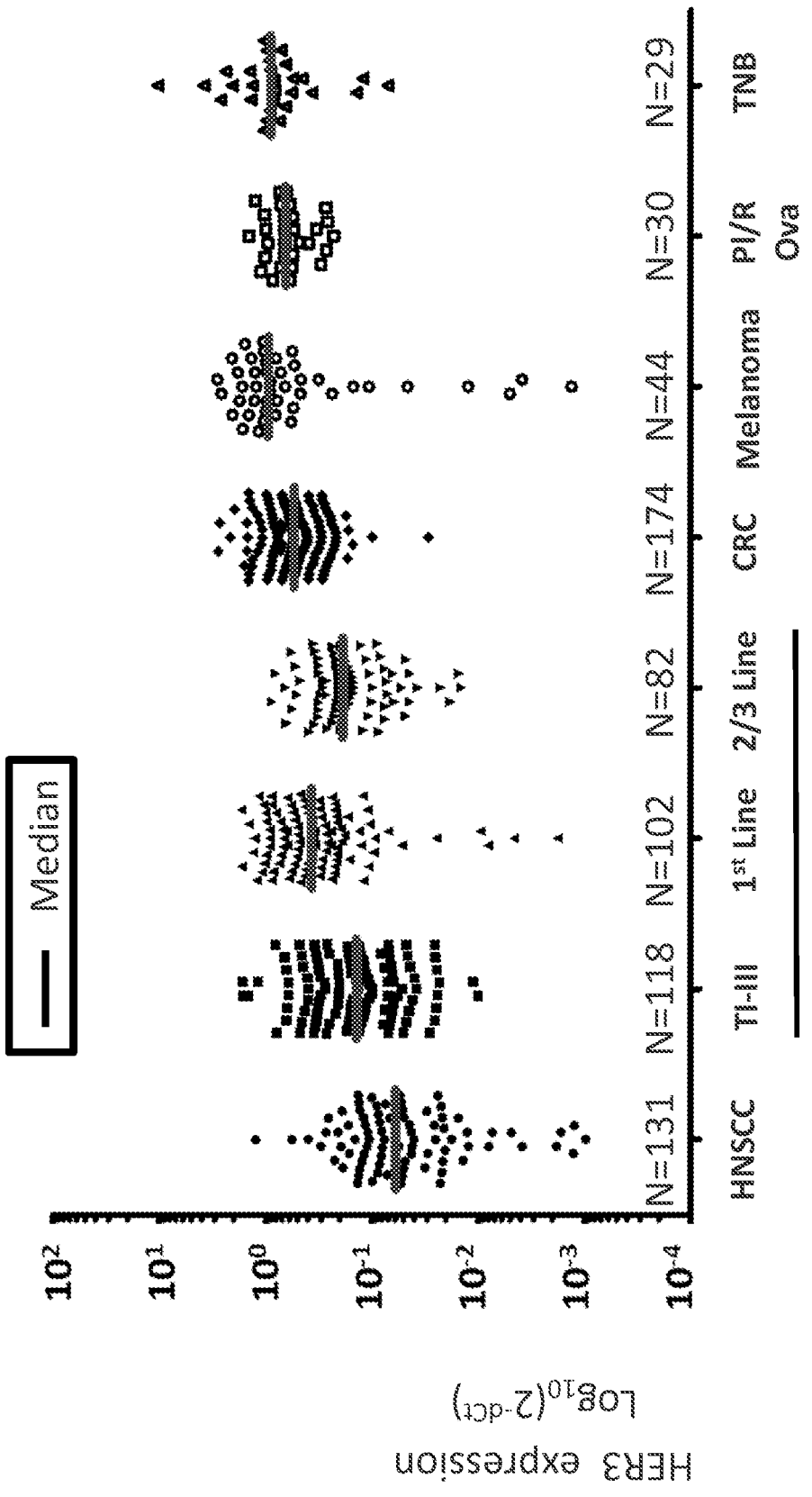

HER3 expression
$Log_{10}(2^{-dCt})$
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}
10^{-4}
Median
N=131
N=118
N=102
N=82
N=174
N=44
N=30
N=29
HNSCC
TI-IIII
1st Line
2/3 Line
CRC
Melanoma
PI/R Ova
TNB
NSCLC

FIG. 5B

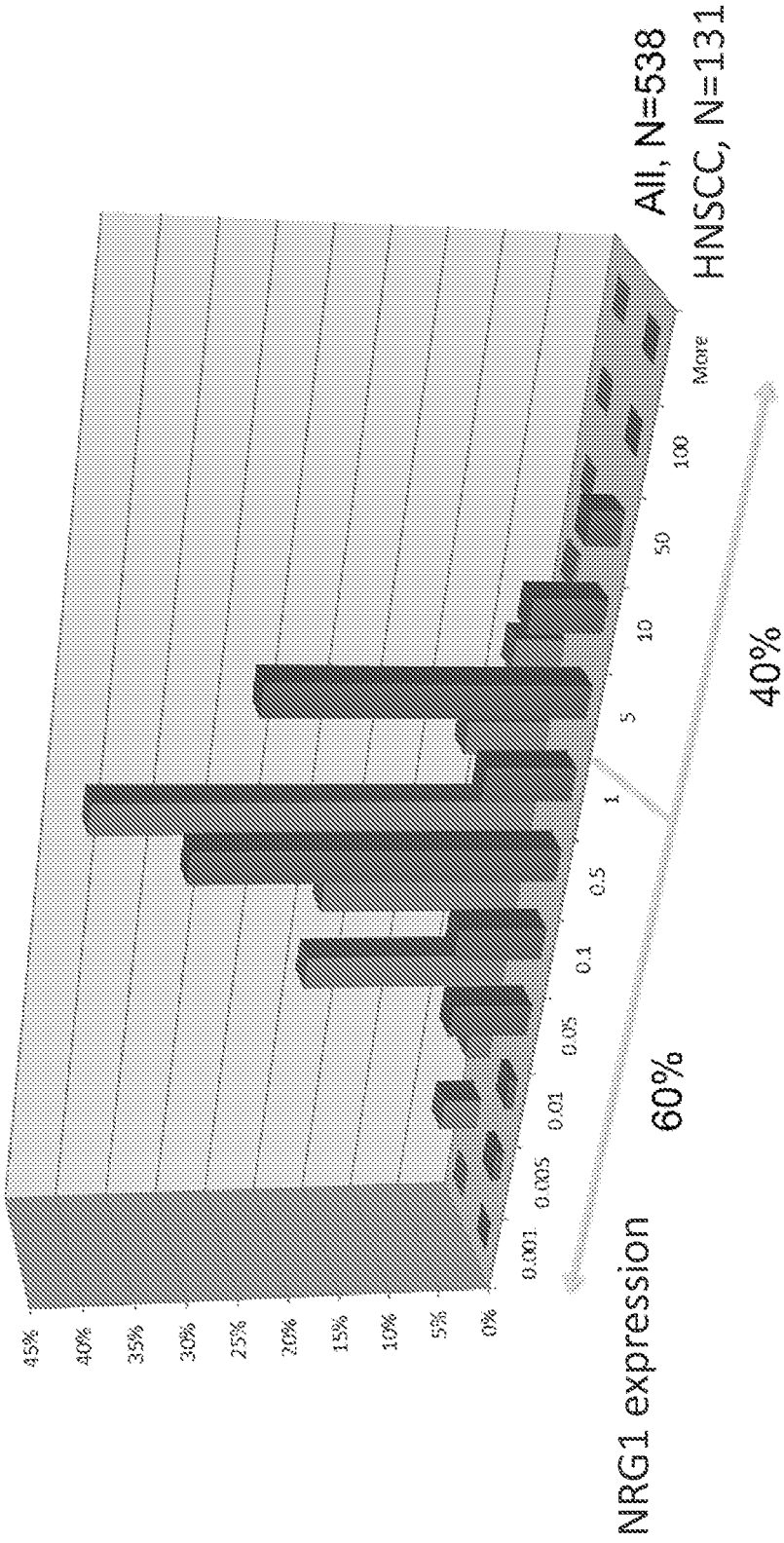

All, N=538
HNSCC, N=131
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
0.001
0.005
0.01
0.05
0.1
0.5
1
5
10
50
100
More
NRG1 expression
60%
40%

FIG. 6

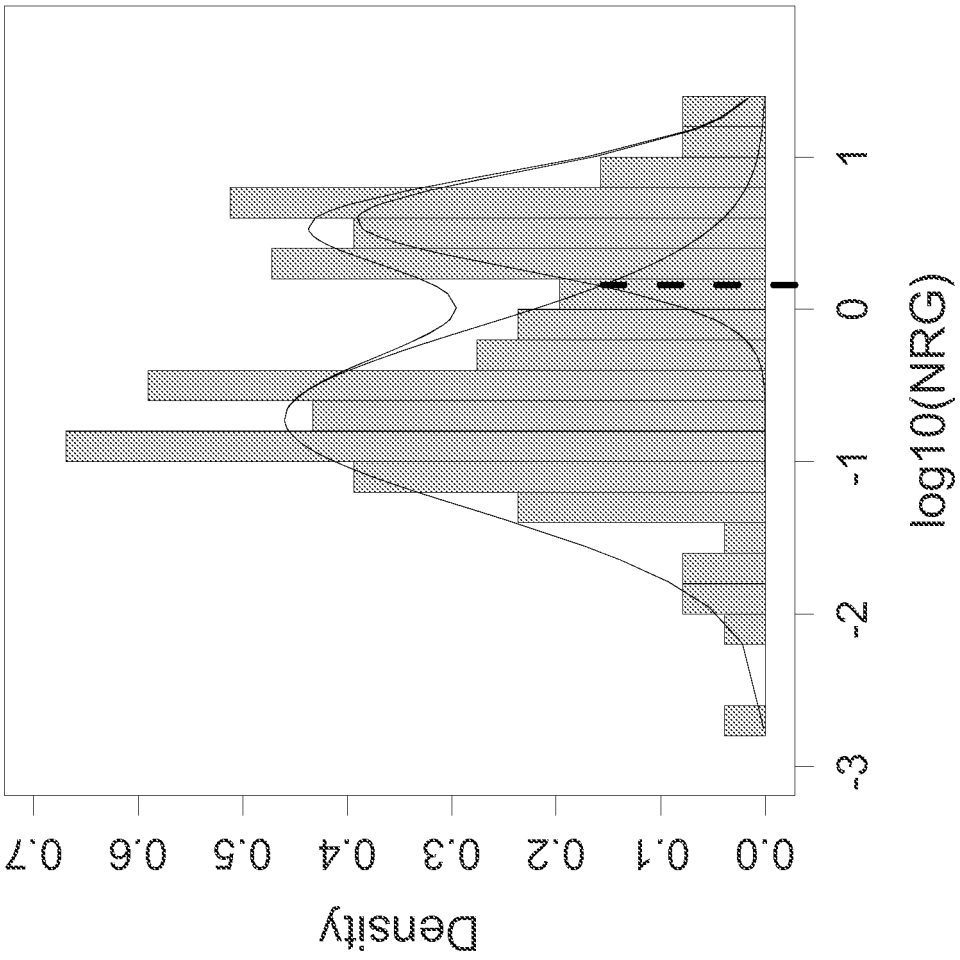


FIG. 7

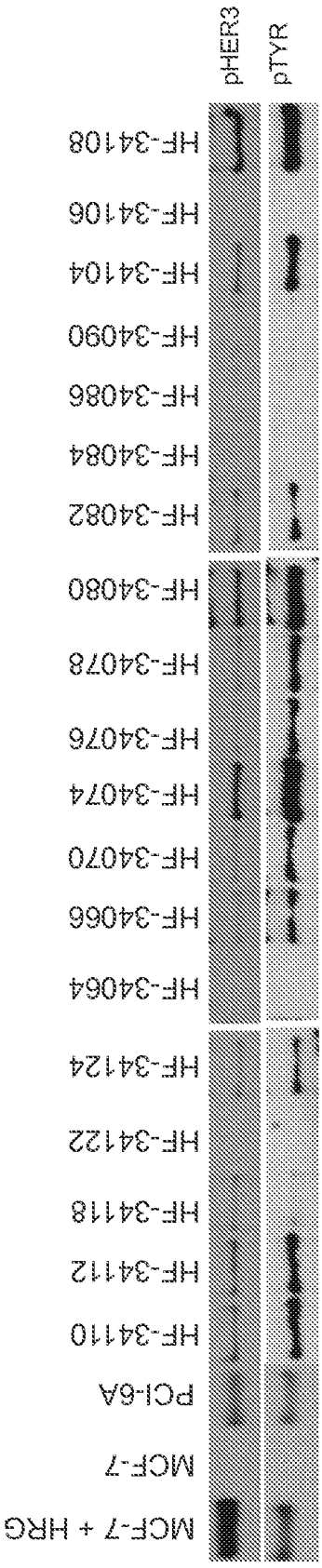

pHER3
pTYR
HF-34108
HF-34106
HF-34104
HF-34090
HF-34086
HF-34084
HF-34082
HF-34080
HF-34078
HF-34076
HF-34074
HF-34070
HF-34066
HF-34064
HF-34124
HF-34122
HF-34118
HF-34112
HF-34110
PCI-6A
MCF-7
MCF-7 + HRG

FIG. 8

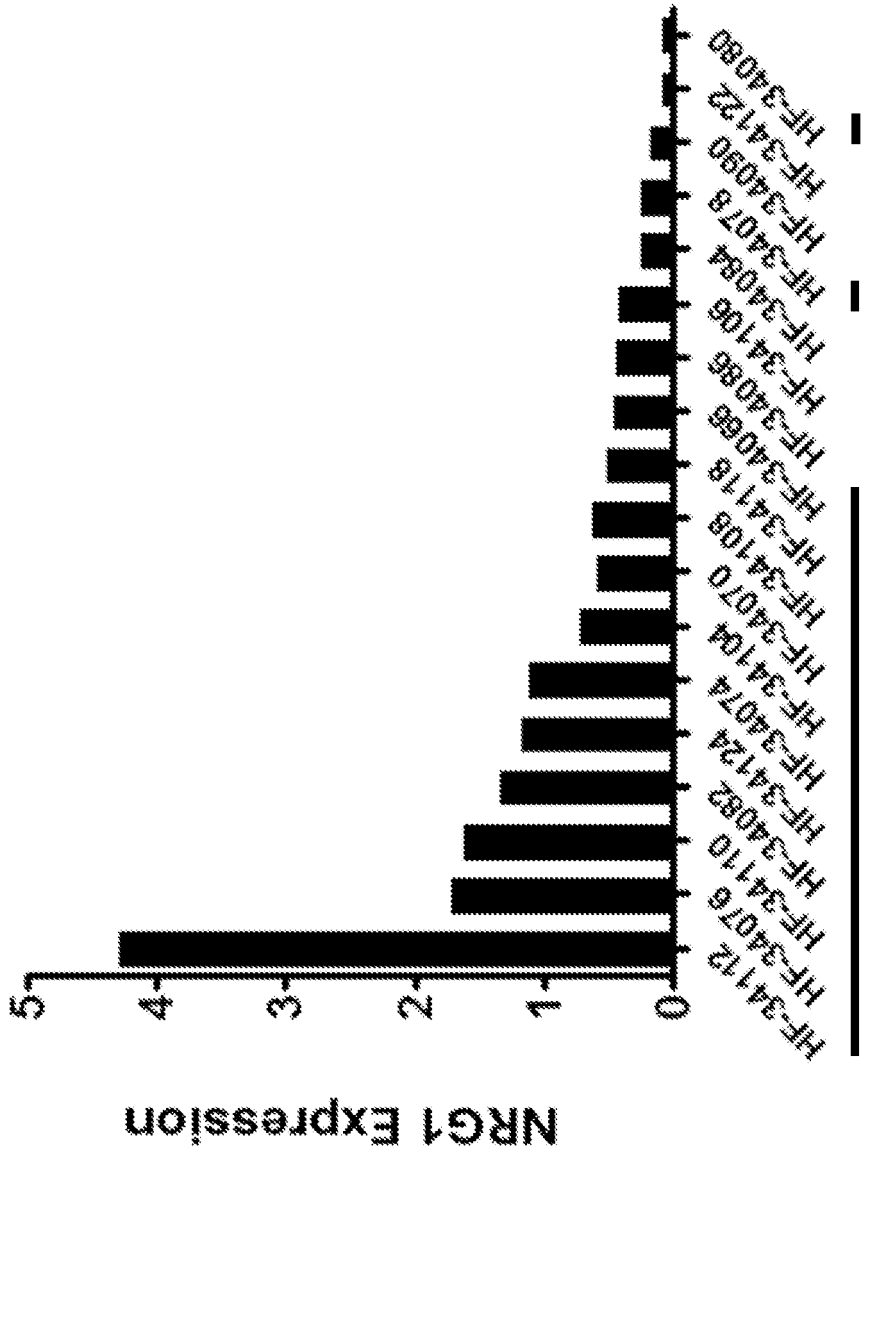

NRG1 Expression
0
1
2
3
4
5
HF_3412
HF_340F6
HF_34110
HF_340B2
HF_34124
HF_340F4
HF_34104
HF_340F0
HF_34108
HF_34118
HF_340E6
HF_340B6
HF_34106
HF_340B4
HF_340F8
HF_340B0
HF_34122
HF_340E0
Positive by IP-western

FIG. 9

Primary	NRG1	HER3	% Autocrine MatLab	Recurrance	PT ID	NRG1	HER3	% Autocrine MatLab
Primary1	0.768	2.055	8.4%	Recurrance1	10720/10	2.381	5.703	10.1%
Primary2	13.705	3.361	4.4%	Recurrance2	12777/08	4.093	5.829	4.3%
Primary3	1.769	4.884	7.6%	Recurrance3	13174/10	7.176	6.149	15.0%
Primary4	8.985	0.621	#N/A	Recurrance4	13699/10	36.133	2.017	10.0%
Primary5	2.028	11.678	#N/A	Recurrance5	14972/10	3.527	12.438	12.7%
Primary6	0.455	6.577	3.2%	Recurrance6	1555/10	0.770	6.885	2.1%
Primary7	3.280	3.074	#N/A	Recurrance7	15706/09	6.320	5.485	5.5%
Primary8	1.920	4.229	24.0%	Recurrance8	1611/10	3.904	5.505	#N/A
Primary9	1.741	1.456	17.4%	Recurrance9	17651/09	40.271	6.633	6.9%
Primary10	1.008	3.094	5.5%	Recurrance10	18742/09	1.801	3.950	#N/A
Primary11	5.909	5.099	8.0%	Recurrance11	1955/10	6.930	9.085	2.9%
Primary12	7.715	4.347	9.9%	Recurrance12	20391/09	7.145	7.664	1.8%
Primary13	0.837	6.161	14.9%	Recurrance13	20696/08	5.441	5.691	14.0%
Primary14	1.254	0.343	5.4%	Recurrance14	2141/08	2.174	2.398	#N/A
Primary15	8.883	2.141	0.3%	Recurrance15	21563/08	14.431	3.131	6.6%
Primary16	18.102	7.724	27.3%	Recurrance16	22612/08	6.186	2.908	1.9%
Primary17	0.978	7.119	16.6%	Recurrance17	2327/11	1.079	8.241	11.0%
Primary18	0.252	1.328	9.6%	Recurrance18	2783/11	0.719	4.410	8.0%
Primary19	0.479	2.534	#N/A	Recurrance19	2851/11	1.016	2.812	17.8%
Primary20	5.751	3.899	#N/A	Recurrance20	3549/11	44.208	3.283	14.7%
Primary21	0.149	2.319	7.7%	Recurrance21	6106/10	4.760	5.350	13.9%
Primary22	0.683	0.030	1.5%	Recurrance22	6310/09	0.426	0.073	0.4%
Primary23	2.683	2.161	18.5%	Recurrance23	6539/08	1.010	8.169	4.5%
Primary24	3.010	1.336	1.4%	Recurrance24	6653/10	8.250	2.029	22.1%
Primary25	0.272	2.395	0.3%	Recurrance25	7824/09	2.620	1.903	#N/A
Primary26	2.349	11.530	18.6%	Recurrance26	7983/09	37.507	2.387	4.4%
Primary27	8.014	7.472	25.6%	Recurrance27	9500/10	10.063	5.412	48.3%
Primary28	1.235	4.954	8.9%	Recurrance28	9856/07	8.718	1.713	11.3%

FIG. 10

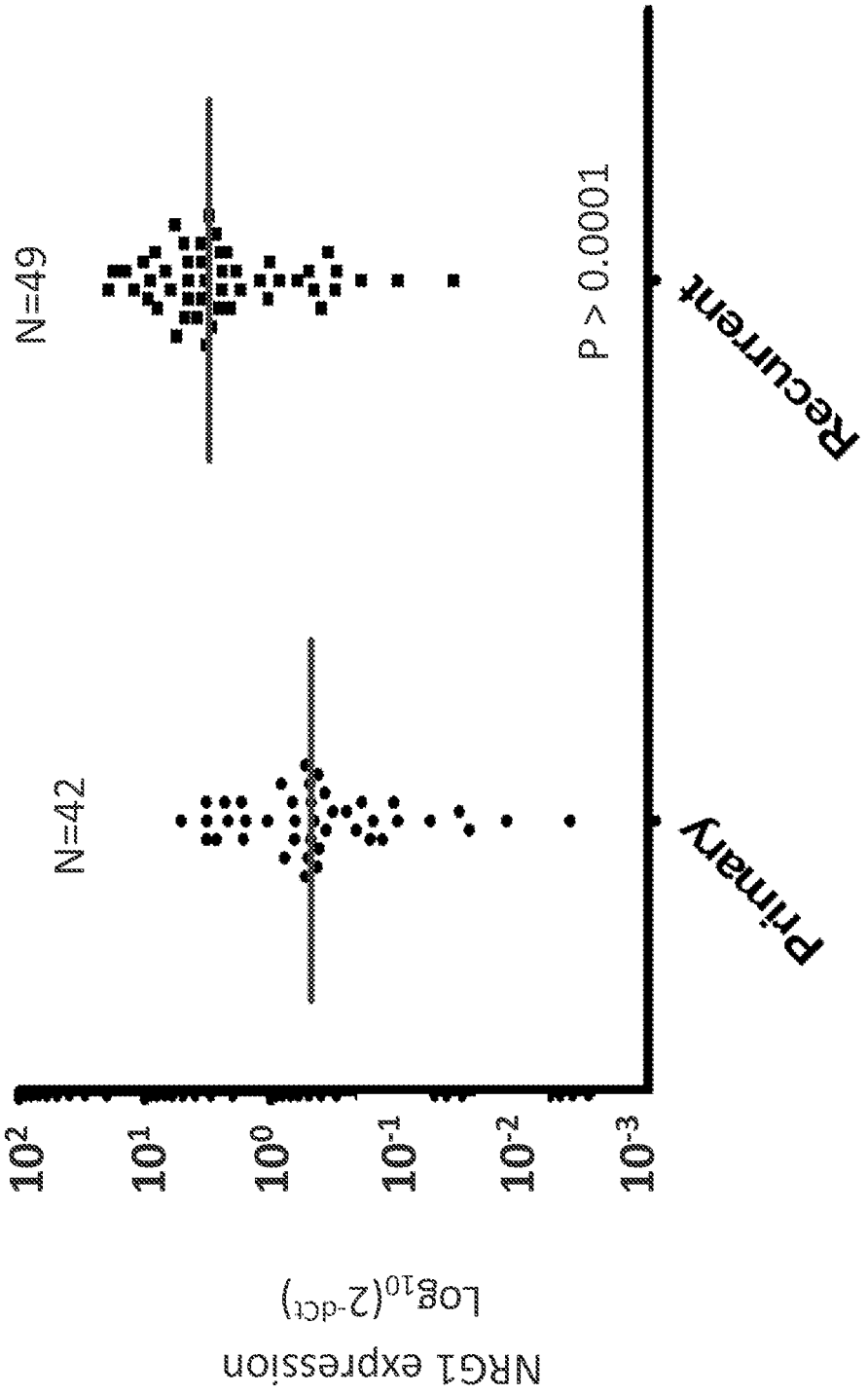

NRG1 expression
$Log_{10}(2^{-dCt})$
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
10^{-3}
N=42
N=49
P > 0.0001
Primary
Recurrent

FIG. 11

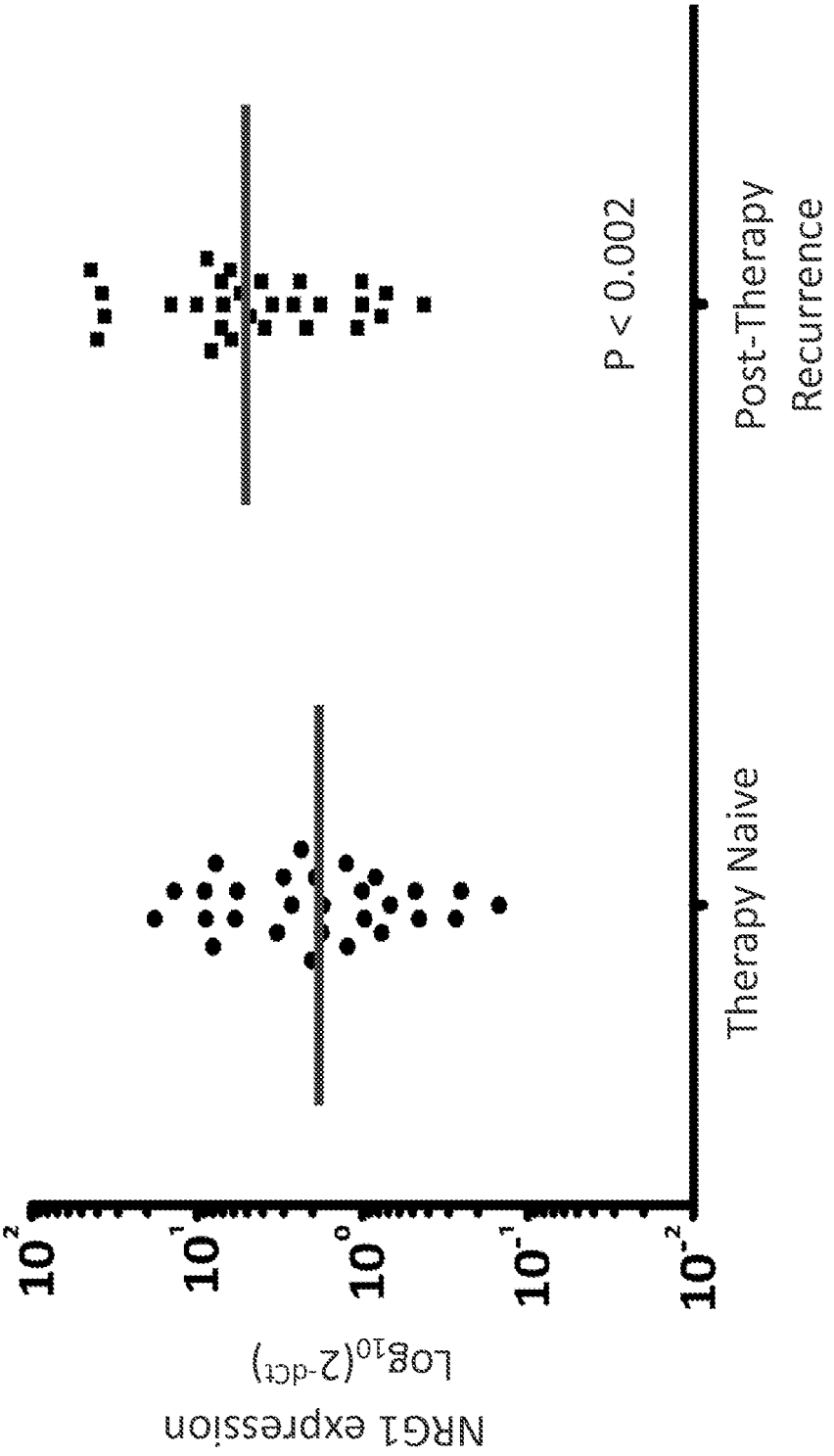

NRG1 expression
$Log_{10}(2^{-dCt})$
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-2}
Therapy Naive
Post-Therapy Recurrence
P < 0.002

FIG. 12

Comparison	Rx Naïve	Post-Rx	Signficance*
NRG1	3.72 (1.99 - 4.45)	9.61 (4.6 - 14.62)	0.002
HER3	4.07 (2.9 - 4.24)	4.9 (3.84 - 5.96)	0.026
Autocrine (MatLab)	10.65 (7.12 - 14.19)	10.43 (6.62 - 14.59)	NS
Autocrine (Definiens Cells)	38.04 (31.68 - 44.41)	37.4 (30.59 - 44.21)	NS
Autocrine (Definiens Area)	26.89 (21.01 - 32.77)	26.25 (19.65 - 32.85)	NS

*Wilcoxon rank sign test for paired samples

FIG. 13

Primary	NRG1	HER3	% Autocrine			Recurrance	NRG1	HER3	% Autocrine		
			MatLab	Tumor Cells*	Tumor Area*				MatLab	Tumor Cells*	Tumor Area*
Rx Naive 1	0.768	2.055	8.4%	38.0%	19.2%	Post-Chemo 1	2.381	5.703	10.1%	36.8%	27.5%
Rx Naive 2	13.705	3.361	4.4%	21.3%	10.3%	Post-Chemo 2	4.093	5.829	4.3%	17.9%	8.3%
Rx Naive 3	1.769	4.884	7.6%	27.6%	13.6%	Post-Chemo 3	7.176	6.149	15.0%	36.9%	24.8%
Rx Naive 4	8.985	0.621	#N/A	#N/A	#N/A	Post-Chemo 4	36.133	2.017	10.0%	34.6%	24.0%
Rx Naive 5	2.026	11.678	#N/A	#N/A	#N/A	Post-Chemo 5	3.527	12.438	12.7%	40.4%	25.0%
Rx Naive 6	0.455	6.577	3.2%	41.8%	29.7%	Post-Chemo 6	0.770	6.885	2.1%	42.9%	27.9%
Rx Naive 7	3.280	3.074	#N/A	#N/A	#N/A	Post-Chemo 7	6.320	5.485	5.5%	30.0%	15.7%
Rx Naive 8	1.920	4.229	24.0%	47.6%	39.1%	Post-Chemo 8	3.904	5.505	#N/A	#N/A	#N/A
Rx Naive 9	1.741	1.456	17.4%	40.3%	31.5%	Post-Chemo 9	40.271	6.633	6.9%	37.5%	24.7%
Rx Naive 10	1.008	3.094	5.5%	35.7%	23.3%	Post-Chemo 10	1.801	3.950	#N/A	#N/A	#N/A
Rx Naive 11	5.909	5.099	8.0%	31.8%	20.9%	Post-Chemo 11	6.930	9.085	2.9%	23.9%	12.7%
Rx Naive 12	7.715	4.347	9.9%	31.3%	18.9%	Post-Chemo 12	7.145	7.664	1.8%	10.9%	3.5%
Rx Naive 13	0.837	6.161	14.9%	54.9%	45.9%	Post-Chemo 13	5.441	5.691	14.0%	32.3%	18.7%
Rx Naive 14	1.254	0.343	5.4%	26.7%	17.2%	Post-Chemo 14	2.174	2.398	#N/A	#N/A	#N/A
Rx Naive 15	8.883	2.141	0.3%	7.8%	3.7%	Post-Chemo 15	14.431	3.131	5.6%	26.5%	14.9%
Rx Naive 16	18.102	7.724	27.3%	58.6%	38.5%	Post-Chemo 16	6.186	2.908	1.9%	13.0%	5.9%
Rx Naive 17	0.978	7.119	16.6%	46.0%	37.6%	Post-Chemo 17	1.079	8.241	11.0%	37.1%	27.1%
Rx Naive 18	0.252	1.328	9.6%	53.9%	39.3%	Post-Chemo 18	0.719	4.410	8.0%	67.1%	56.5%
Rx Naive 19	0.479	2.534	#N/A	#N/A	#N/A	Post-Chemo 19	1.016	2.812	17.8%	62.4%	48.5%
Rx Naive 20	5.751	3.899	#N/A	#N/A	#N/A	Post-Chemo 20	44.208	3.283	14.7%	51.3%	43.5%
Rx Naive 21	0.149	2.319	7.7%	35.6%	22.7%	Post-Chemo 21	4.760	5.350	13.9%	47.3%	37.0%
Rx Naive 22	0.683	0.030	1.5%	8.9%	3.0%	Post-Chemo 22	0.426	0.073	0.4%	16.5%	6.4%
Rx Naive 23	2.683	2.161	18.5%	60.2%	48.3%	Post-Chemo 23	1.010	8.169	4.5%	43.0%	30.0%
Rx Naive 24	3.010	1.336	1.4%	41.0%	28.2%	Post-Chemo 24	8.250	2.029	22.1%	56.6%	44.0%
Rx Naive 25	0.272	2.395	0.3%	29.9%	21.1%	Post-Chemo 25	2.620	1.903	#N/A	#N/A	#N/A
Rx Naive 26	2.349	11.530	18.6%	57.9%	49.8%	Post-Chemo 26	37.507	2.387	4.4%	31.5%	20.9%
Rx Naive 27	8.014	7.472	25.6%	61.2%	39.7%	Post-Chemo 27	10.063	6.412	48.3%	71.3%	61.7%
Rx Naive 28	1.235	4.954	8.9%	26.9%	16.9%	Post-Chemo 28	8.718	1.719	11.3%	30.0%	21.1%

FIG. 14

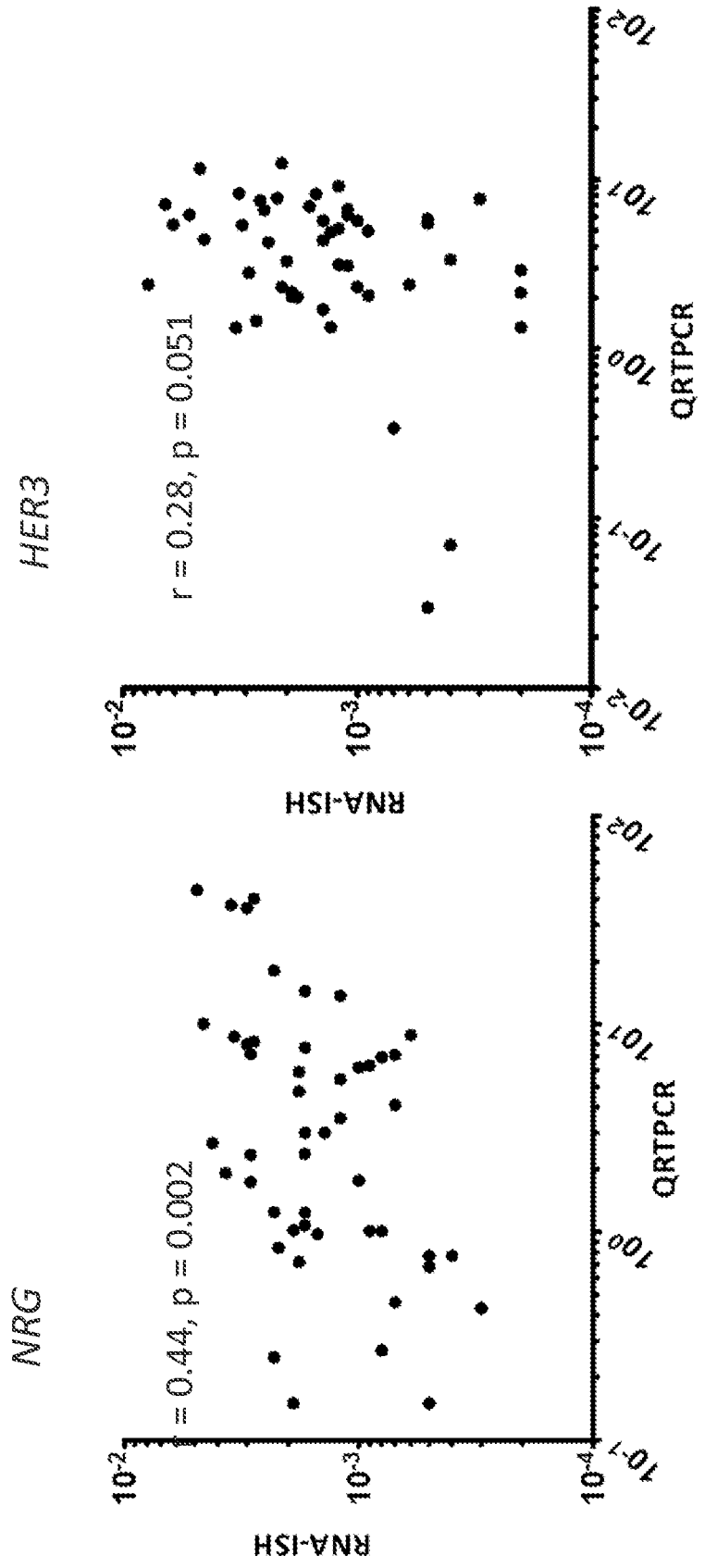

HER3
r = 0.28, p = 0.051
RNA-ISH
QRTPCR
B
NRG
= 0.44, p = 0.002
RNA-ISH
QRTPCR
A

FIG. 15

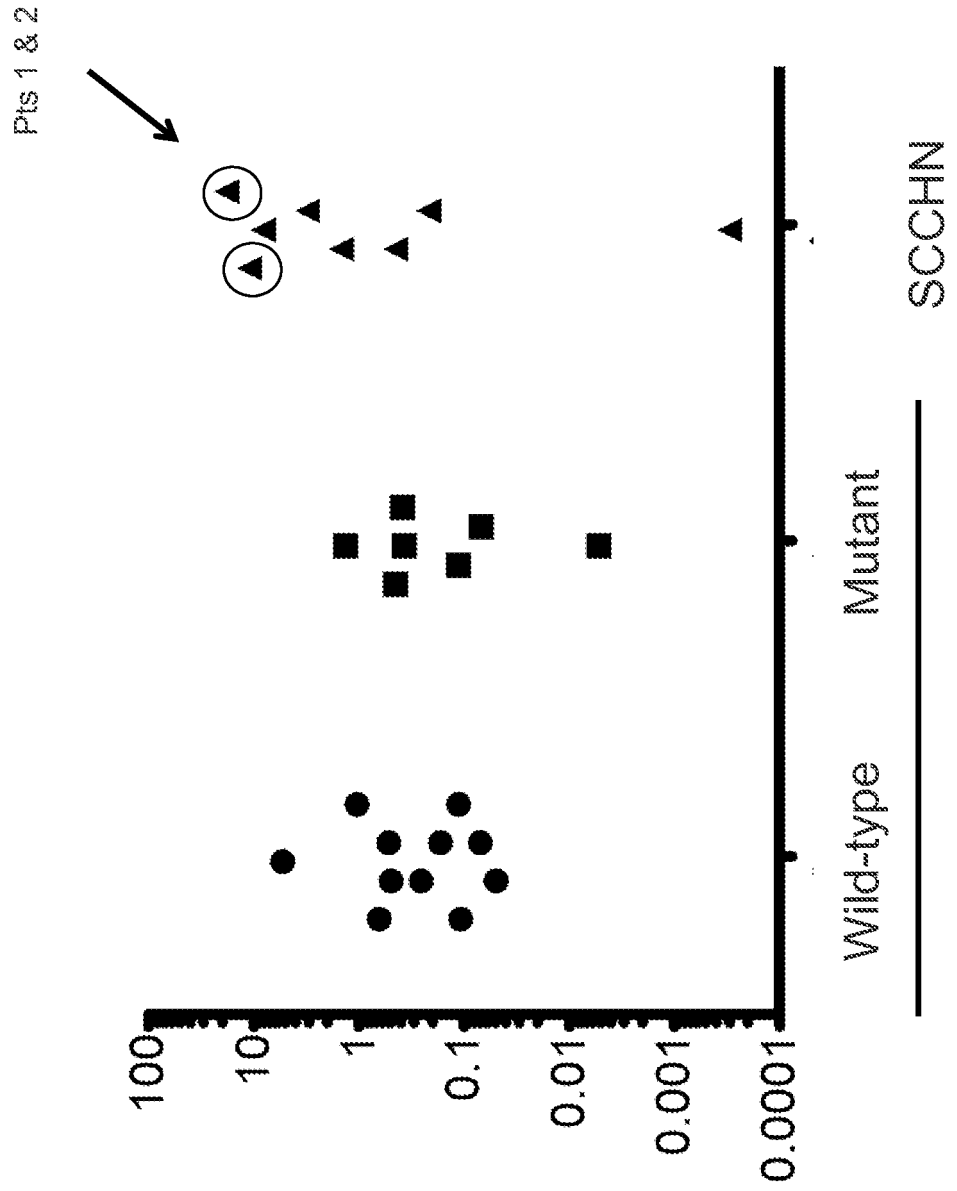


FIG. 16

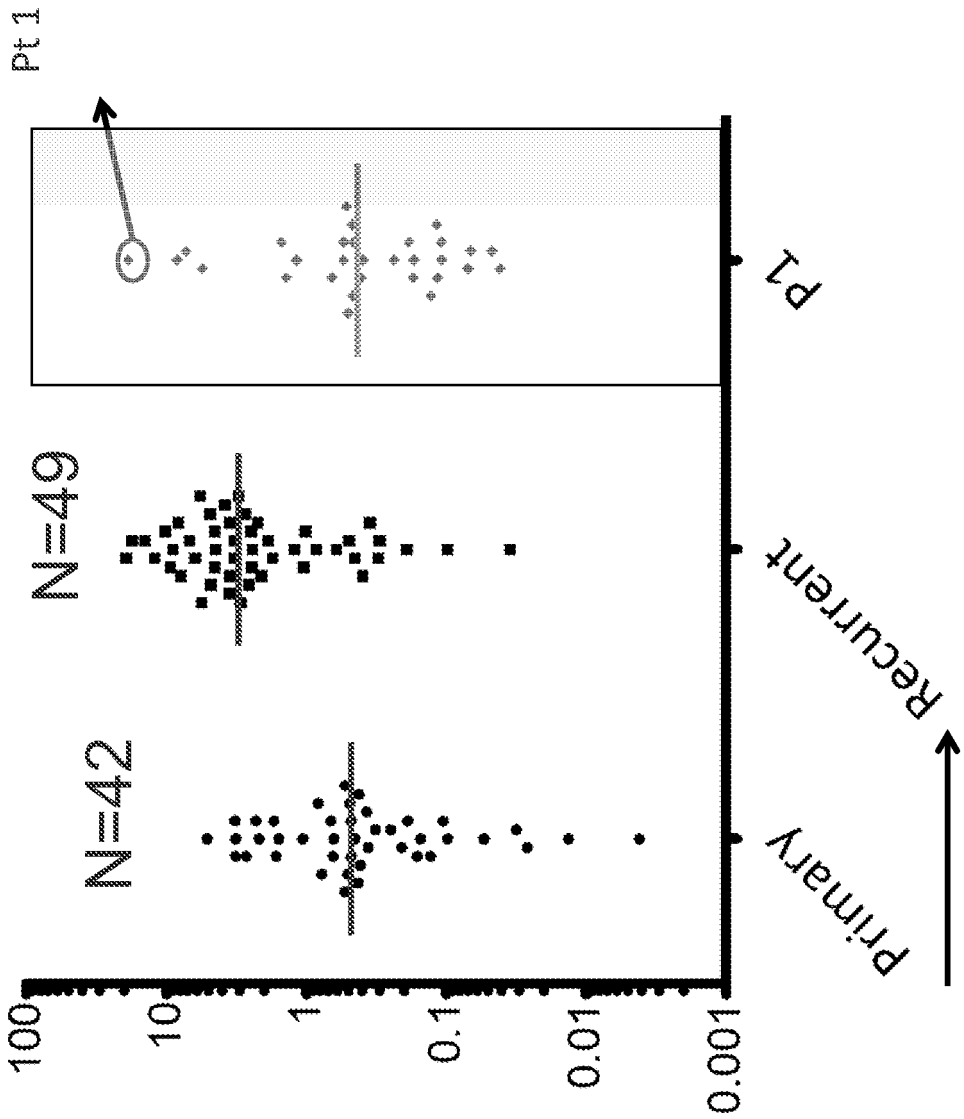


FIG. 17

```
Kabat#   1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 A  B  36 37 38 39 40 41
DL11f    E  V  Q  L  V  E  S  G  G  G  L  V  Q  P  G  G  S  L  R  L  S  C  A  A  S  G  F  T  L  S  G  D  W  I  H        W  V  R  Q  A  P

Kabat#   42 43 44 45 46 47 48 49 50 51 52 a  b  c  53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80
DL11f    G  K  G  L  E  W  V  G  E  I  S  A        A  G  G  Y  T  D  Y  A  D  S  V  K  G  R  F  T  I  S  A  D  T  S  K  N  T  A  Y  L

Kabat#   81 82 A  B  C  83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100A B  C  D  E  F  G  H  I  J  K  101 102 103 104 105 106 107 108 109
DL11f    Q  M  N  S  L  R  A  E  D  T  A  V  Y  Y  Y  C  A  R  E  S  R  V  S  F  E  A  A                    M  D  Y  W  G  Q  G  T  L  V
```

SEQ ID NO: 1

```
Kabat#   1  2  3  4  5  6  7  8  9  10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 A  B  C  D  E  F  28 29 30 31 32 33 34 35 36 37
DL11f    D  I  Q  M  T  Q  S  P  S  S  L  S  A  S  V  G  D  R  V  T  I  T  C  R  A  S  Q                    N  I  A  T  D  V  A  W  Y  Q

Kabat#   38 39 40 41 42 43 44 45 46 47 48 A  49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80
DL11f    Q  K  P  G  K  A  P  K  L  L  I  I        Y  S  A  S  F  L  Y  S  G  V  P  S  R  F  S  G  S  G  S  G  T  D  F  T  L  T  I  S  S  L  Q  P

Kabat#   81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 A  B  C  D  E  F  96 97 98 99 100 101 102 103 104 105 106 107 108 109
DL11f    E  D  F  A  T  Y  Y  C  Q  Q  S  E  P  E  P                    Y  T  F  G  Q  G  T  K  V  E  I  K  R
```

SEQ ID NO: 2

FIG. 18