FIG. 1

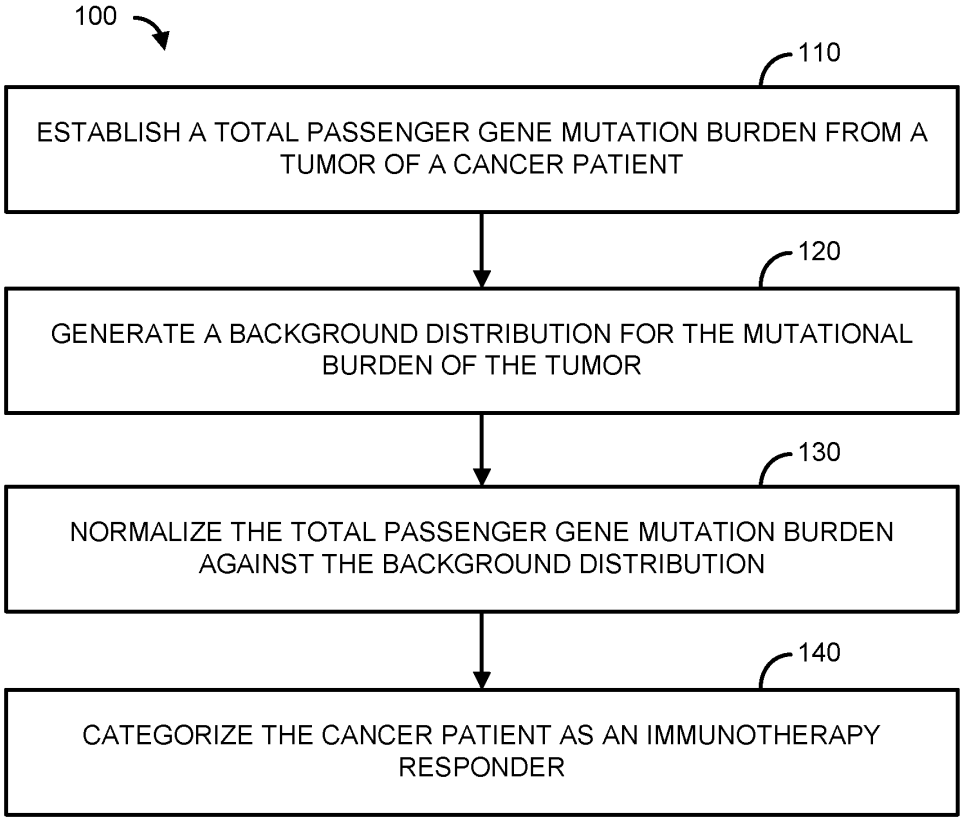

100
110
ESTABLISH A TOTAL PASSENGER GENE MUTATION BURDEN FROM A TUMOR OF A CANCER PATIENT
120
GENERATE A BACKGROUND DISTRIBUTION FOR THE MUTATIONAL BURDEN OF THE TUMOR
130
NORMALIZE THE TOTAL PASSENGER GENE MUTATION BURDEN AGAINST THE BACKGROUND DISTRIBUTION
140
CATEGORIZE THE CANCER PATIENT AS AN IMMUNOTHERAPY RESPONDER

FIG. 2

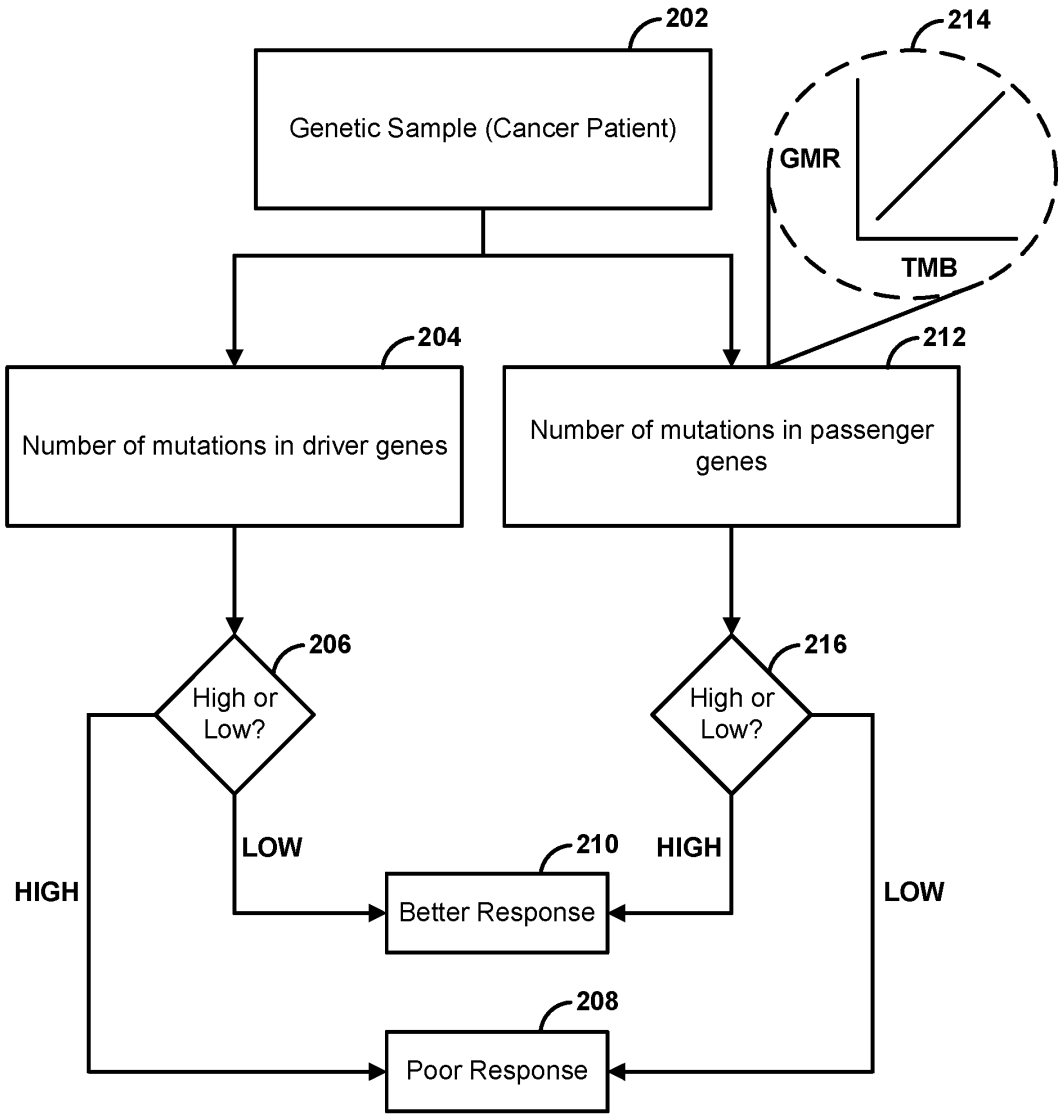

202
Genetic Sample (Cancer Patient)
214
GMR
TMB
204
Number of mutations in driver genes
212
Number of mutations in passenger genes
206
High or Low?
216
High or Low?
LOW
HIGH
210
Better Response
HIGH
LOW
208
Poor Response

FIG. 3

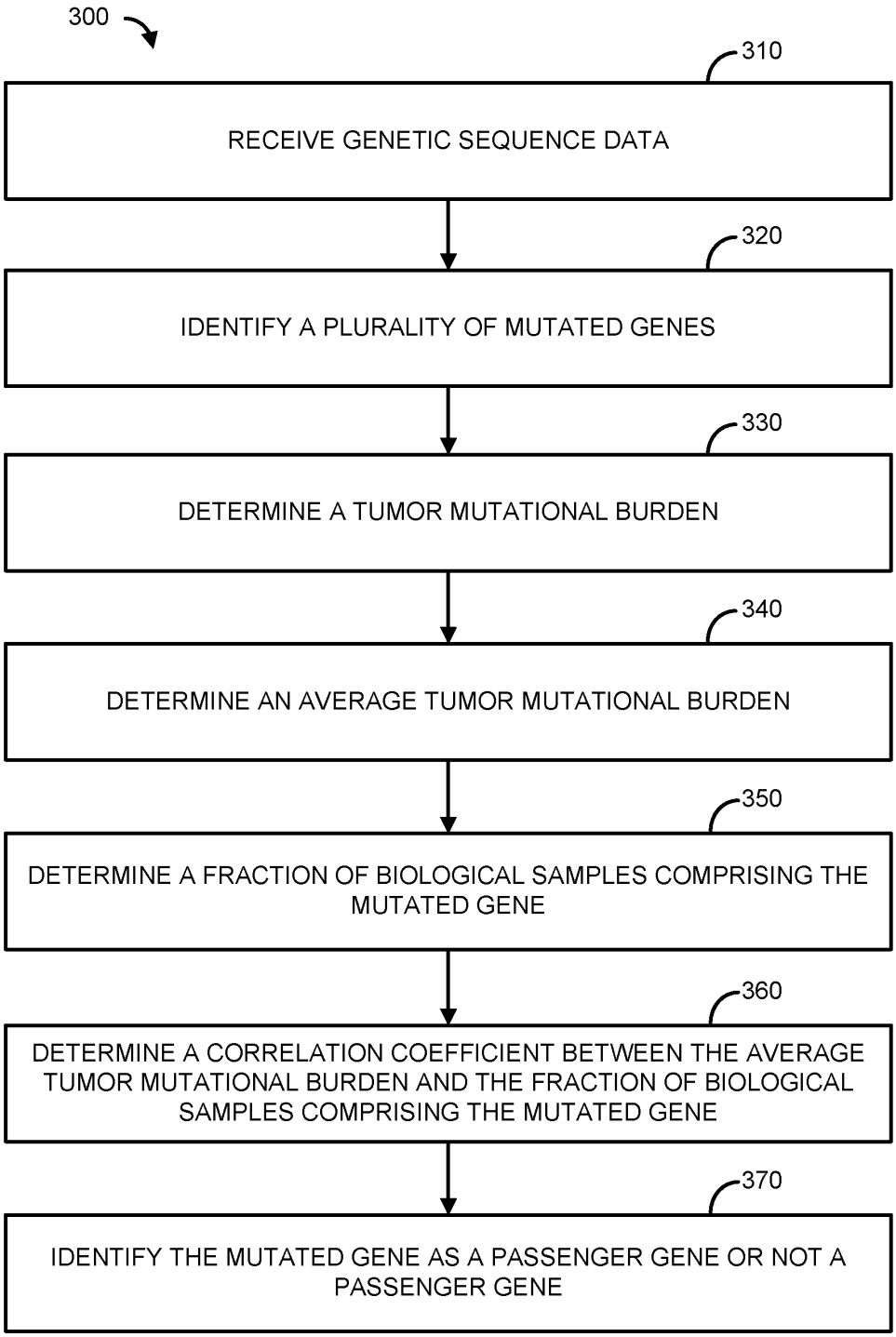
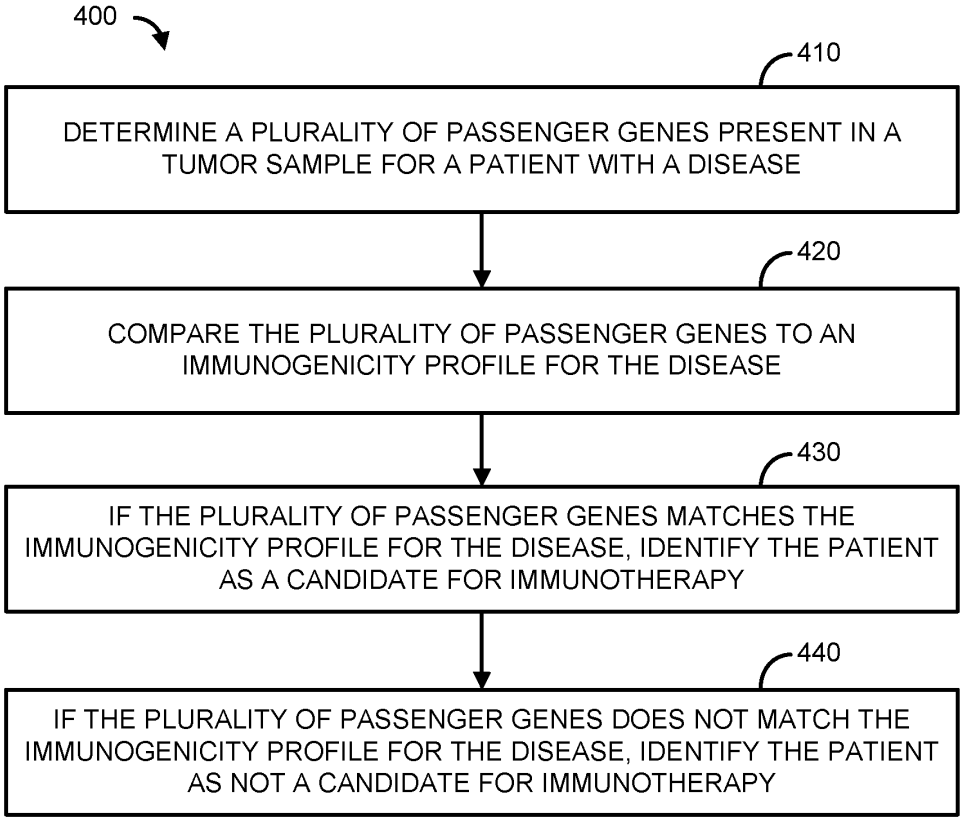

300
310
RECEIVE GENETIC SEQUENCE DATA
320
IDENTIFY A PLURALITY OF MUTATED GENES
330
DETERMINE A TUMOR MUTATIONAL BURDEN
340
DETERMINE AN AVERAGE TUMOR MUTATIONAL BURDEN
350
DETERMINE A FRACTION OF BIOLOGICAL SAMPLES COMPRISING THE MUTATED GENE
360
DETERMINE A CORRELATION COEFFICIENT BETWEEN THE AVERAGE TUMOR MUTATIONAL BURDEN AND THE FRACTION OF BIOLOGICAL SAMPLES COMPRISING THE MUTATED GENE
370
IDENTIFY THE MUTATED GENE AS A PASSENGER GENE OR NOT A PASSENGER GENE

FIG. 4


400
410
DETERMINE A PLURALITY OF PASSENGER GENES PRESENT IN A TUMOR SAMPLE FOR A PATIENT WITH A DISEASE
420
COMPARE THE PLURALITY OF PASSENGER GENES TO AN IMMUNOGENICITY PROFILE FOR THE DISEASE
430
IF THE PLURALITY OF PASSENGER GENES MATCHES THE IMMUNOGENICITY PROFILE FOR THE DISEASE, IDENTIFY THE PATIENT AS A CANDIDATE FOR IMMUNOTHERAPY
440
IF THE PLURALITY OF PASSENGER GENES DOES NOT MATCH THE IMMUNOGENICITY PROFILE FOR THE DISEASE, IDENTIFY THE PATIENT AS NOT A CANDIDATE FOR IMMUNOTHERAPY

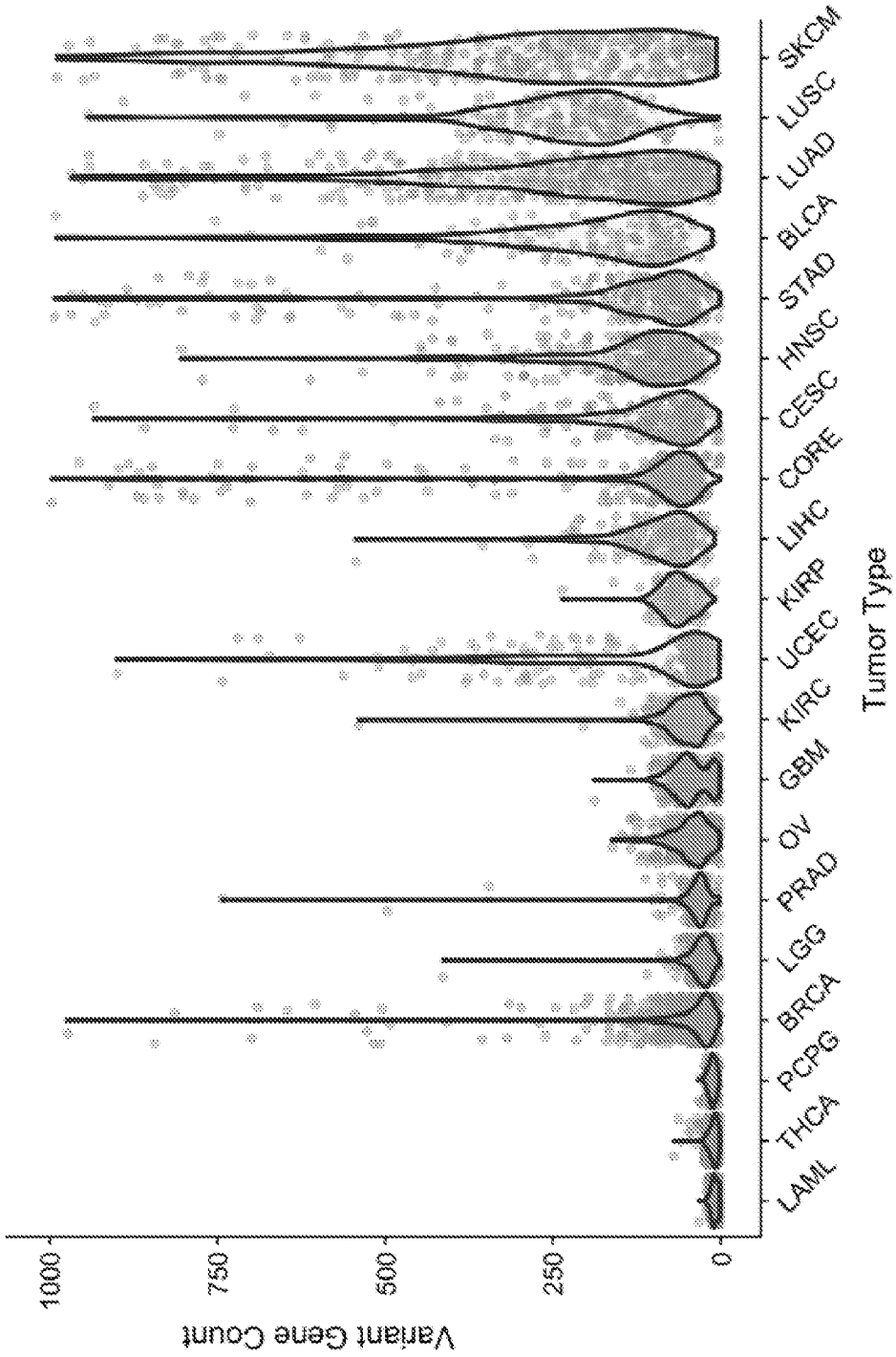

Variant Gene Count
1000
750
500
250
0
LAML
THCA
PCPG
BRCA
LGG
PRAD
OV
GBM
KIRC
UCEC
KIRP
LIHC
CORE
CESC
HNSC
STAD
BLCA
LUAD
LUSC
SKCM
Tumor Type

FIG. 5

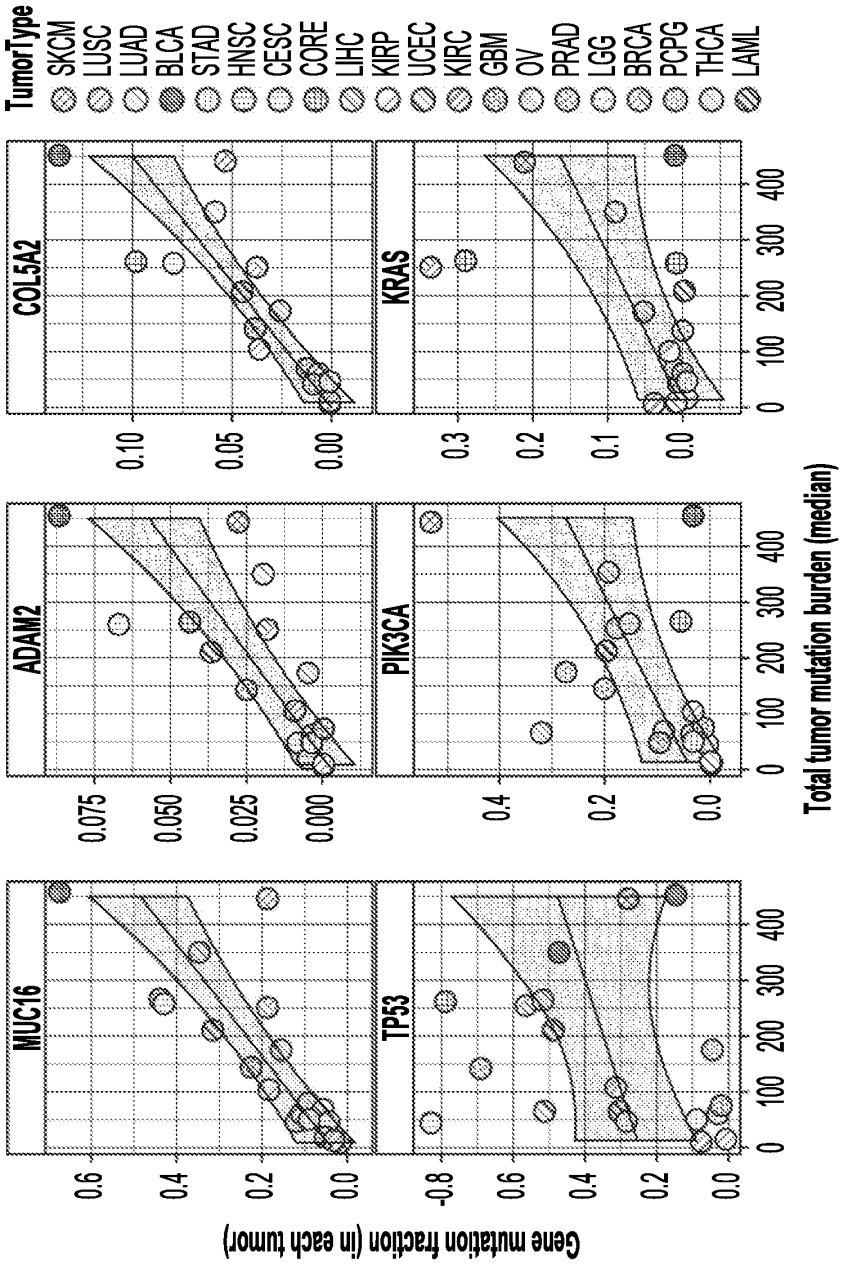

TumorType
SKCM
LUSC
LUAD
BLCA
STAD
HNSC
CESC
CORE
LIHC
KIRP
UCEC
KIRC
GBM
OV
PRAD
LGG
BRCA
PCPG
THCA
LAML
MUC16
ADAM2
COL5A2
TP53
PIK3CA
KRAS
Gene mutation fraction (in each tumor)
Total tumor mutation burden (median)

FIG. 6

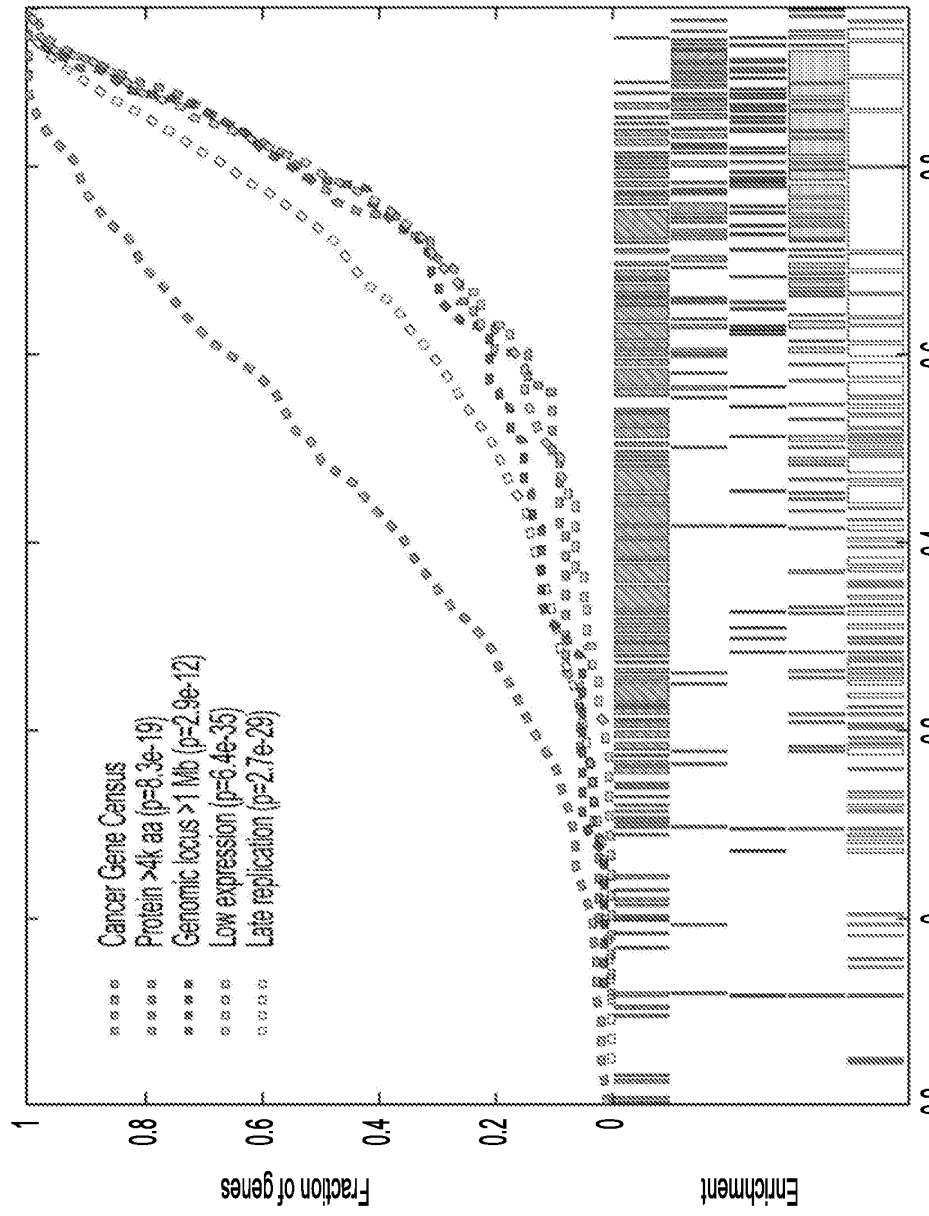

Cancer Gene Census
Protein >4k aa (p=8.3e-19)
Genomic locus > 1 Mb (p=2.9e-12)
Low expression (p=6.4e-35)
Late replication (p=2.7e-29)
Fraction of genes
Enrichment
Passenger Gene Index (PGI)
1
0.8
0.6
0.4
0.2
0
-0.2
0
0.2
0.4
0.6
0.8

FIG. 7

FIG. 8

Gene	PGI	Type	Perc
KDR	0.94	skcm	0.14
PDE4DIP	0.89	skcm	0.15
PDGFRA	0.88	skcm	0.10
TFE3	0.87	skcm	0.03
PBX1	0.87	skcm	0.04
CRLF2	0.86	skcm	0.03
RANBP17	0.86	skcm	0.06
COL1A1	0.86	skcm	0.12
MLL3	0.85	blca	0.22
ROS1	0.85	skcm	0.18
ARID2	0.85	skcm	0.13
KIAA1549	0.84	skcm	0.10
PRDM16	0.84	skcm	0.08
HIP1	0.84	skcm	0.04
USP6	0.83	skcm	0.09
NTRK3	0.83	luad	0.08
SRGAP3	0.83	skcm	0.10
IL7R	0.83	skcm	0.11
PDGFRB	0.83	skcm	0.06
ZNF331	0.83	skcm	0.06
POT1	0.83	luad	0.03
CREB3L2	0.82	skcm	0.03
PAX7	0.81	stad	0.03
SLC34A2	0.81	skcm	0.06
PRDM1	0.81	skcm	0.06
STL	0.81	skcm	0.04
C15orf55	0.81	skcm	0.09
BCL11A	0.81	skcm	0.10
LCK	0.81	skcm	0.04
CHN1	0.80	skcm	0.02

Gene	PGI	Type	Perc
CREB1	0.17	ucec	0.02
CCND1	0.16	ucec	0.07
NF2	0.16	kirp*	0.06
CBFB	0.16	brca	0.02
TCF7L2	0.16	coad*	0.08
RPL22	0.16	ucec	0.13
YWHAE	0.13	ucec*	0.04
APC	0.12	coad*	0.71
PIK3CA	0.12	ucec	0.54
CIC	0.11	lgg*	0.18
SMARCB1	0.10	stad	0.04
AKT1	0.09	ucec	0.03
PBRM1	0.09	kirc*	0.33
PTEN	0.05	ucec*	0.69
MAX	0.04	ucec	0.05
FLT3	0.03	laml*	0.30
PHF6	0.02	ucec	0.04
NACA	0.02	ucec	0.07
ATRX	0.01	lgg*	0.44
FAM22B	0.00	ucec*	0.02
PIK3R1	0.00	ucec	0.38
U2AF1	-0.03	laml	0.04
DNMT3A	-0.08	laml*	0.23
VHL	-0.08	kirc*	0.48
FIP1L1	-0.10	ucec	0.04
IDH1	-0.17	lgg*	0.76
RUNX1	-0.17	laml*	0.10
CEBPA	-0.19	laml*	0.07
NPM1	-0.24	laml*	0.26
IDH2	-0.28	laml	0.10

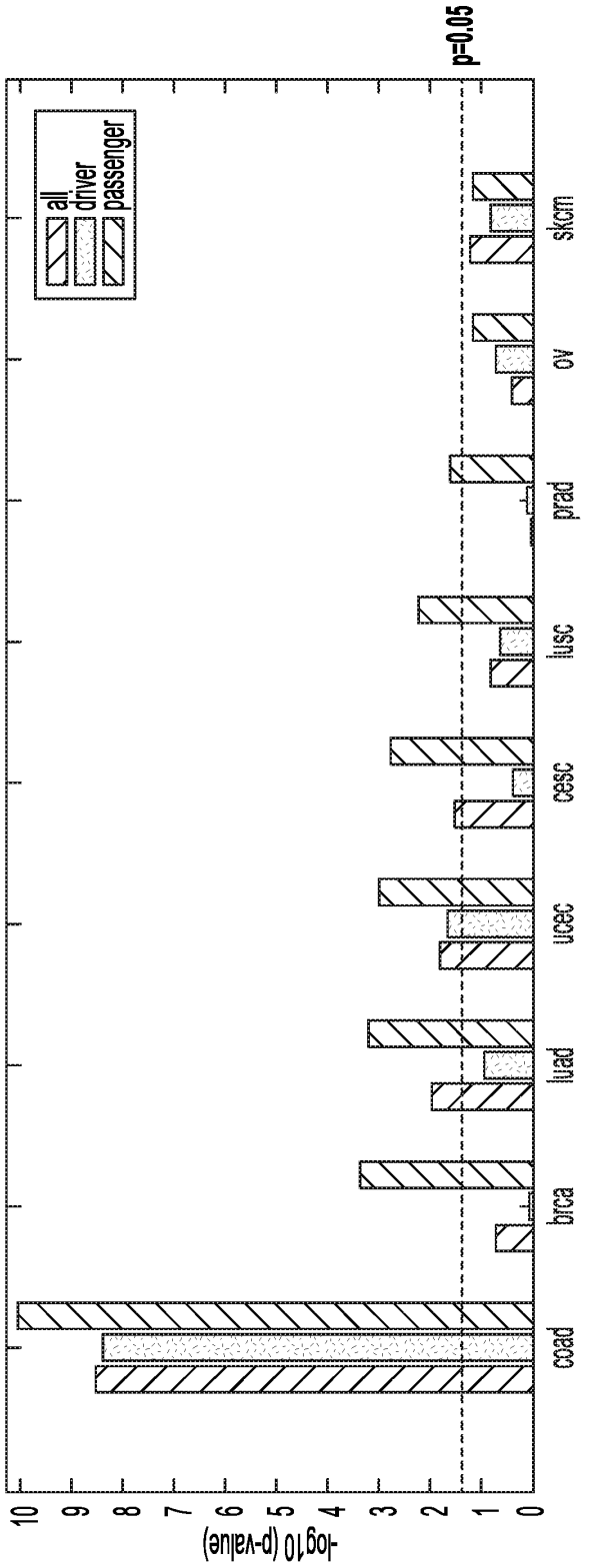

p=0.05
all
driver
passenger
-log10 (p-value)
0
1
2
3
4
5
6
7
8
9
10
coad
brca
luad
ucec
cesc
lusc
prad
ov
skcm

FIG. 9A

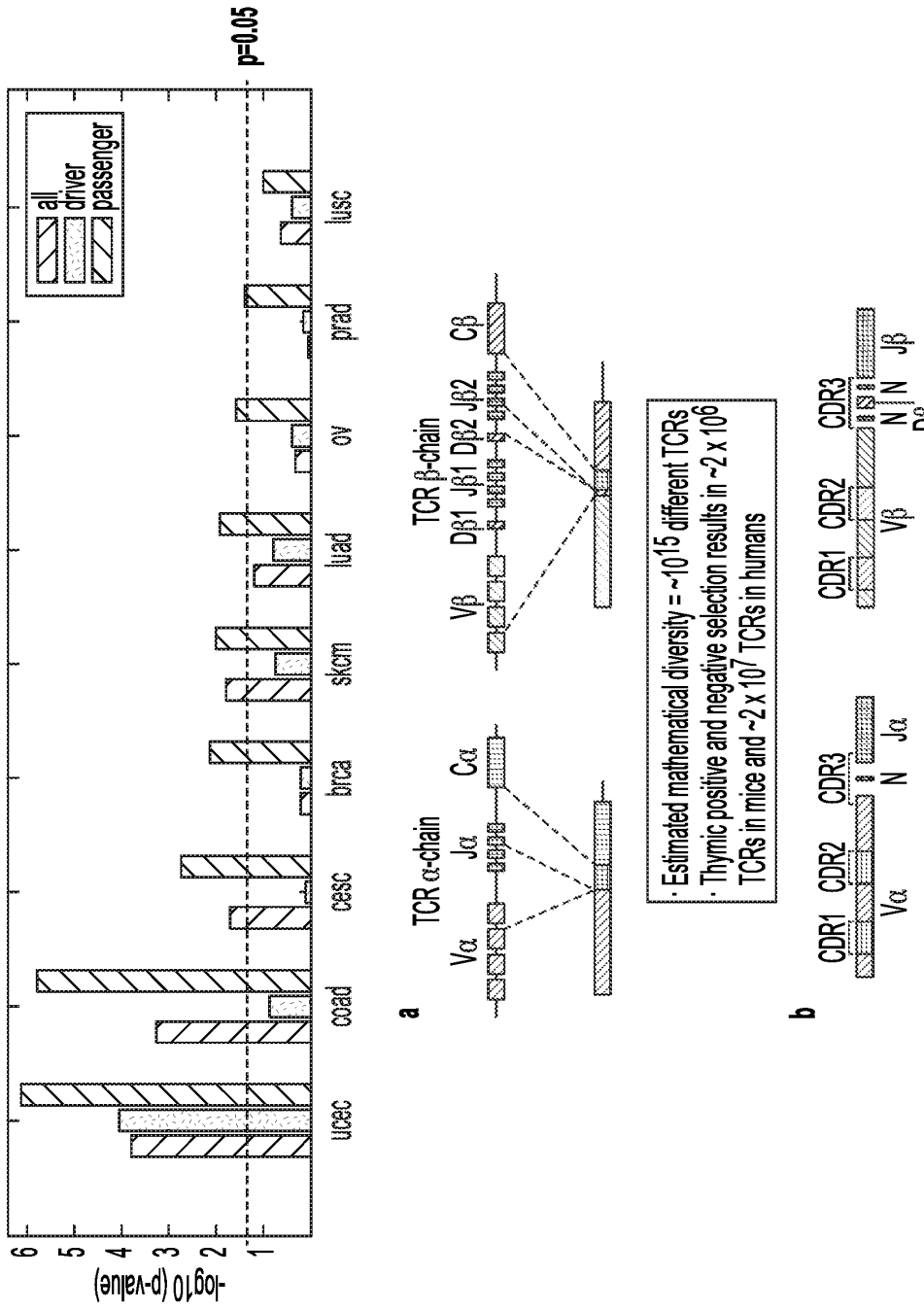

p=0.05
all
driver
passenger
-log10 (p-value)
6
5
4
3
2
1
ucec
coad
cesc
brca
skcm
luad
ov
prad
lusc
a
TCR α-chain
Vα
Jα
Cα
TCR β-chain
Vβ
Dβ1 Jβ1 Dβ2 Jβ2
Cβ
· Estimated mathematical diversity = ~10^15 different TCRs
· Thymic positive and negative selection results in ~2 x 10^6 TCRs in mice and ~2 x 10^7 TCRs in humans
b
CDR1
CDR2
CDR3
Vα
N
Jα
CDR1
CDR2
CDR3
Vβ
N
N
Dβ
Jβ

FIG. 9B

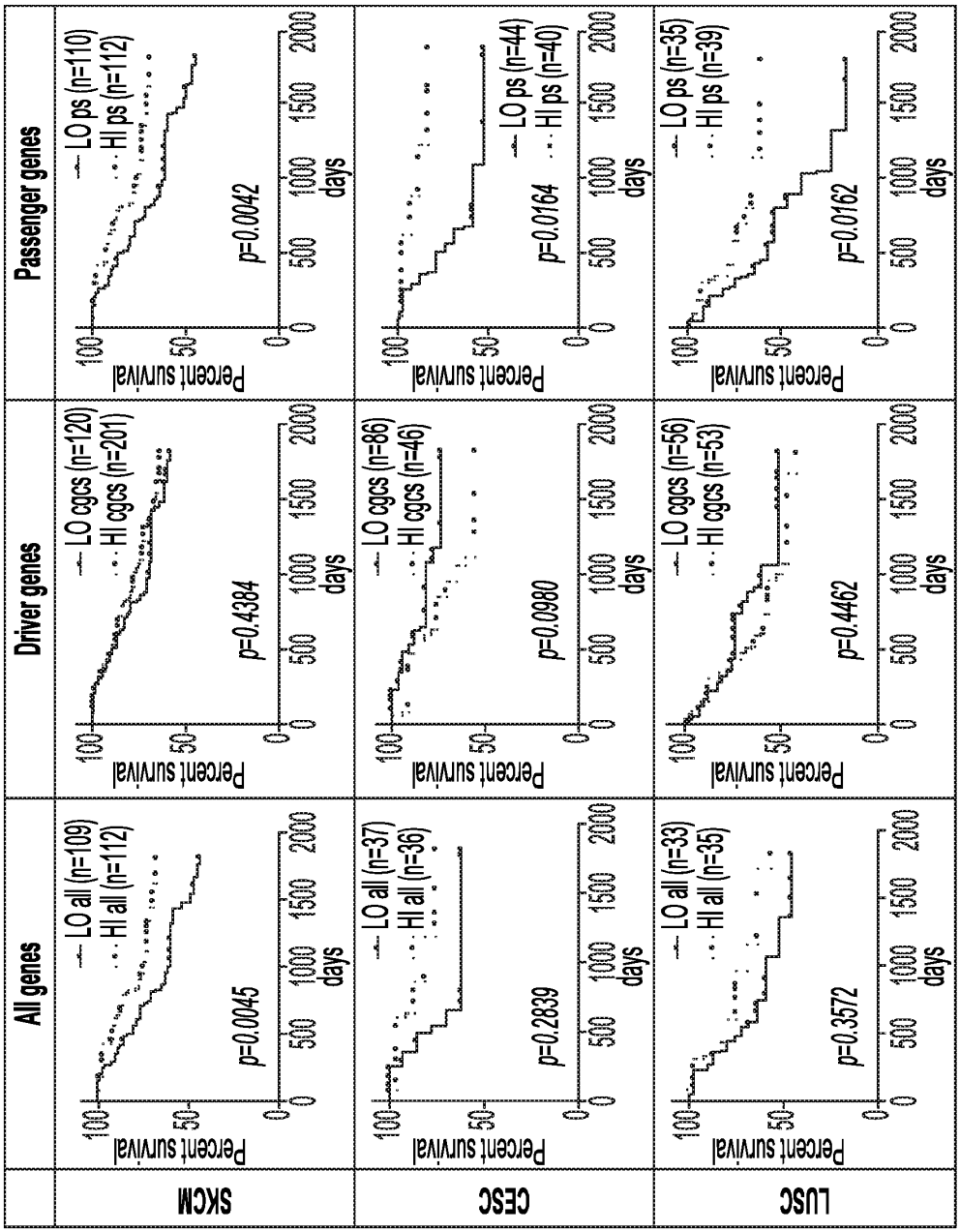

All genes
Driver genes
Passenger genes
SKCM
CESC
LUSC
LO all (n=109)
HI all (n=112)
LO cgcs (n=120)
HI cgcs (n=201)
LO ps (n=110)
HI ps (n=112)
LO all (n=37)
HI all (n=36)
LO cgcs (n=86)
HI cgcs (n=46)
LO ps (n=44)
HI ps (n=40)
LO all (n=33)
HI all (n=35)
LO cgcs (n=56)
HI cgcs (n=53)
LO ps (n=35)
HI ps (n=39)
Percent survival
100
50
0
0
500
1000
1500
2000
days
p=0.0045
p=0.4384
p=0.0042
p=0.2839
p=0.0980
p=0.0164
p=0.3572
p=0.4462
p=0.0162

FIG. 9C

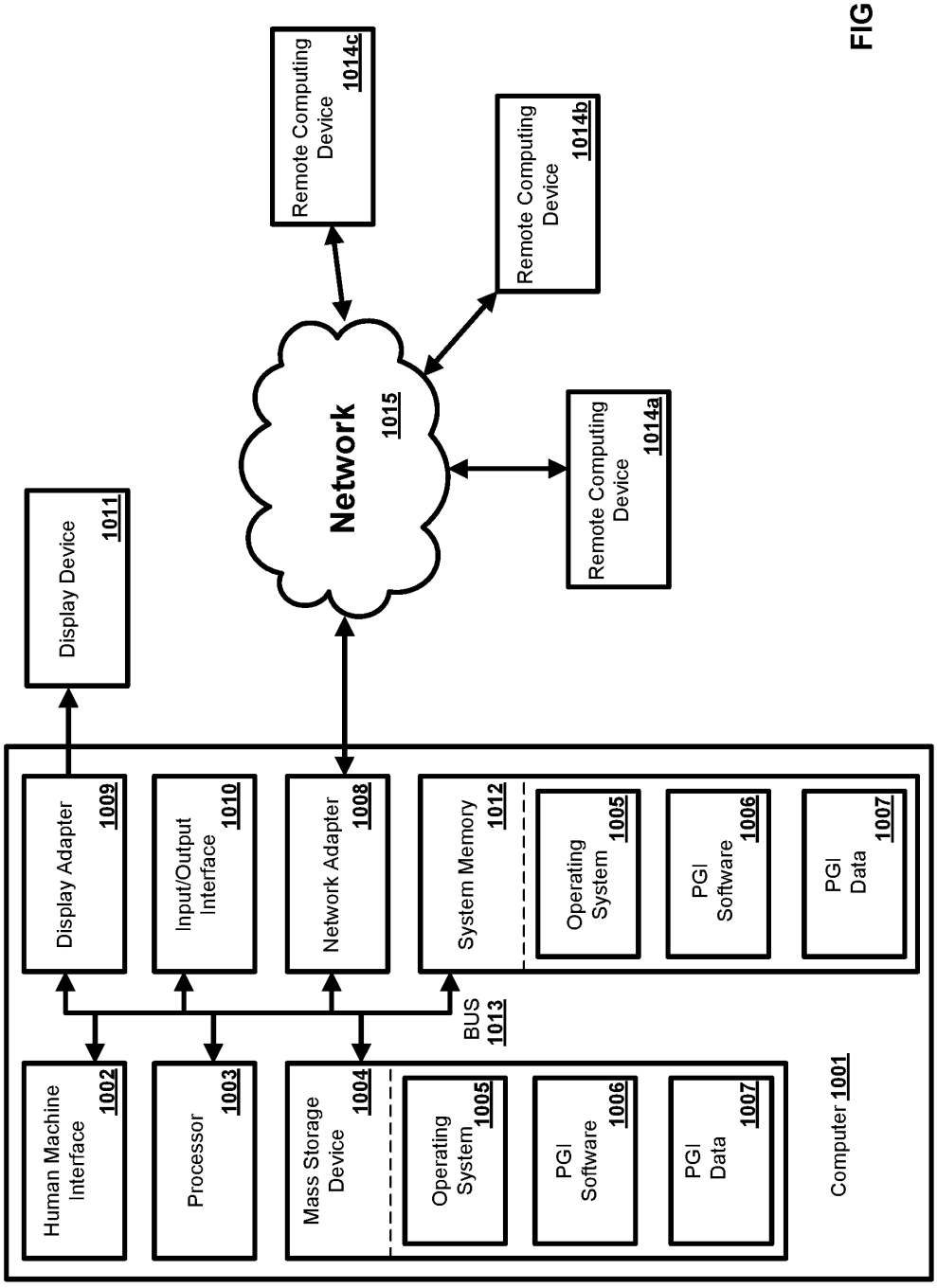
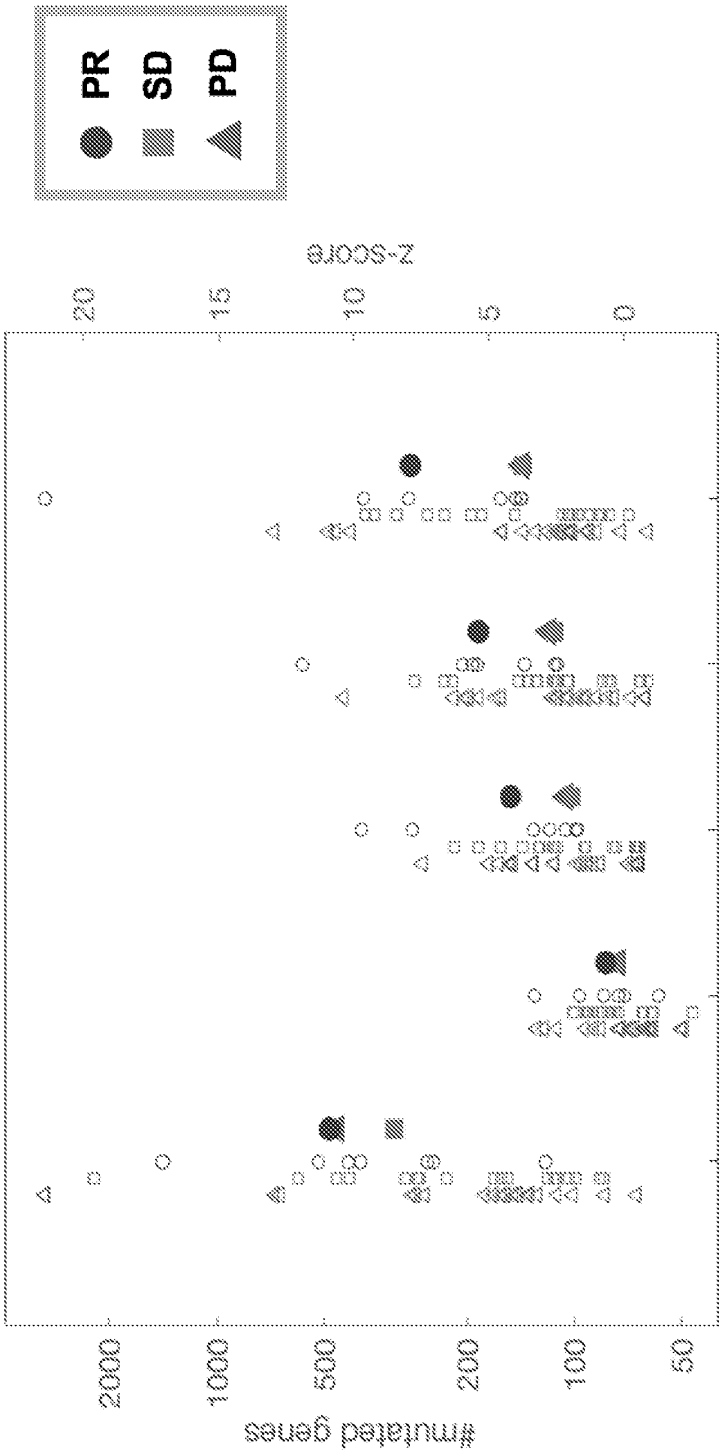

Remote Computing Device 1014c
Remote Computing Device 1014b
Remote Computing Device 1014a
Network 1015
Display Device 1011
Display Adapter 1009
Input/Output Interface 1010
Network Adapter 1008
System Memory 1012
Operating System 1005
PGI Software 1006
PGI Data 1007
BUS 1013
Human Machine Interface 1002
Processor 1003
Mass Storage Device 1004
Operating System 1005
PGI Software 1006
PGI Data 1007
Computer 1001

FIG. 10



PR vs PD	p=0.48	p=0.24	p=0.039	p=0.026	p=0.021
PR vs PD+SD	p=0.38	p=0.24	p=0.017	p=0.010	p=0.006

FIG. 11

FIG. 12

1	MUC16
2	PKHD1L1
3	PAPPA2
4	CTNND2
5	NEB
6	TRPV5
7	FLG2
8	FLG
9	C1orf173
10	MUC17
11	XIRP2
12	TTN
13	KRTAP12-3
14	RNASE3
15	OR2G2
16	MYH2
17	SLC4A10
18	CDH18
19	OR4A47
20	OR10R2
21	TPTE
22	OR4N4
23	BBOX1
24	OR5A2
25	MAGEB18
26	ADAM2
27	PDE1C
28	TAS2R16
29	CD177
30	SORCS3
31	GRM8
32	HRNR
33	SPHKAP
34	EPHA6
35	CSMD2
36	FAM83C
37	PEG3
38	OR5AC2
39	USP29
40	ZNF208
41	COL5A2
42	OR52N4

43	CRB1
44	CNTN5
45	ADAMTS20
46	OR4M1
47	LILRA2
48	CNTNAP2
49	TNN
50	LRFN2
51	GABRG1
52	GPR98
53	UNC13A
54	DNAH7
55	COL6A6
56	NLRP8
57	LTBP1
58	PRB1
59	ADCYAP1R1
60	RELN
61	OR10S1
62	ACAN
63	NLRP7
64	APOB
65	ACSM5
66	ZFP14
67	FAM5C
68	RIT2
69	DNAH8
70	OR4C15
71	COL22A1
72	OR11L1
73	RFX6
74	PSKH2
75	MYH15
76	KALRN
77	TNR
78	OR4B1
79	FCRL5
80	NUP210L
81	ZNF99
82	F5
83	MYH1
84	EXPH5

85	LAMA2
86	HS3ST4
87	GH1
88	RBP3
89	SMR3A
90	OR4M2
91	SCN1A
92	GRID2
93	CFHR4
94	DMBT1
95	CSMD1
96	COL11A2
97	RPS4Y2
98	PCLO
99	BCLAF1
100	ZNF831
101	CRISP3
102	RGS5
103	EPHA7
104	OR52B4
105	VWA3B
106	PLCB1
107	CD1E
108	SLC9A4
109	OR2G3
110	OR2T1
111	TMEM132D
112	ZNF804A
113	KCNT2
114	NTRK3
115	FAM47A
116	PTGDR
117	OR4N2
118	ZNF536
119	OR2G6
120	LRP1B
121	OR2T6
122	ZSCAN1
123	OR5R1
124	TRAT1
125	OR6F1
126	FIBIN

127	PKP2
128	DYSF
129	SLC8A1
130	STON1-GTF2A1L
131	OR5D13
132	CNTNAP4
133	MAGEA6
134	OR51A4
135	KIAA1210
136	NBPF1
137	NDST4
138	PRIM2
139	COL11A1
140	DNAH9
141	MAGEC1
142	PLXNA4
143	C2CD3
144	CALCR
145	SLCO1B1
146	OR8H1
147	ITGAD
148	CACNA1C
149	OR51L1
150	PTPRT
151	CACNA1I
152	CATSPERD
153	ZFHX4
154	C2orf78
155	CHAT
156	SPAG17
157	UNC13C
158	POTEA
159	GRIN3A
160	FAM5B
161	MORC1
162	NLRP14
163	OR8B2
164	ACSM2B
165	IRGC
166	ADCY8
167	KIAA1462
168	VEGFC

FIG. 12
(continued)

169	OR5J2
170	GRIN2B
171	FAM47C
172	MROH2B
173	DACH1
174	FAM135B
175	TAC1
176	FER1L6
177	DUSP27
178	OR2M3
179	LPA
180	FREM1
181	CD163
182	PRUNE2
183	PTPRB
184	NAALAD2
185	OR4D5
186	SPANXN2
187	HYDIN
188	TCHHL1
189	COL9A1
190	OR8B4
191	LDB2
192	KLK5
193	LEPR
194	CSMD3
195	MYH13
196	ADAM12
197	RIMS2
198	USH2A
199	CDHR1
200	NEUROD1
201	FAT3
202	SELV
203	C2orf16
204	CPA3
205	SEZ6L2
206	ASF1B
207	COL19A1
208	NPTXR
209	CLEC6A
210	CRISP2

211	MYH8
212	HSD3B2
213	OR8I2
214	RTP3
215	OR52J3
216	RP1
217	THSD7B
218	DGKK
219	CLVS2
220	SNTG2
221	NPC1L1
222	CDH6
223	WDR49
224	FAM24A
225	OR2L13
226	OR3A1
227	KANK4
228	OR2F1
229	UNC79
230	SYT4
231	ANKRD30A
232	POM121L12
233	KCNB2
234	SHROOM3
235	LRRC7
236	CNGB3
237	CTNNA3
238	SPTA1
239	ABCA13
240	ASTN1
241	AMER3
242	LY86
243	ANKS1B
244	ACTRT2
245	NLRP5
246	PSG2
247	SKP1
248	TRIOBP
249	SAMD3
250	DNAH5
251	MRRF
252	OC90

253	ROBO4
254	UBA3
255	NEU4
256	SCN3A
257	TRIM10
258	AK024141
259	TMEM200A
260	FAM188B
261	OR5B17
262	HDAC9
263	NAA11
264	LILRB1
265	OR51M1
266	TRIM58
267	NLRP4
268	OR4L1
269	OR4K1
270	F13A1
271	GABRB3
272	FOLH1B
273	SYNDIG1L
274	PXDNL
275	MYH4
276	OR2T3
277	TIGD3
278	OR8H3
279	MAGI2
280	SLC6A19
281	CACNA1S
282	FSTL5
283	KDR
284	OR5D14
285	OR8H2
286	VN1R4
287	PREX2
288	GIMAP6
289	AHNAK
290	UGT3A1
291	OR4N5
292	IMPG1
293	OR10A2
294	CDR1

295	SI
296	AOX1
297	TRHDE
298	RGS7
299	OR52B2
300	BAI3
301	NLRP13
302	DGKI
303	CFHR5
304	PDE4DIP
305	GPR111
306	ZDHHC19
307	SPATA31D1
308	FSHR
309	CWH43
310	OR9Q2
311	TENM3
312	TMEM132B
313	CA10
314	PLCH1
315	ZCCHC12
316	LAIR2
317	OR5B2
318	OR2T34
319	TLR4
320	SIGLEC14
321	GCK
322	DNAH3
323	C6
324	ADAM29
325	OR2L3
326	OR5L1
327	PDILT
328	UNC5D
329	RNF133
330	OR2M7
331	GPR123
332	OR52E4
333	OR2F2
334	ESRRG
335	KCNH1
336	PRR23B

FIG. 12
(continued)

337	PCDH15
338	LRP2
339	STAB2
340	OR9A2
341	COL2A1
342	JAM2
343	NPAP1
344	DCAF4L2
345	MYLK3
346	MYOCD
347	ITGA7
348	OR8K5
349	CLSTN2
350	CFTR
351	PCK1
352	TECRL
353	RYR1
354	PTPRD
355	MXRA5
356	NPAS4
357	CDS1
358	SLC6A18
359	ROS1
360	BLK
361	NPFFR2
362	OR51T1
363	GRXCR1
364	SLCO1B3
365	CAPN13
366	SELP
367	SCN11A
368	TDRD5
369	UGT3A2
370	DZIP3
371	LPAR4
372	ZDBF2
373	TSHZ2
374	PCDHGA3
375	HOXB1
376	PSG7
377	MYO18B
378	NKAIN2

379	SCN2A
380	SLC5A8
381	PARD3B
382	CSH2
383	NCKAP1L
384	DAB1
385	GPR142
386	OR2B6
387	SEMA5B
388	OR10C1
389	ENTHD1
390	LCT
391	PI16
392	SLC35G3
393	SLC5A7
394	FOLH1
395	PAK7
396	FLT1
397	CNR1
398	ASXL3
399	NLRP3
400	CIB4
401	ADCY10
402	DENND2A
403	OR51S1
404	DNAH11
405	ALPK2
406	SPATA16
407	EMILIN3
408	SLC17A8
409	SIGLEC9
410	DCC
411	OR4C3
412	KRTAP12-4
413	KCNK10
414	CEACAM8
415	HCN1
416	NOS1
417	TPO
418	GRIN2A
419	PPAPDC1A
420	OR2A12

421	STON2
422	RYR2
423	GRM7
424	SLCO6A1
425	PDGFRA
426	TRPC5
427	OR4F17
428	SLC17A6
429	ARPP21
430	CPED1
431	OR10G7
432	OR2M4
433	NCKAP5
434	OR5AP2
435	KIF4B
436	RP1L1
437	KRTAP13-3
438	OR1J4
439	OR4A15
440	BPIFB4
441	MYO7B
442	OR10G8
443	ITGA4
444	MYF5
445	SLIT2
446	PCDHGA1
447	SERPINI2
448	ZSWIM2
449	GPC5
450	OR2T11
451	OR8K1
452	C7
453	CLCN1
454	CYP11B2
455	C8orf34
456	ZNF676
457	COMMD1
458	PCDHB7
459	OR11A1
460	KCNH7
461	MYH3
462	FCRL3

463	OR52E6
464	SALL1
465	RYR3
466	FUT9
467	ZNF274
468	LCE3D
469	MYT1L
470	DNM3
471	TNXB
472	ST6GAL2
473	CCNB3
474	DNAH10
475	MBL2
476	GABRB1
477	PCDHB4
478	COL17A1
479	TIE1
480	PYDC2
481	KCNV1
482	BTK
483	AMPH
484	CNGA2
485	OR4X2
486	BCAS1
487	ADAM22
488	PHLDB2
489	WNT3A
490	DCDC5
491	GAB4
492	OR8B12
493	ELTD1
494	LPHN3
495	NXF5
496	OR8G2
497	ADAMTS16
498	FSTL1
499	MYCT1
500	PMFBP1