

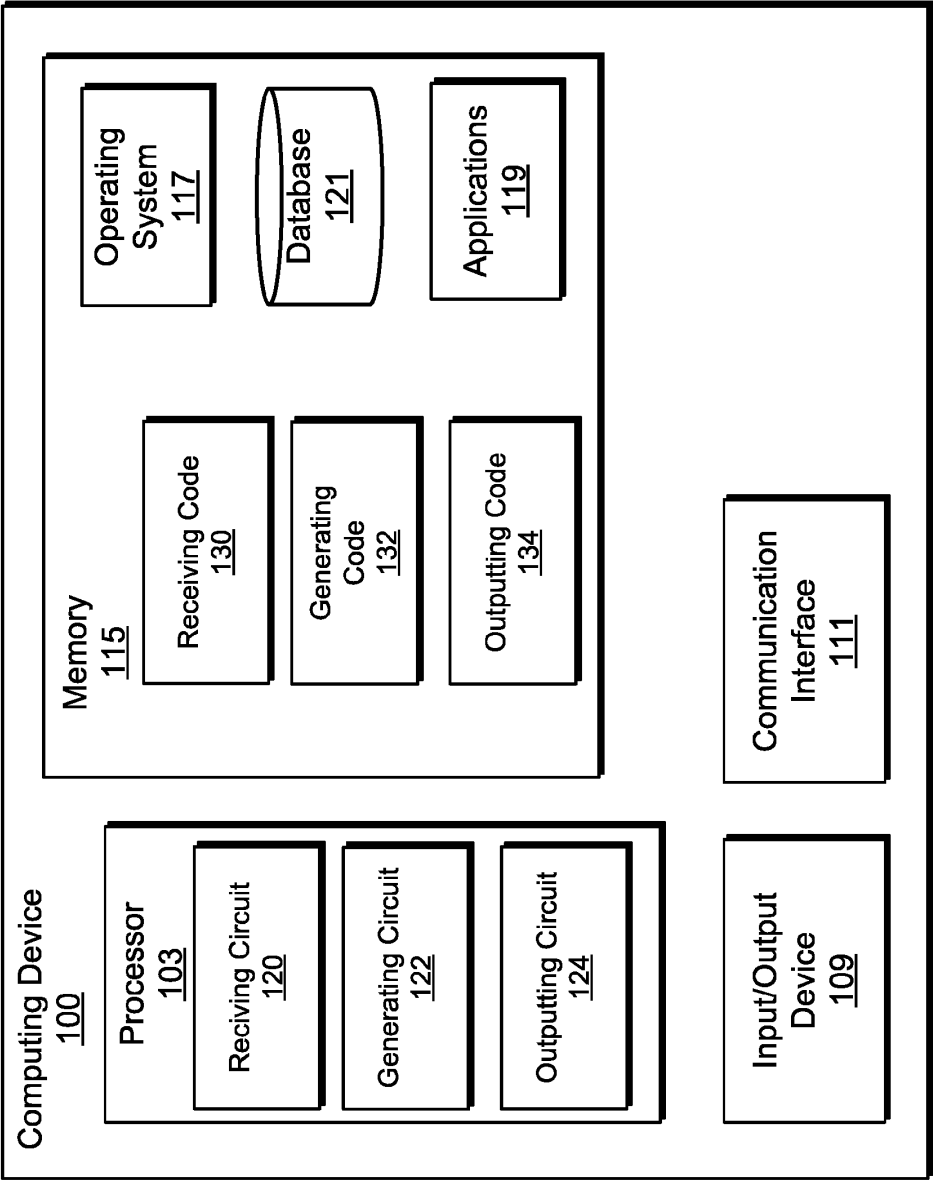


FIG. 1

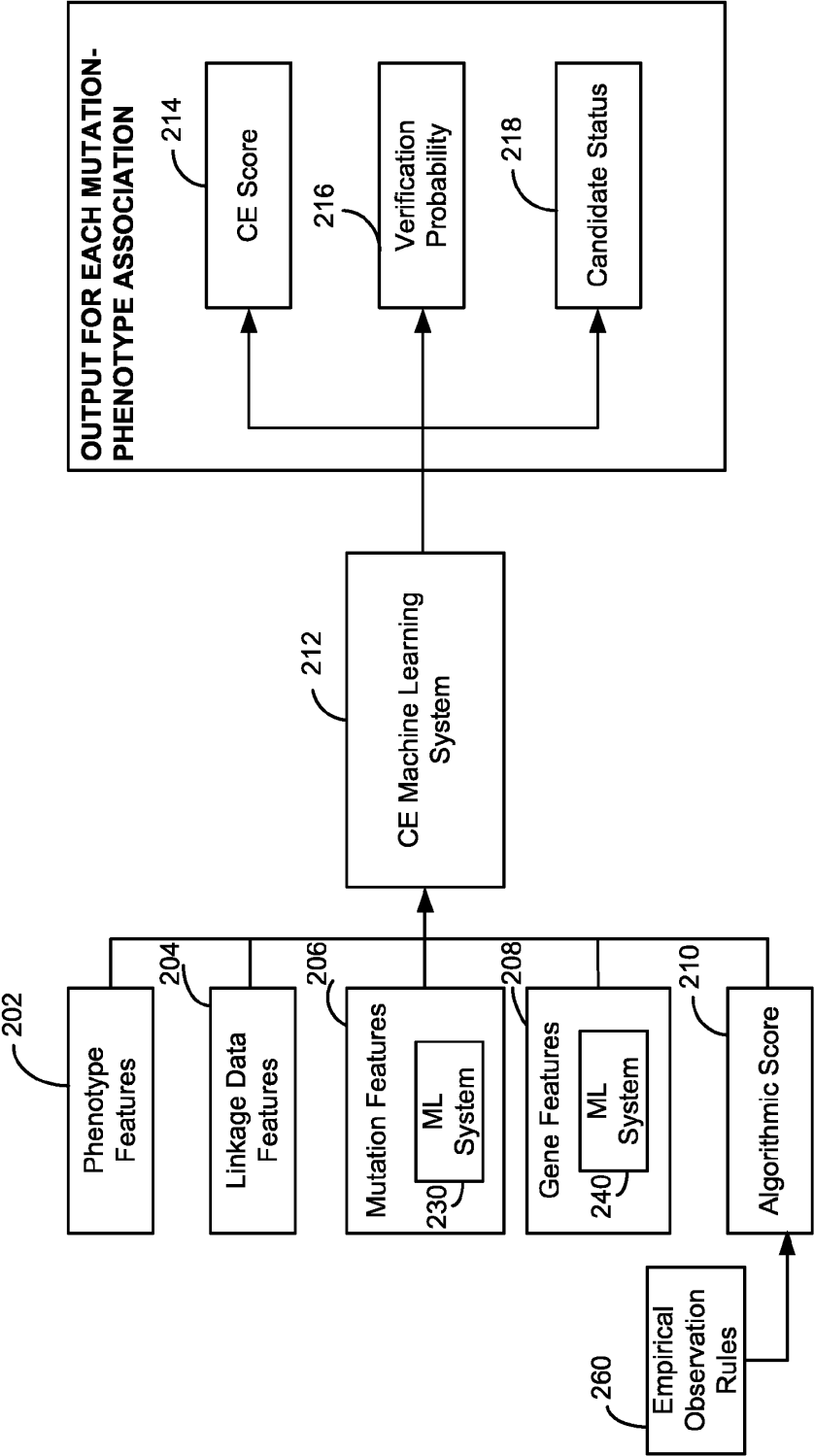
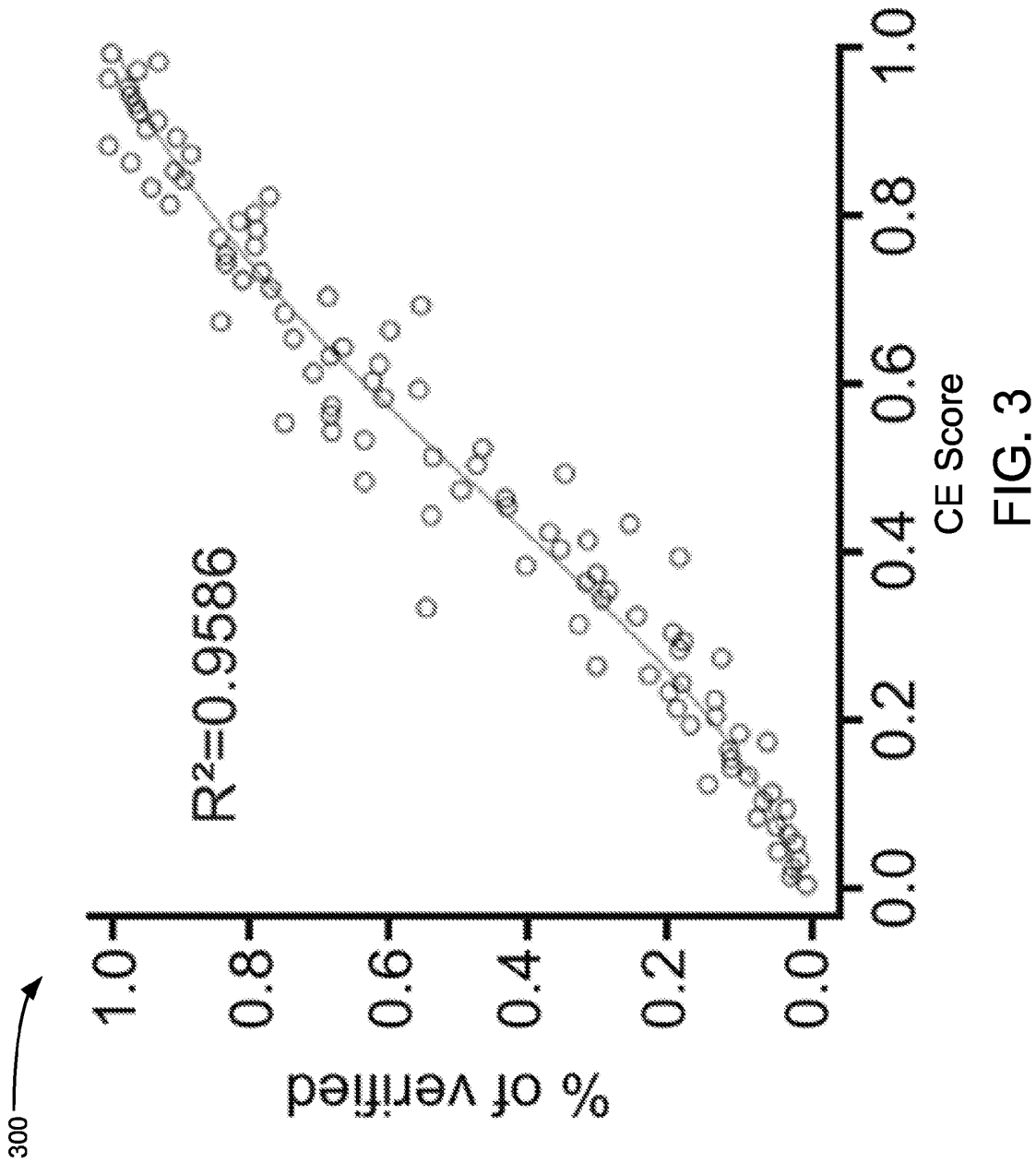


FIG. 2



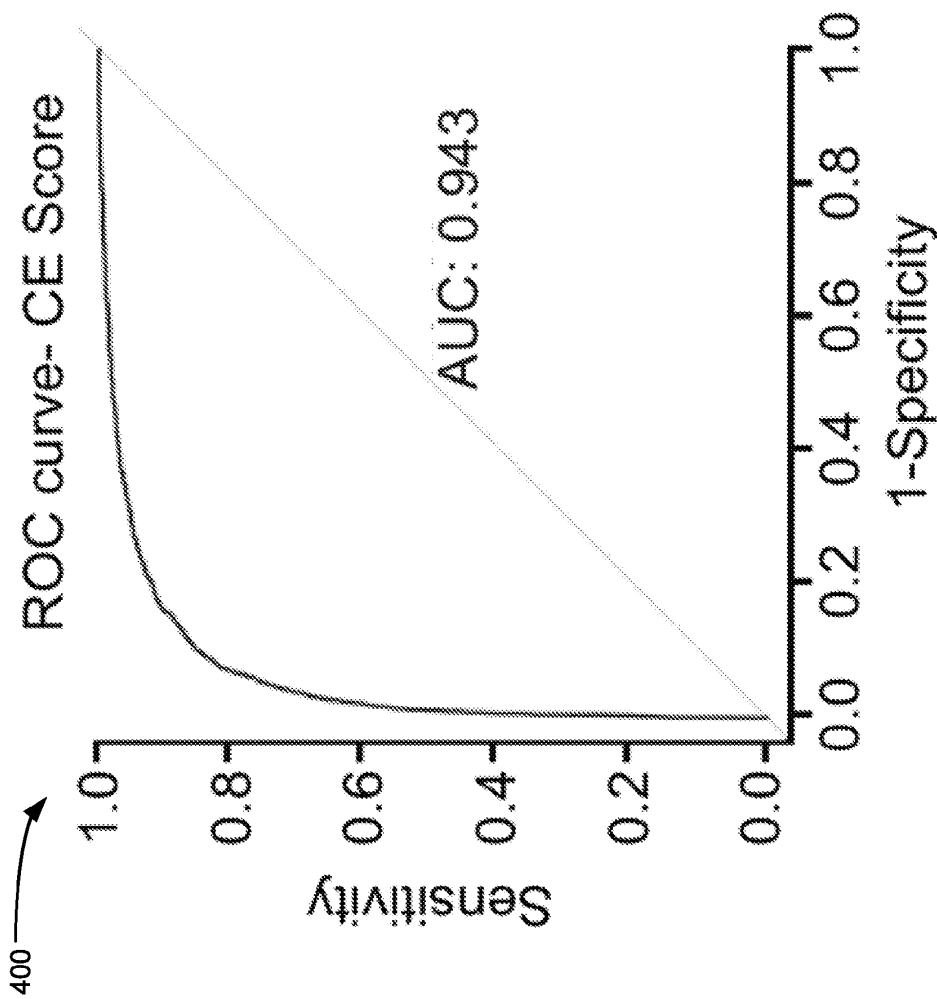


FIG. 4

500

Table 1. CE performance for flow cytometry phenotypes

Cutoff	True positives	False positives	True negatives	False negatives	Recall, %	Accuracy, %	Precision, %
Mutation-phenotype associations (n = 96,022; 1,310 verified, 1,757 excluded, 92,955 untested)							
Excellent	838	176	1,581	472	63.97	78.87	82.64
Good and above	1,140	286	1,471	170	87.02	85.13	79.94
Potential and above	1,209	669	1,088	101	92.29	74.89	64.38
Not good and above	1,310	1,757	0	0	100	42.71	42.71
Alleles (n = 3,020 named alleles; 275 verified, 112 excluded, 2,633 untested)							
Excellent	215	14	98	60	78.18	80.88	93.89
Good and above	246	21	91	29	89.45	87.08	92.13
Potential and above	257	59	53	18	93.45	80.10	81.33
Not good and above	275	112	0	0	100	71.06	71.06
Genes (n = 15,313; 146 causative, 108 noncausative, 15,059 untested)							
Excellent	114	19	89	32	78.08	79.92	85.71
Good and above	132	24	84	14	90.41	85.04	84.62
Potential and above	139	69	39	7	95.21	70.08	66.83
Not good and above	146	108	0	0	100	57.48	57.48

FIG. 5A

501 ↗

2. CE performance in scoring colocalizing mutations				
No. of colocalized genes	Total cases	CE ranked correctly	% Correct	
2	591	514	87.0	
3	233	208	89.3	
4	91	76	83.5	
5	32	22	68.8	
6	6	5	83.3	
7	6	6	100	
8	1	0	0	
10	1	1	100	

FIG. 5B

600

Table 3. Features of input data in CE prediction algorithm

Input data	Features
Phenotype data	The percentage of VAR mice whose screen results overlap with those of B6 mice The percentage of VAR mice whose screen results overlap with those of REF mice Difference between HET and VAR results Direction of the results (whether the average of VAR screening results is greater or less than the average of REF screening results) Difference between REF and VAR results Number of female HET mice Number of female REF mice Number of male REF mice Number of male HET mice Number of male VAR mice Number of female VAR mice The identity of the phenotype (e.g., FACS T cell) The group identity of the phenotype (e.g., FACS screen or bone screens) The number of outliers in REF mice The number of outliers in HET mice The number of outliers in VAR mice Difference between REF and B6 results Difference between REF and HET results Whether the variance of REF is big Whether the variance of HET is big Whether the variance of VAR is big Whether the average age of the mice for this mutation/phenotype is older than the average age of all mice tested for this phenotype Whether the average age of the VAR mice is younger than the average age of the REF mice Number of pedigrees this gene/phenotype has The direction of the position superpedigree results for this mutation/phenotype Number of significant* single pedigrees in the significant position superpedigree for this mutation/phenotype Number of pedigrees included in the significant position superpedigree results for this mutation/phenotype The direction of the gene superpedigree results (null alleles) for this phenotype The direction of the gene superpedigree results (null+missense alleles) for this phenotype Whether there are corresponding trimmed results for the untrimmed data (only when VAR results are greater than REF results)* How closely VAR results resemble B6 results How closely HET results resemble B6 results How closely REF results resemble B6 results Whether REF and B6 results are different
Linkage data	Average number of Linkage Analyzer runs with $P < 0.00005$ for each allele of this gene Number of phenotypes with significant selective gene superpedigree results for this gene Number of Linkage Analyzer runs with $P < 0.00005$ for this gene Number of pedigrees in the selective gene superpedigree and whether the result is significant for this gene/phenotype Number of pedigrees contributing to a significant gene superpedigree result (null alleles) Number of pedigrees in a significant gene superpedigree result (null alleles) The minimum P value of single Linkage Analyzer result for this mutation/phenotype The percentage of body weight screens with $P < 0.0001$ for this mutation The percentage of FACS screens with $P < 0.0001$ for this mutation Whether the gene superpedigree results are significant (null+missense) for this phenotype Whether P value is significant in both raw and normalized assays for this mutation/phenotype Whether the minimum P value is for a recessive model of inheritance (rather than dominant or additive) Whether this phenotype is driven by another mutation The percentage of DSS screens with $P < 0.0001$ for this mutation Number of FACS phenotypes with $P < 0.0001$ for this mutation Number of DSS phenotypes with $P < 0.0001$ for this mutation Number of body weight phenotypes with $P < 0.0001$ for this mutation Whether the position superpedigree results are significant for this mutation/phenotype Whether the gene superpedigree results are significant (null alleles) for this phenotype Whether the gene superpedigree results are significant (missense alleles) for this phenotype
Mutation data	Damage score for this mutation Number of alleles this gene has Whether the mutation is autosomal Whether the mutation is colocalized with another mutation for this phenotype Whether the mutation is colocalized with a verified mutation for this phenotype Whether the mutation is colocalized with an excluded mutation for this phenotype Whether the mutation is colocalized with a mutation of higher damage score The number of splice variants for the gene containing this mutation The ratio of number of named mutations vs. number of incidental mutations for this amino acid change
Gene data	The P value for a lethal phenotype The probability that the gene is an essential gene (E-score)
Other	Number of phenotypes with algorithmic score greater or equal to -0.5 for this mutation Algorithmic score for this mutation/phenotype

FIG. 6

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700

Feature	Points
REF outliers*	-1
HET outliers*	-1
VAR outliers*	-1
HET results have big variance [†]	-1
VAR results have big variance [†]	-1
REF and B6 results are different [‡]	-1
REF and VAR results overlap [§]	-1 to -3
B6 and VAR results overlap [§]	-0.5
HET results more similar than REF results to B6 results*	-1 to -2
VAR results more similar than REF results to B6 results*	-1 to -2
Magnitude of change less than 2-fold for FACS B-1 B cell phenotype	-0.5
Magnitude of change less than 1.5-fold for FACS B-1 B cell phenotype	-3
Magnitude of change less than 2-fold for FACS B-2 B cell phenotype	-0.5
Magnitude of change less than 1.5-fold for FACS B-2 B cell phenotype	-3
Magnitude of change less than 2-fold for FACS DC phenotype	-0.5
Insignificant position superpedigree result	-1
Significant position superpedigree result (only minority of pedigrees contributed)	-1
In opposite direction of significant position superpedigree result	-3
Significant position superpedigree result	1.5
In opposite direction of significant gene superpedigree result (null alleles)	-3
Insignificant gene superpedigree result (null allele)	-1
Significant gene superpedigree result (null alleles)	1
In opposite direction of significant gene superpedigree result (null+missense alleles)	-0.5
Insignificant gene superpedigree result (null+missense alleles)	-0.5
Significant gene superpedigree result (null+missense alleles)	0.5
In opposite direction of significant gene superpedigree result (missense alleles)	-0.5
Insignificant gene superpedigree result (missense alleles)	-0.5
Significant gene superpedigree result (missense alleles)	0.5
Significant selective gene superpedigree result with more than two pedigrees	3
Significant selective gene superpedigree result with two pedigrees	2
In opposite direction of insignificant selective gene superpedigree result	1
In opposite direction of significant selective gene superpedigree result with two pedigrees	-2
In opposite direction of significant selective gene superpedigree result with more than two pedigrees	-3
Insignificant selective gene superpedigree result	-1
Significant selective gene superpedigree result exists for other phenotypes	0.5
Mutation is linked to a more damaging mutation	-1
Mutation is linked to an excluded mutation	1
Mutation is linked to a verified mutation	-3
No corresponding trimmed result	-3
Phenotype is driven by another mutation	-1

B6, C57BL/6J.

A screen result is considered as an outlier if its value is outside the range of mean $\pm 3 \times$ standard deviation (SD).[†]The variance of REF, HET, or VAR results is considered big if the SD is more than 30% of the absolute difference between the maximum screening result and the minimum screening result.[‡]REF and B6 results are considered different if the absolute difference between the REF mean and B6 mean is more than $2 \times$ REF SD and $2 \times$ B6 SD.[§]REF or B6 results overlap with VAR results if they are within the range of VAR mean $\pm 1 \times$ VAR SD.^{}HET results are considered more similar than REF results to B6 results if the absolute difference between the B6 mean and REF mean is more than half of REF SD and more than the absolute difference between HET mean and B6 mean.^{*}VAR results are considered more similar than REF results to B6 results if the absolute difference between the B6 mean and REF mean is more than half of REF SD and more than the absolute difference between VAR mean and B6 mean.[†]Significant pedigree refers to linkage analysis of a pedigree or superpedigree by AMM in which $P < 0.05$ for a mutation-phenotype association.

FIG. 7

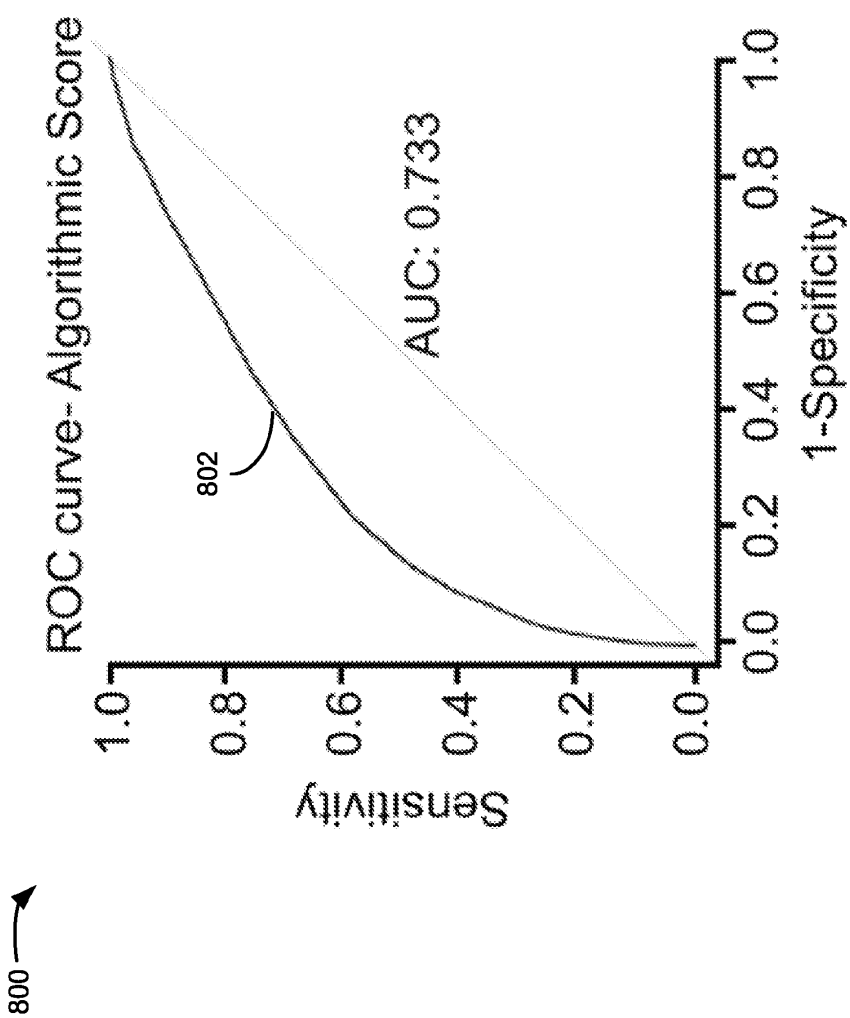


FIG. 8

900

	Parameter
1	B cells
2	B:T cell ratio
3	B-1 B cells
4	B-1a B cells
5	B-1a B cells in B-1 B cells
6	B-1b B cells
7	B-1b B cells in B-1 B cells
8	B-2 B cells
9	B220 MFI
10	CD11b ⁺ DC (gated in CD11c ⁺ cells)
11	CD11c ⁺ DC
12	CD4:CD8 T cell ratio
13	CD4 ⁺ T cells
14	CD4 ⁺ T cells in CD3 ⁺ T cells
15	CD44 MFI on CD4 ⁺ T cells
16	CD44 ⁺ CD4 ⁺ T cells
17	CD44 MFI on CD8 ⁺ T cells
18	CD44 ⁺ CD8 ⁺ T cells
19	CD44 ⁺ T cells
20	CD44 MFI on T cells
21	CD8 ⁺ T cells
22	CD8 ⁺ T cells in CD3 ⁺ T cells
23	CD8 α ⁺ DC (gated in CD11c ⁺ cells)
24	Central memory CD4 ⁺ T cells in CD4 ⁺ T cells
25	Central memory CD8 ⁺ T cells in CD8 ⁺ T cells
26	Effector memory CD4 ⁺ T cells in CD4 ⁺ T cells
27	Effector memory CD8 ⁺ T cells in CD8 ⁺ T cells
28	Effector T cells
29	IgD MFI
30	IgD ⁺ B cells
31	IgM MFI
32	IgM ⁺ B cells
33	Macrophages
34	Memory T cells
35	Naive CD4 ⁺ T cells in CD4 ⁺ T cells
36	Naive CD8 ⁺ T cells in CD8 ⁺ T cells
37	Naive T cells
38	Neutrophils
39	NK cells
40	NK1.1 ⁺ T cells
41	Plasmacytoid DC
42	T cells

Parameters represent frequencies unless otherwise indicated. MFI, mean fluorescence intensity.

FIG. 9

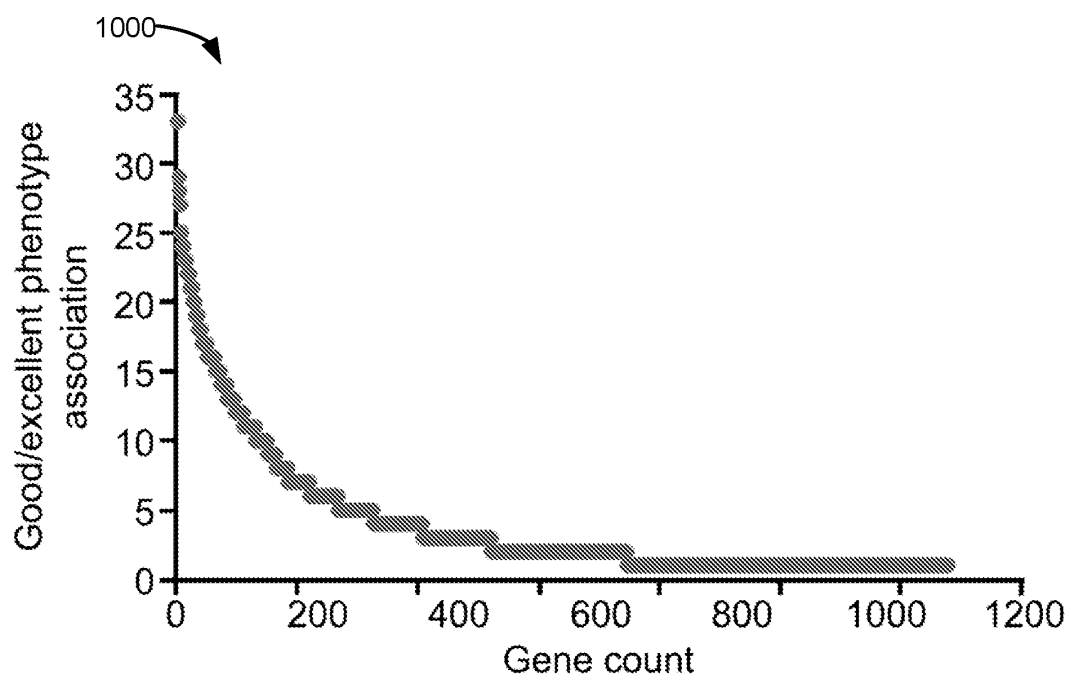
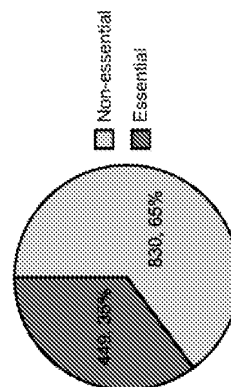
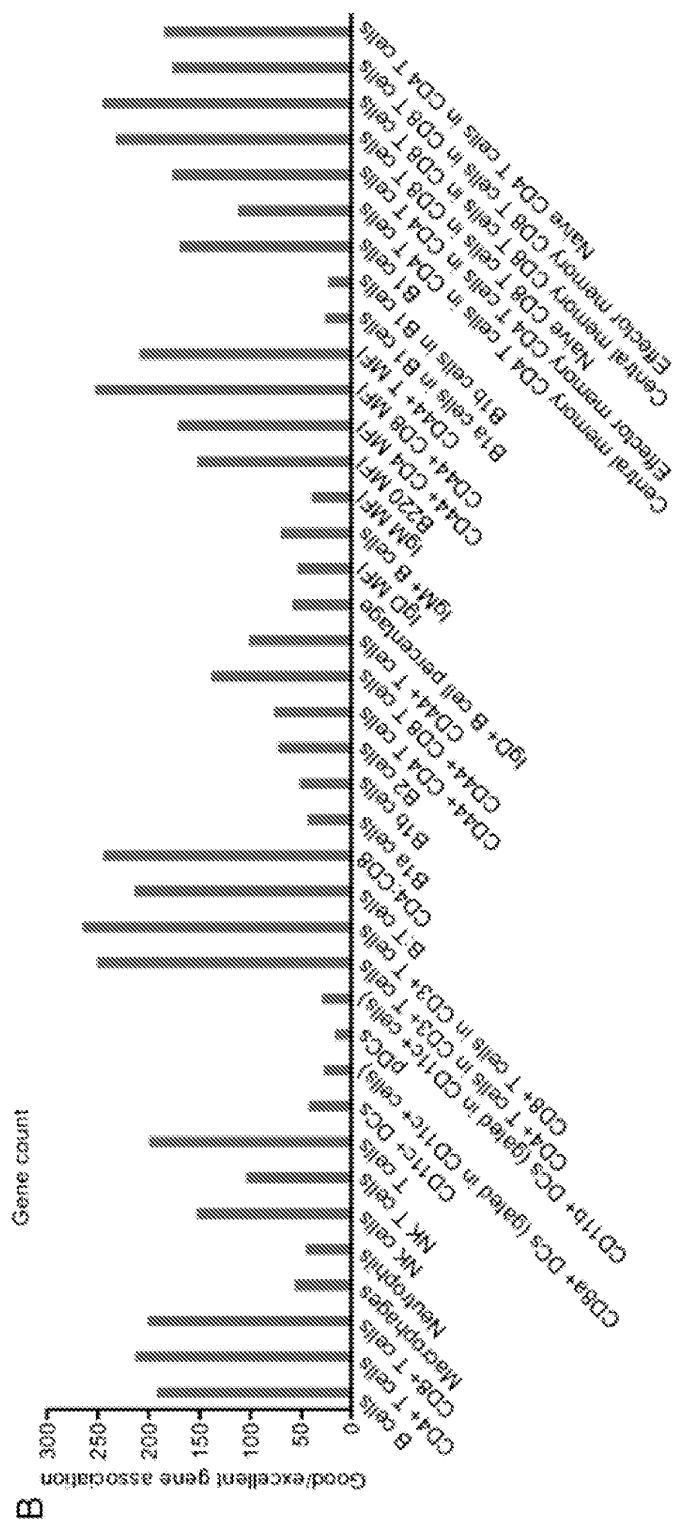


FIG. 10A



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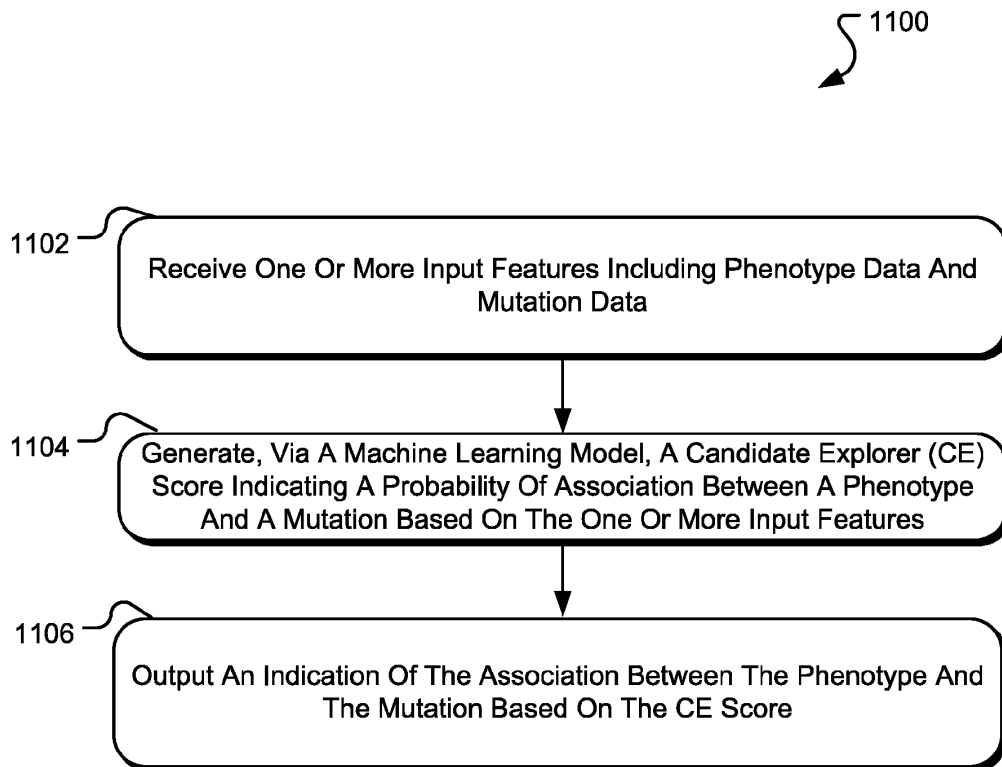


FIG. 11