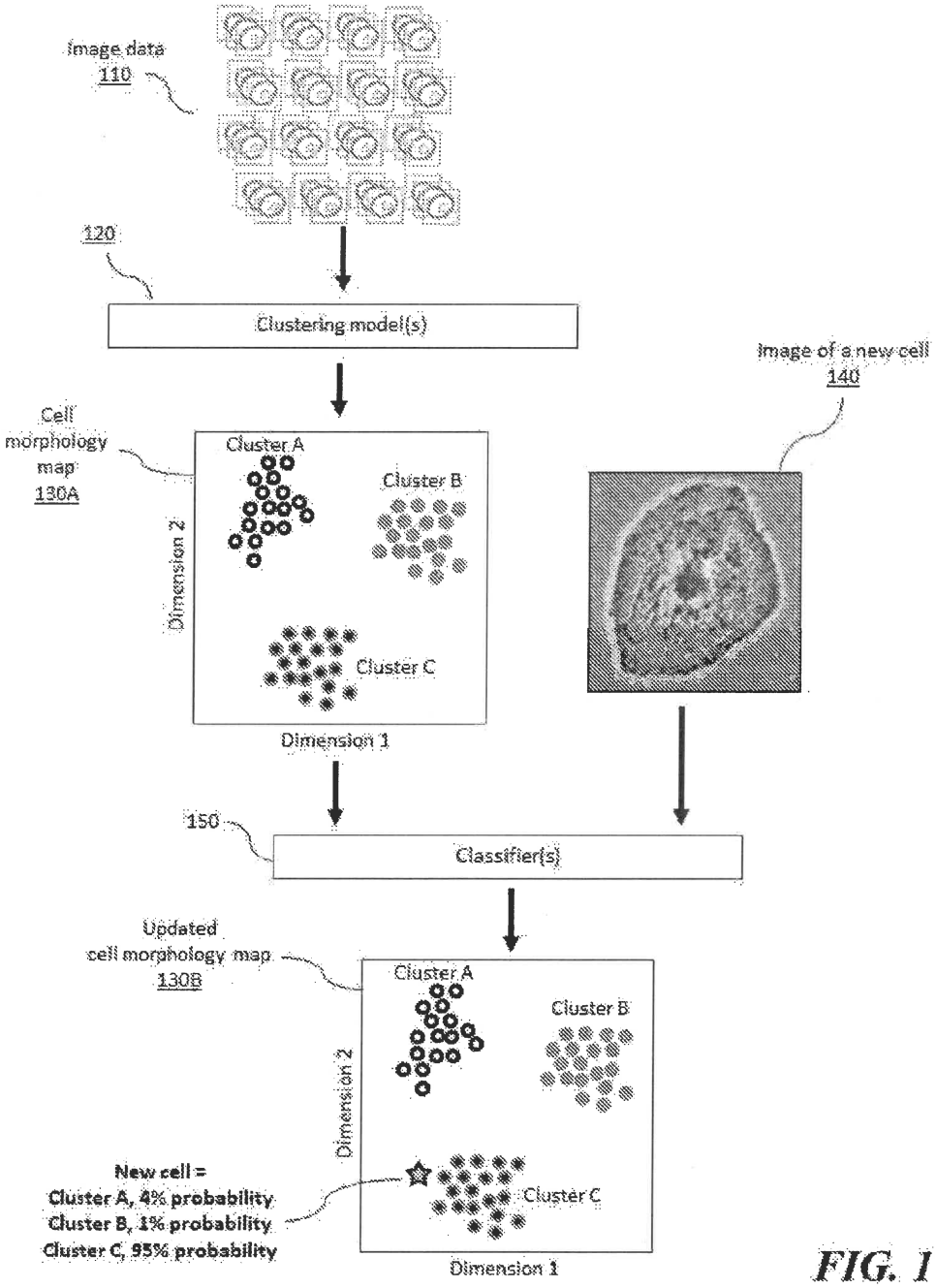

Image data
110
120
Clustering model(s)
Image of a new cell
140
Cell
morphology
map
130A
Cluster A
Cluster B
Cluster C
Dimension 2
Dimension 1
150
Classifier(s)
Updated
cell morphology map
130B
Cluster A
Cluster B
Cluster C
Dimension 2
Dimension 1
New cell =
Cluster A, 4% probability
Cluster B, 1% probability
Cluster C, 95% probability

FIG. 1

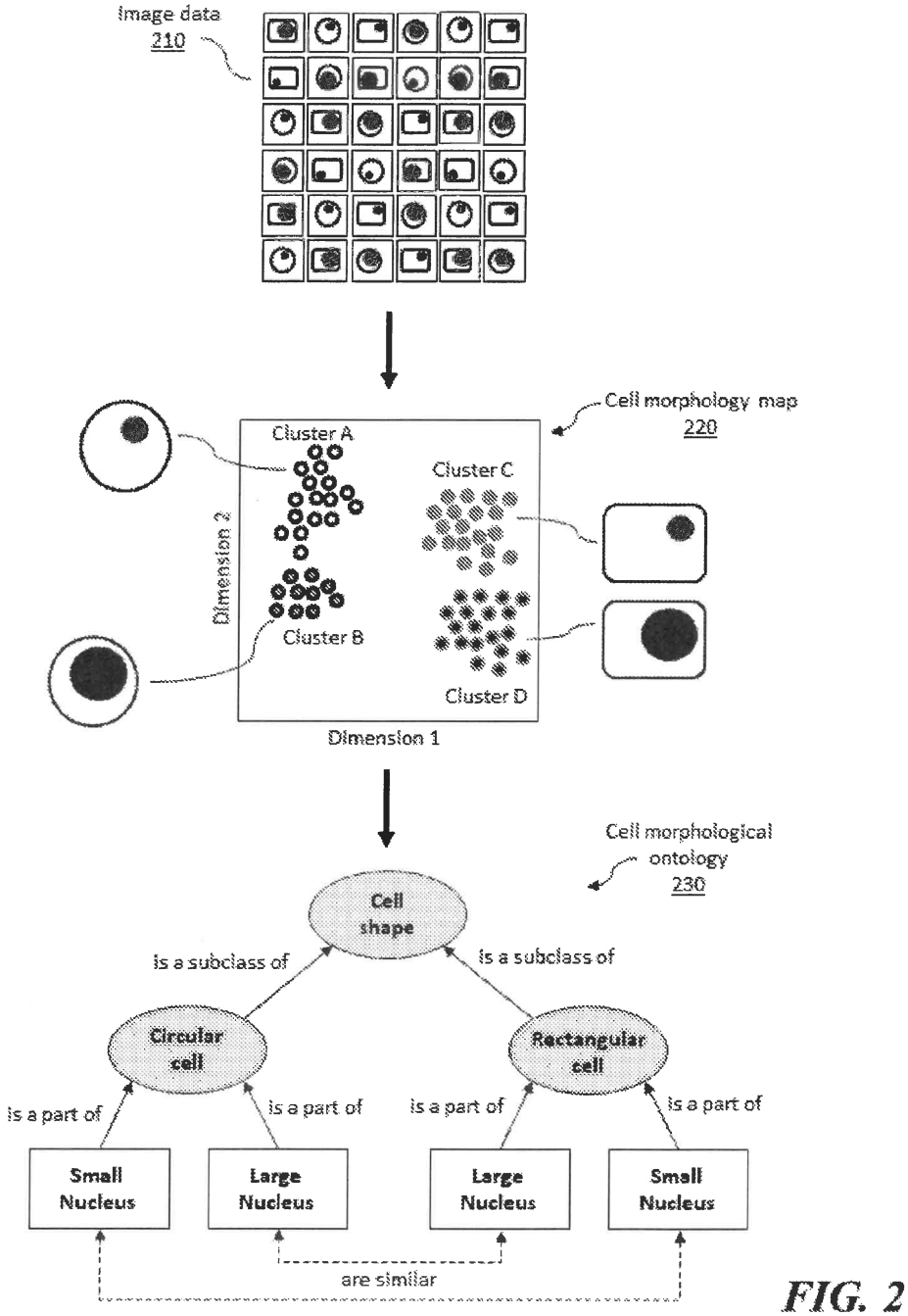

Image data
210
Cell morphology map
220
Cluster A
Cluster B
Cluster C
Cluster D
Dimension 2
Dimension 1
Cell morphological
ontology
230
Cell shape
is a subclass of
is a subclass of
Circular cell
Rectangular cell
is a part of
is a part of
is a part of
is a part of
Small Nucleus
Large Nucleus
Large Nucleus
Small Nucleus
are similar

FIG. 2

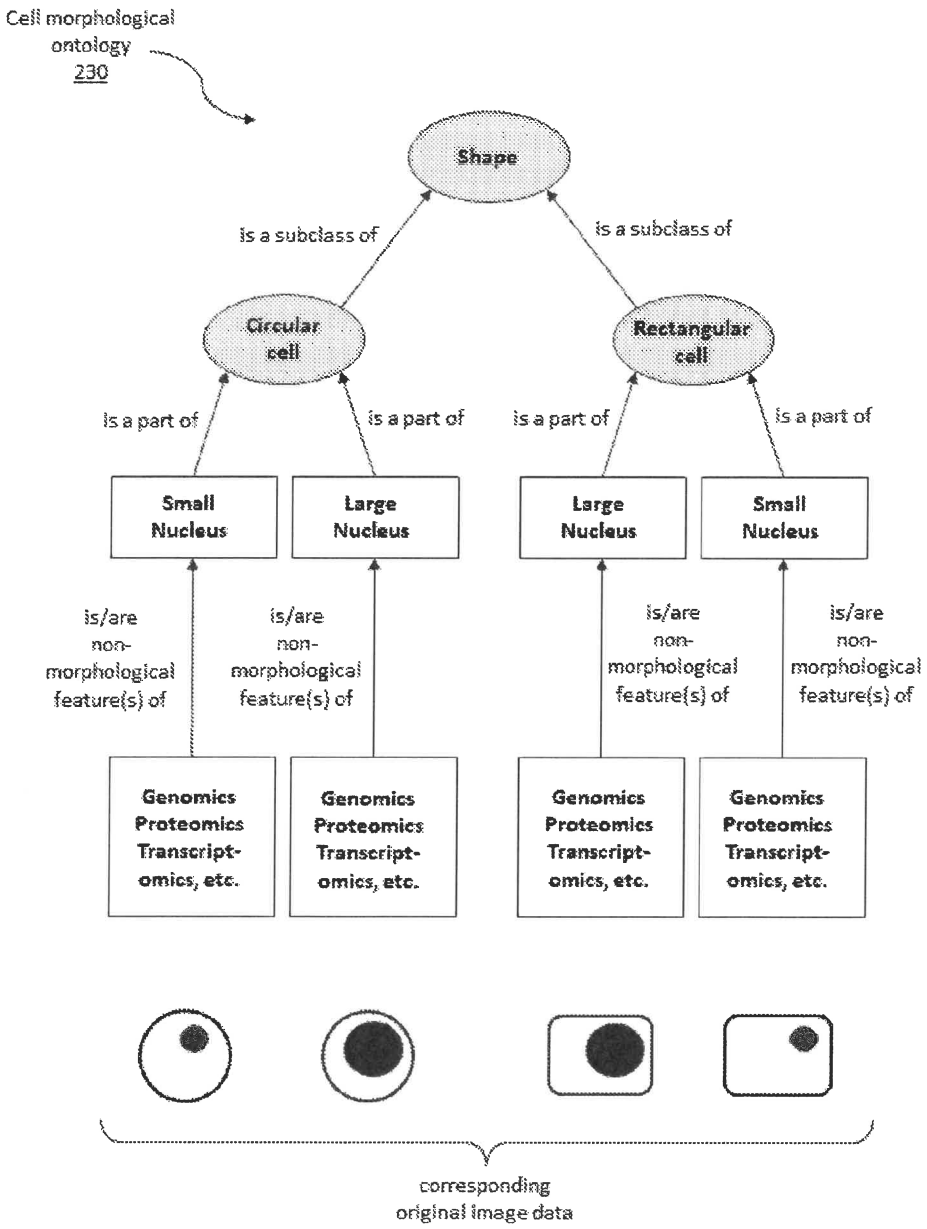

Cell morphological ontology 230
Shape
is a subclass of
is a subclass of
Circular cell
Rectangular cell
is a part of
is a part of
is a part of
is a part of
Small Nucleus
Large Nucleus
Large Nucleus
Small Nucleus
is/are non-morphological feature(s) of
is/are non-morphological feature(s) of
is/are non-morphological feature(s) of
is/are non-morphological feature(s) of
Genomics Proteomics Transcript-omics, etc.
Genomics Proteomics Transcript-omics, etc.
Genomics Proteomics Transcript-omics, etc.
Genomics Proteomics Transcript-omics, etc.
corresponding original image data

FIG. 3

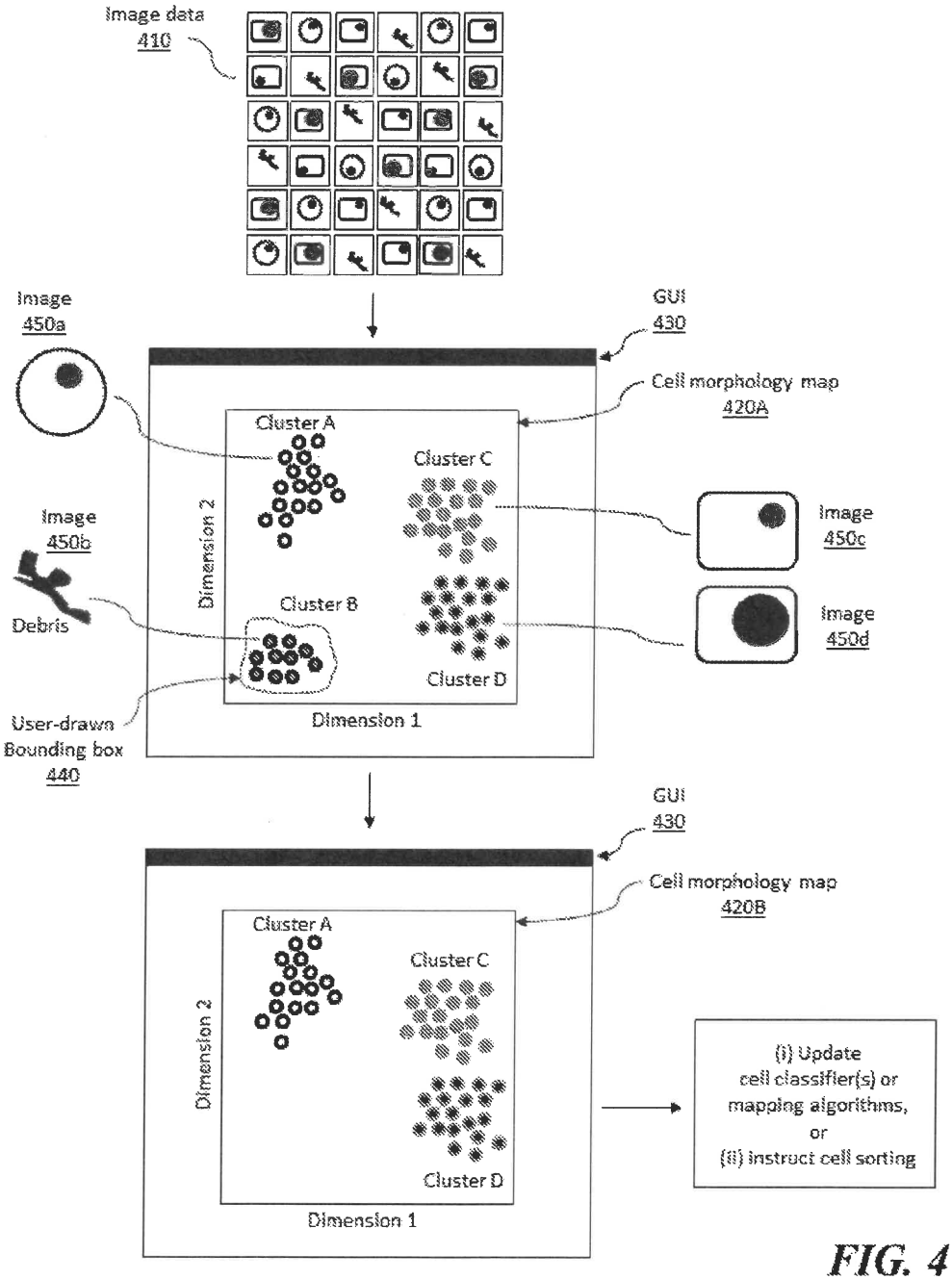

Image data
410
Image
450a
GUI
430
Cell morphology map
420A
Cluster A
Cluster C
Image
450b
Debris
Dimension 2
Cluster B
Cluster D
Image
450c
Image
450d
User-drawn
Bounding box
440
Dimension 1
GUI
430
Cell morphology map
420B
Cluster A
Cluster C
Dimension 2
Cluster D
Dimension 1
(i) Update
cell classifier(s) or
mapping algorithms,
or
(ii) instruct cell sorting

FIG. 4

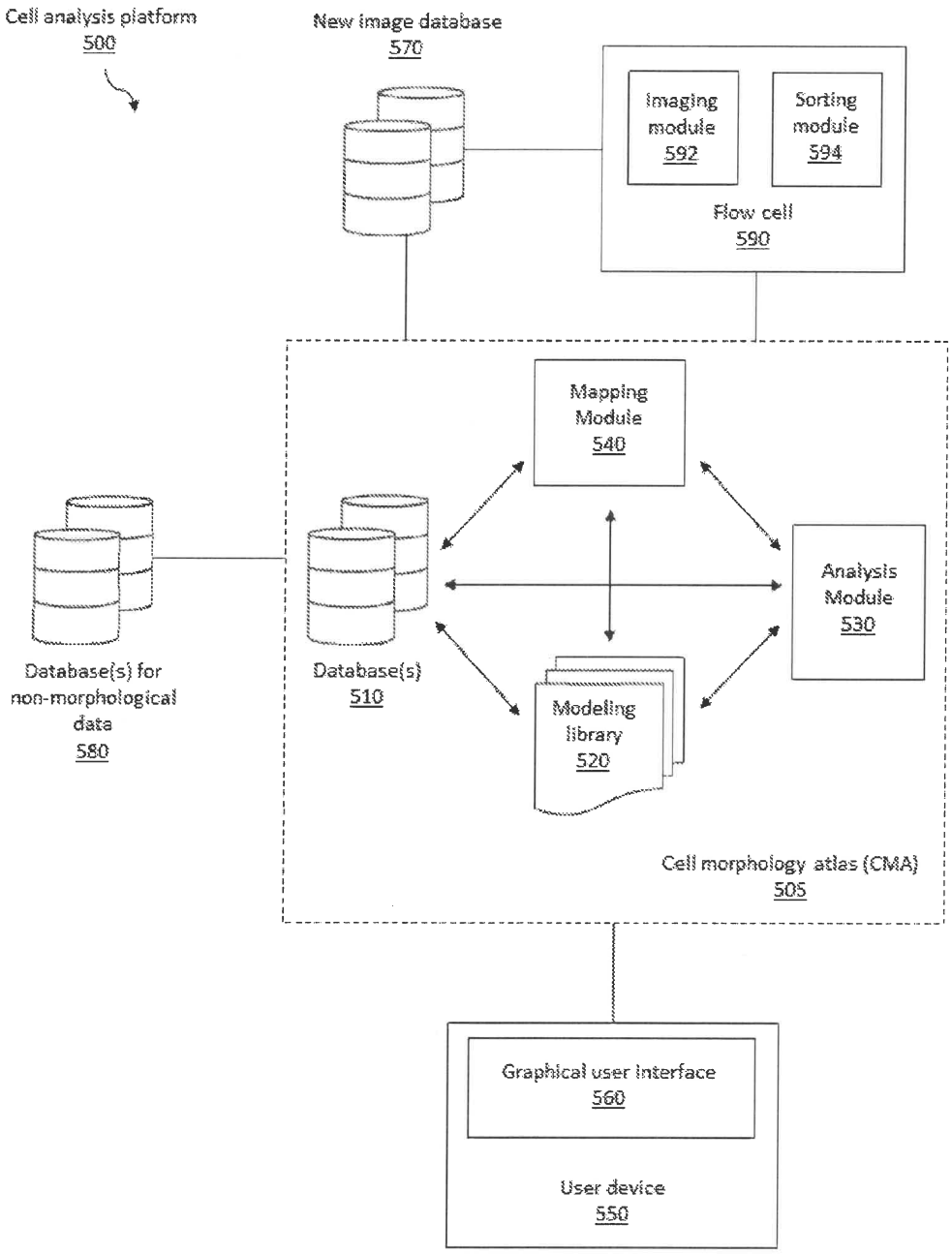

Cell analysis platform
500
New image database
570
Imaging module
592
Sorting module
594
Flow cell
590
Mapping Module
540
Analysis Module
530
Database(s) for non-morphological data
580
Database(s)
510
Modeling library
520
Cell morphology atlas (CMA)
505
Graphical user interface
560
User device
550

FIG. 5

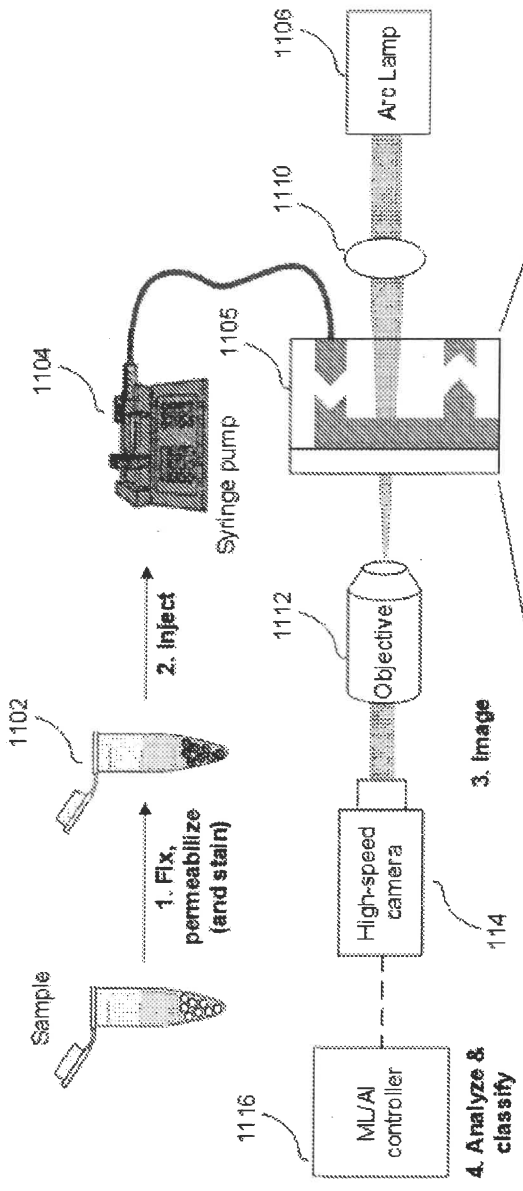

Sample
1. Fix, permeabilize (and stain)
1102
2. Inject
1104
Syringe pump
1105
1106
Arc Lamp
1110
1112
Objective
High-speed camera
114
3. Image
1116
ML/AI controller
4. Analyze & classify

FIG. 6A

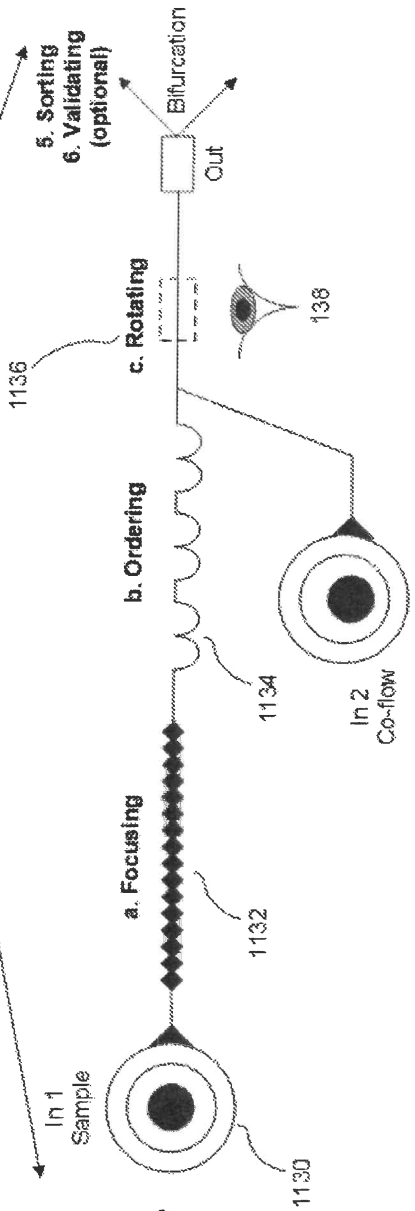

5. Sorting
6. Validating (optional)
Bifurcation
Out
1136
c. Rotating
138
b. Ordering
1134
In 2
Co-flow
a. Focusing
1132
In 1
Sample
1130

FIG. 6B

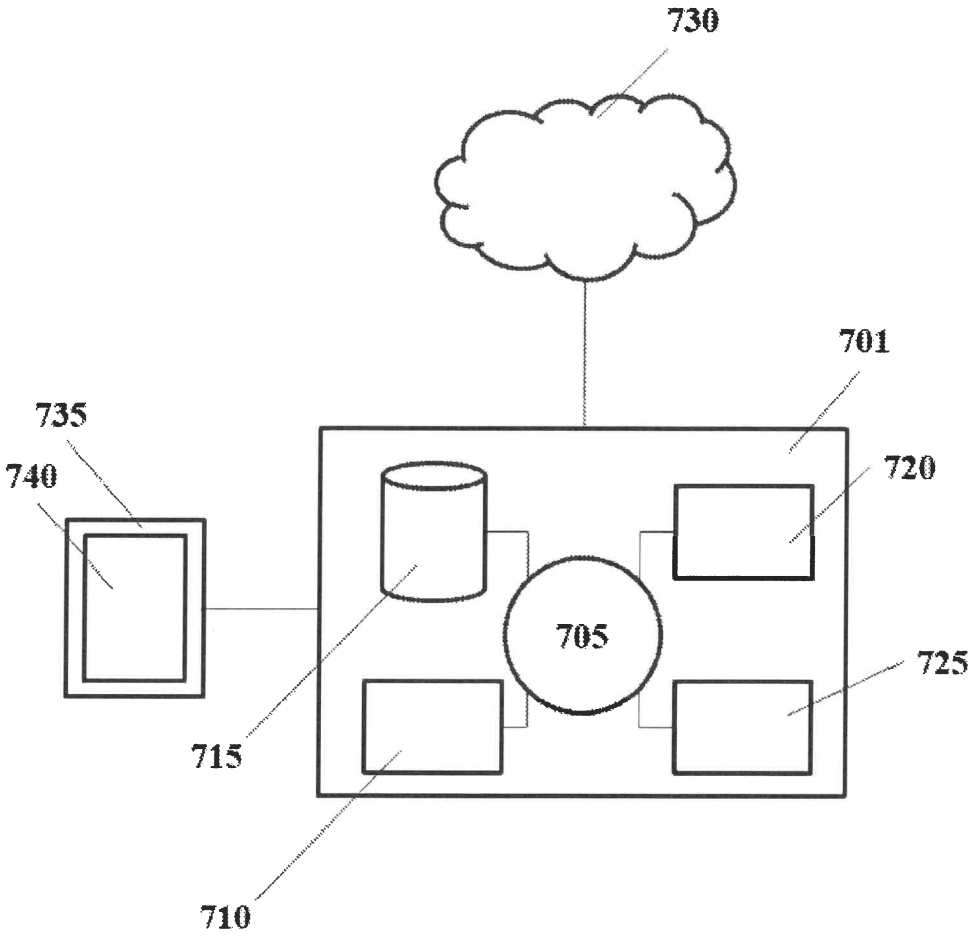


FIG. 7

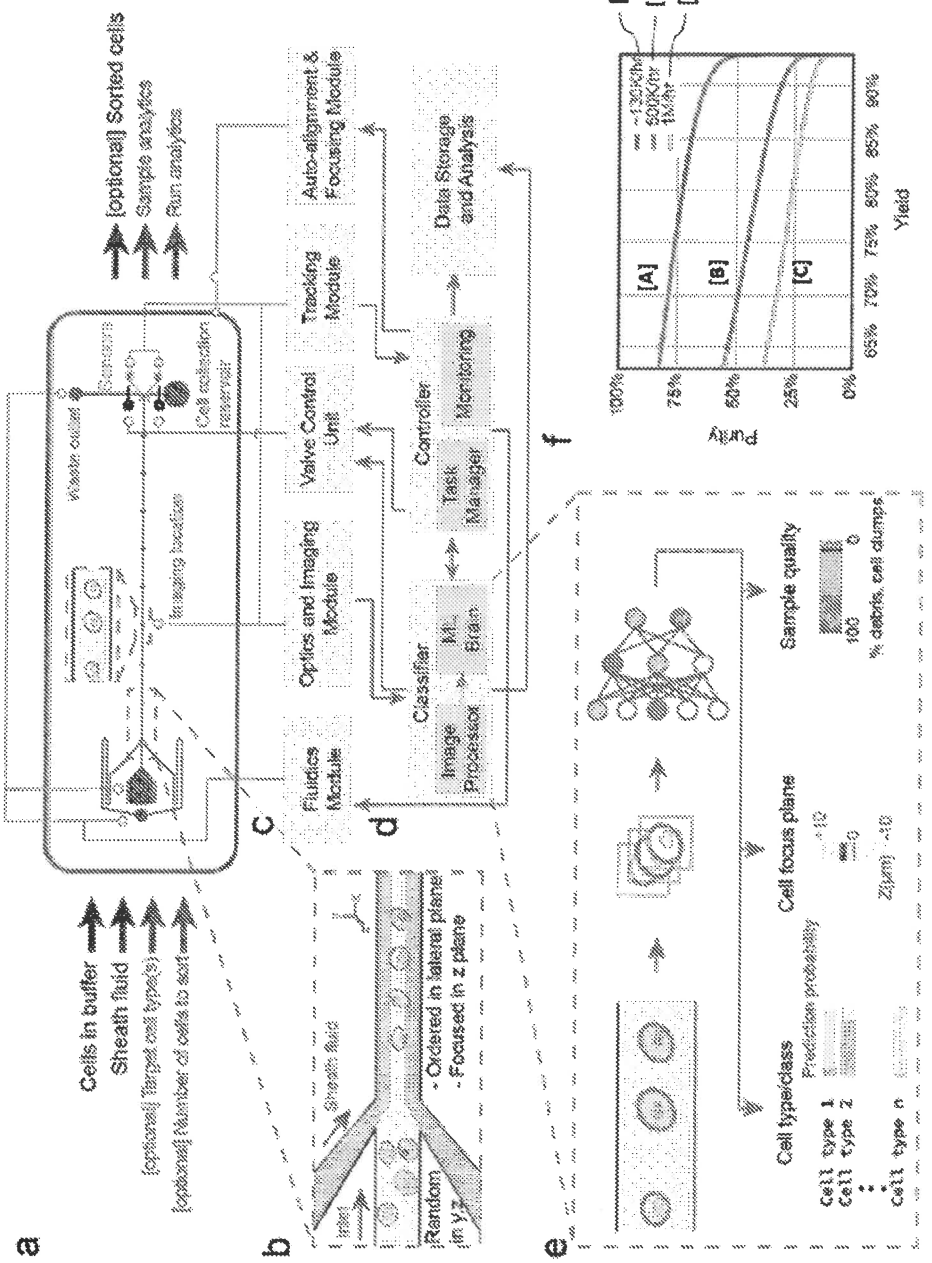

a
Cells in buffer
Sheath fluid
[optional] Target cell type(s)
[optional] Number of cells to sort
[optional] Sorted cells
Sample analytics
Run analytics
Waste outlet
Sensors
Imaging location
Cell collection reservoir
b
Inlet
Sheath fluid
Random in y,z
- Ordered in lateral plane
- Focused in z plane
c
Fluidics Module
Optics and Imaging Module
Valve Control Unit
Tracking Module
Auto-alignment & Focusing Module
d
Classifier
Image Processor
ML Brain
Controller
Task Manager
Monitoring
Data Storage and Analysis
e
Cell type/class
Prediction probability
Cell type 1
Cell type 2
Cell type n
Cell focus plane
Sample quality
% debris, cell clumps
f
[A]
[B]
[C]
Purity
Yield
100%
75%
50%
25%
0%
65%
70%
75%
80%
85%
90%

FIG. 8

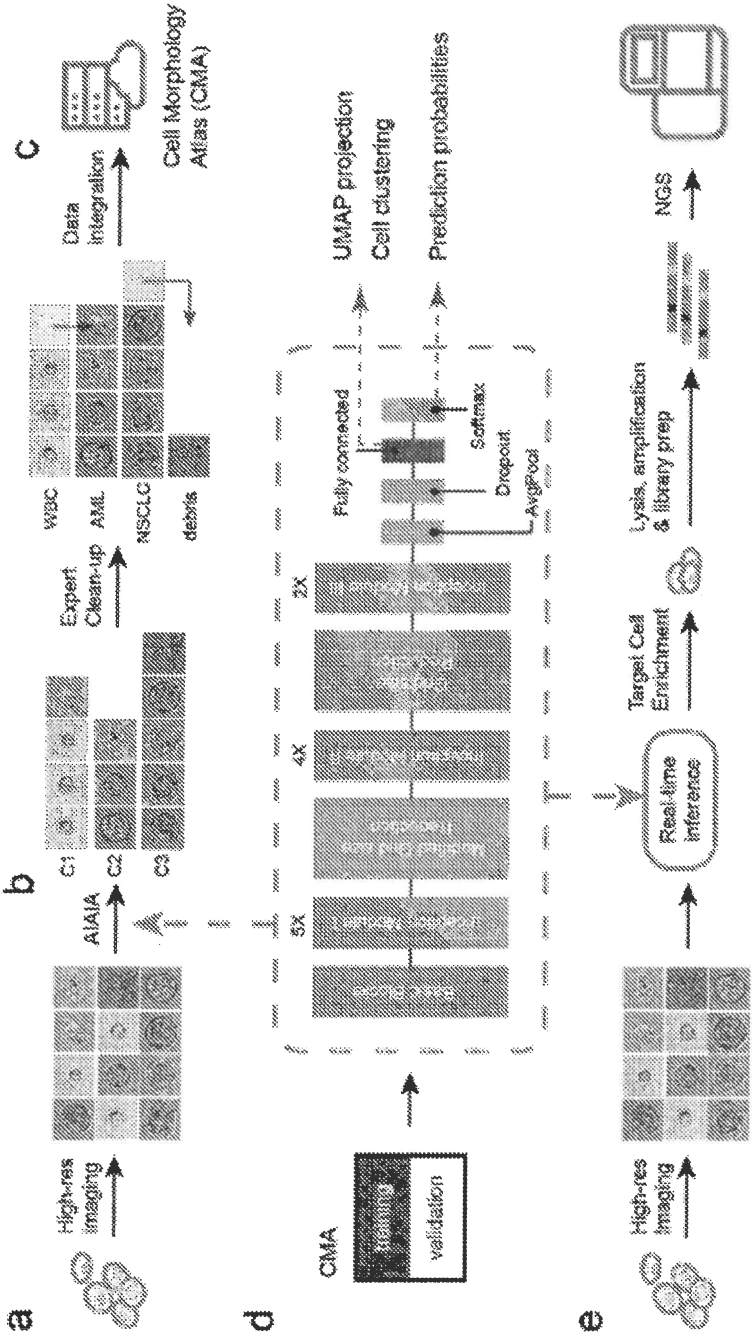

a
High-res imaging
b
AIAIA
C1
C2
C3
Expert Clean-up
WBC
AML
NSCLC
debris
c
Data Integration
Cell Morphology Atlas (CMA)
d
CMA
training
validation
5X
4X
2X
Fully connected
Softmax
Dropout
AvgPool
UMAP projection
Cell clustering
Prediction probabilities
e
High-res imaging
Real-time inference
Target Cell Enrichment
Lysis, amplification & library prep
NGS

FIG. 9

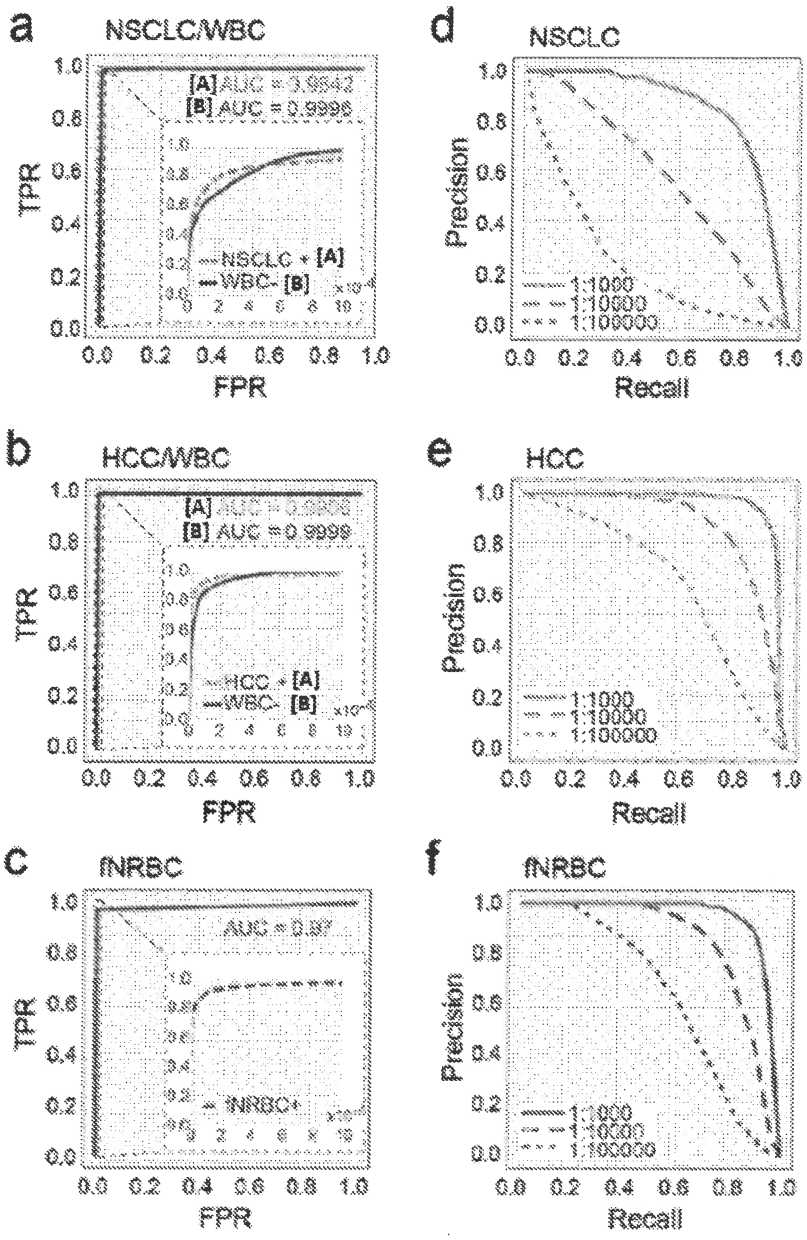

a
NSCLC/WBC
[A] AUC = 0.9842
[B] AUC = 0.9998
TPR
FPR
NSCLC - [A]
WBC - [B]
d
NSCLC
Precision
Recall
1:1000
1:10000
1:100000
b
HCC/WBC
[A] AUC = 0.9842
[B] AUC = 0.9998
HCC - [A]
WBC - [B]
e
HCC
c
fNRBC
AUC = 0.97
fNRBC+
f
fNRBC

FIG. 10

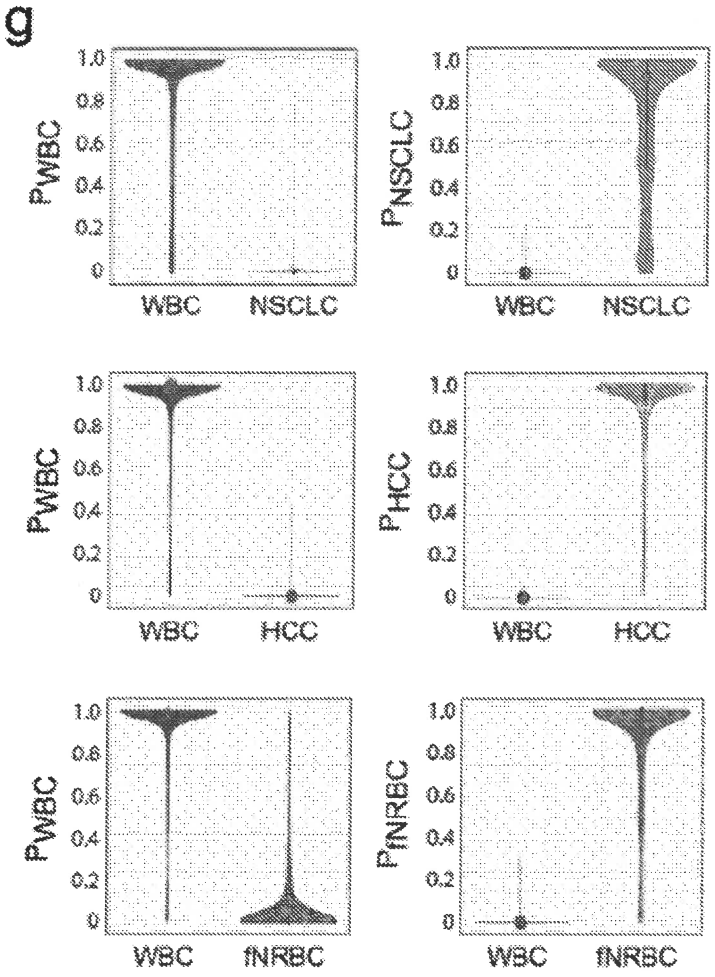

g
P_{WBC}
1.0
0.8
0.6
0.4
0.2
0
WBC
NSCLC
P_{NSCLC}
WBC
NSCLC
P_{WBC}
WBC
HCC
P_{HCC}
WBC
HCC
P_{WBC}
WBC
fNRBC
P_{fNRBC}
WBC
fNRBC

FIG. 10

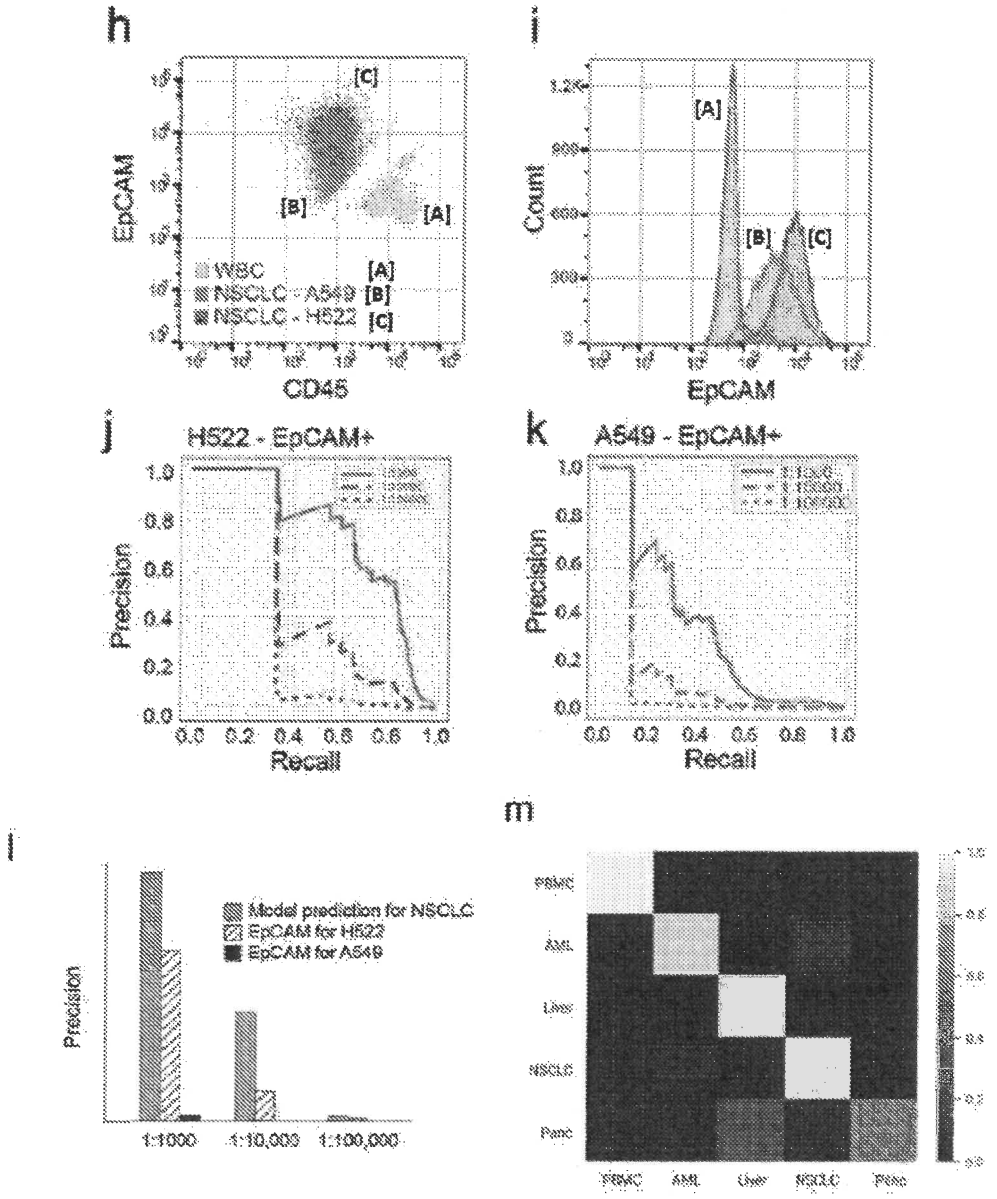

h
EpCAM
CD45
[A]
[B]
[C]
WBC
NSCLC - A549
NSCLC - H522
i
Count
EpCAM
[A]
[B]
[C]
j
H522 - EpCAM+
Precision
Recall
k
A549 - EpCAM+
Precision
Recall
l
Precision
Model prediction for NSCLC
EpCAM for H522
EpCAM for A549
1:1000
1:10,000
1:100,000
m
PBMC
AML
Liver
NSCLC
Panc

FIG. 10

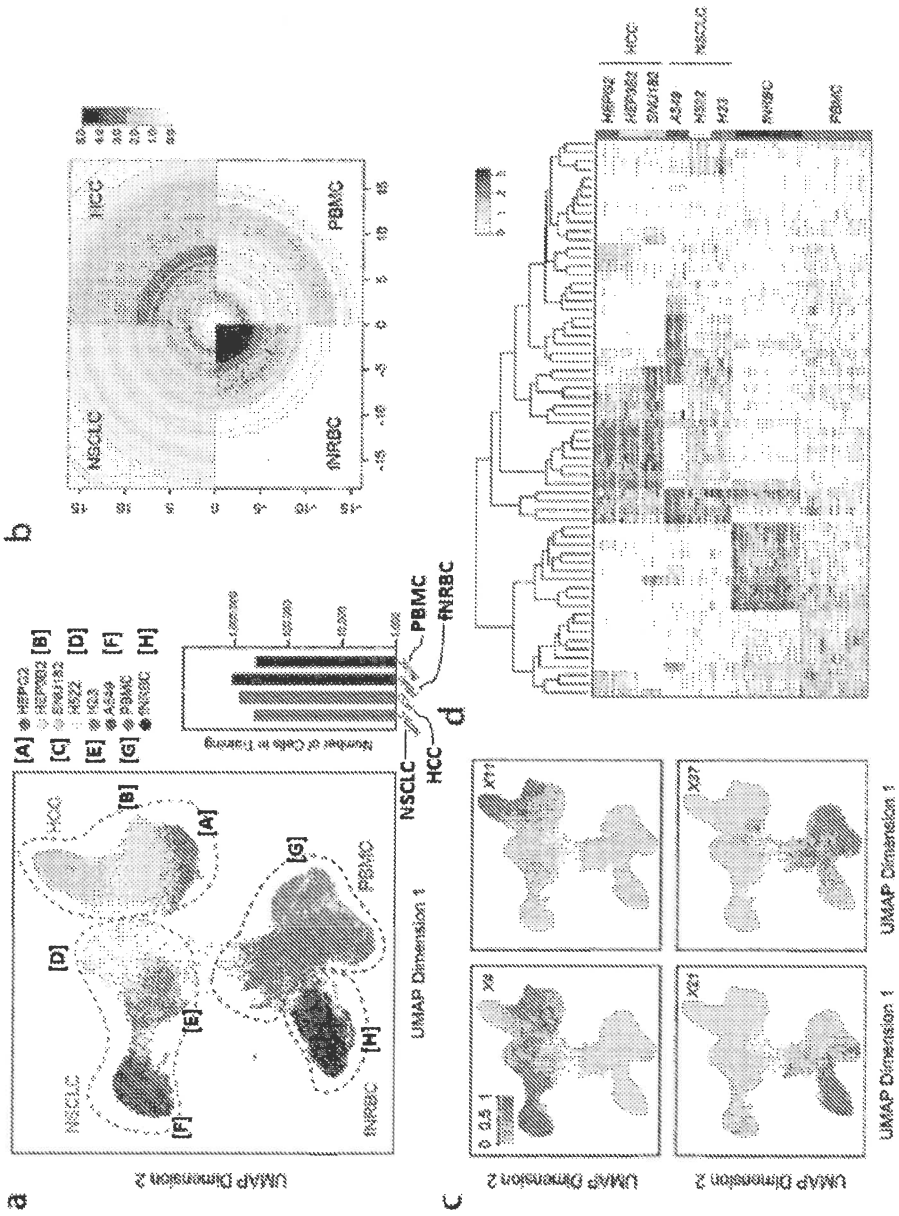

a
b
c
d
UMAP Dimension 2
UMAP Dimension 1
NSCLC
HCC
PBMC
fNRBC
[A]
[B]
[C]
[D]
[E]
[F]
[G]
[H]
Number of Cells in Training
MSPC2
HEP3B2
SNU182
A549
H23
H23
fNRBC
PBMC
HCC
NSCLC

FIG. 11

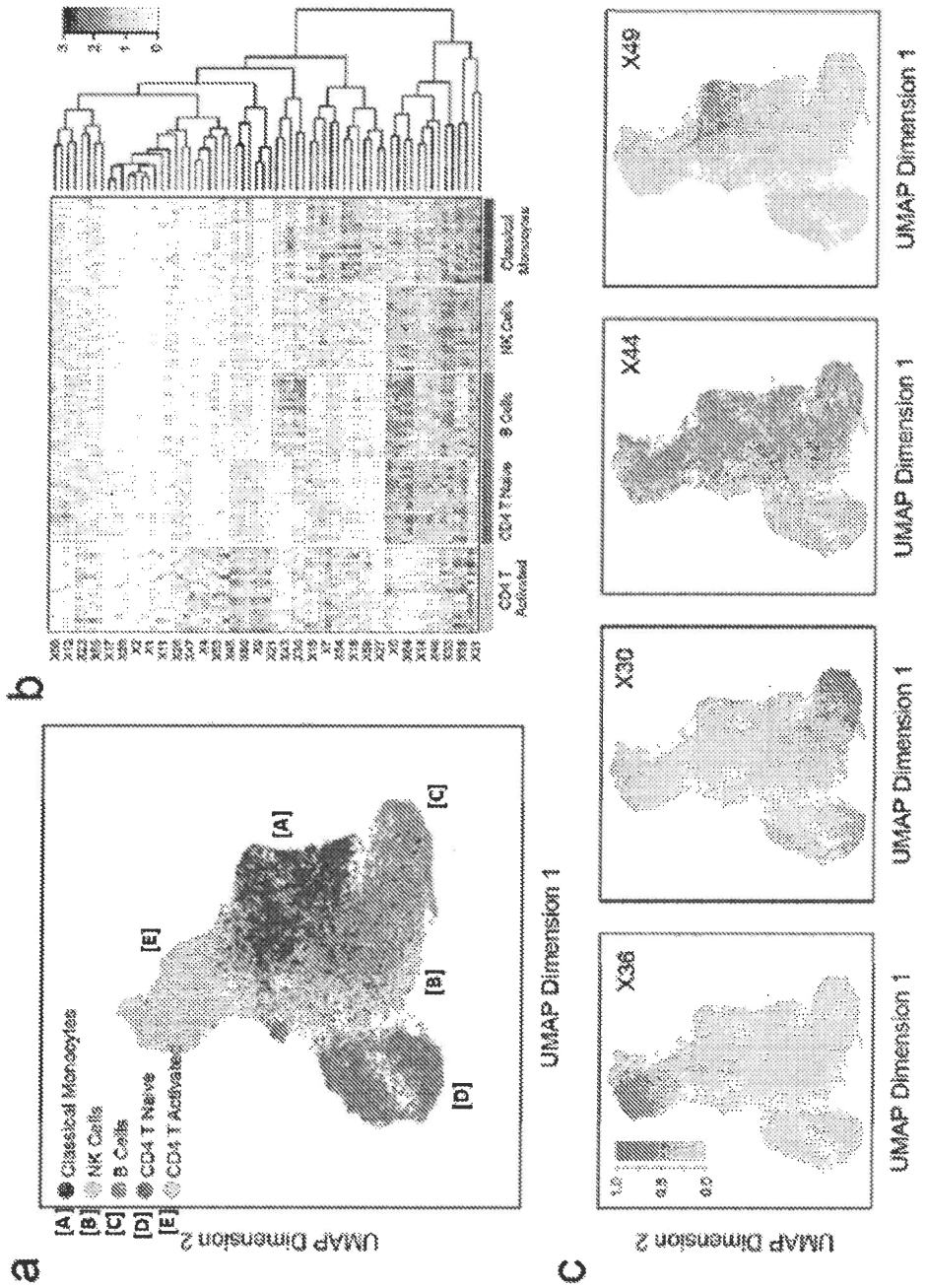

a
b
c
[A]
[B]
[C]
[D]
[E]
Classical Monocytes
NK Cells
B Cells
CD4 T Naive
CD4 T Activated
UMAP Dimension 2
UMAP Dimension 1
X36
X30
X44
X49
Classical Monocytes
NK Cells
B Cells
CD4 T Naive
CD4 T Activated

FIG. 12

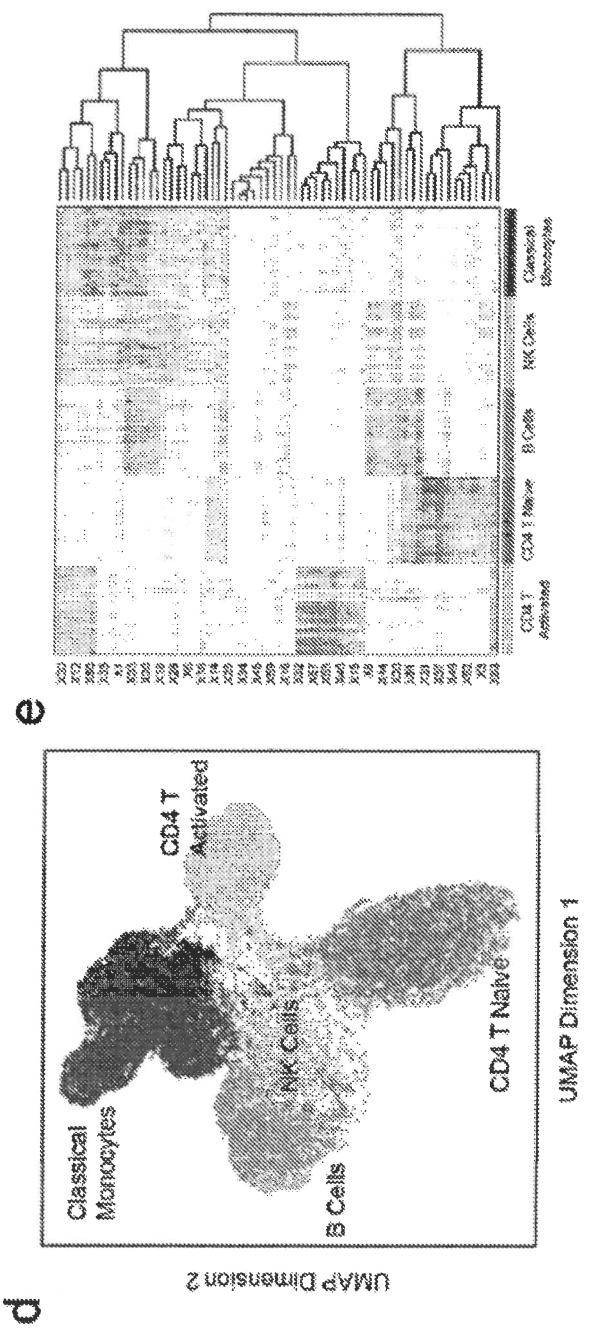

e
d
Classical Monocytes
CD4 T Activated
NK Cells
B Cells
CD4 T Naive
UMAP Dimension 1
UMAP Dimension 2

FIG. 12

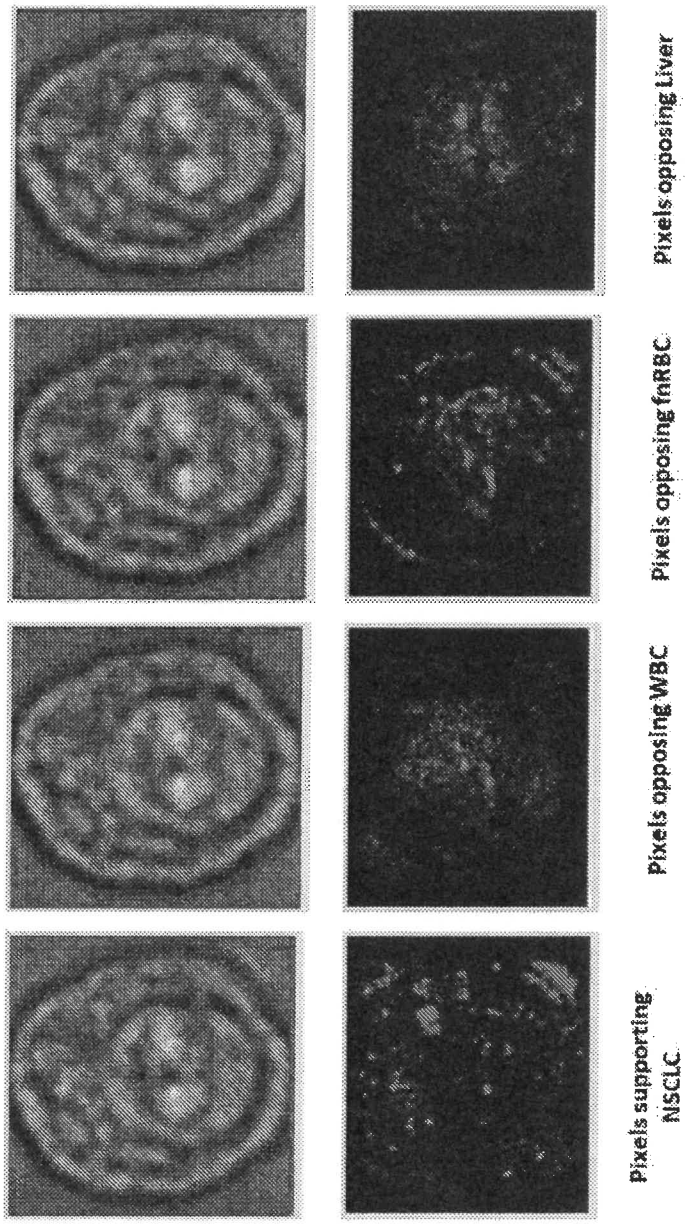
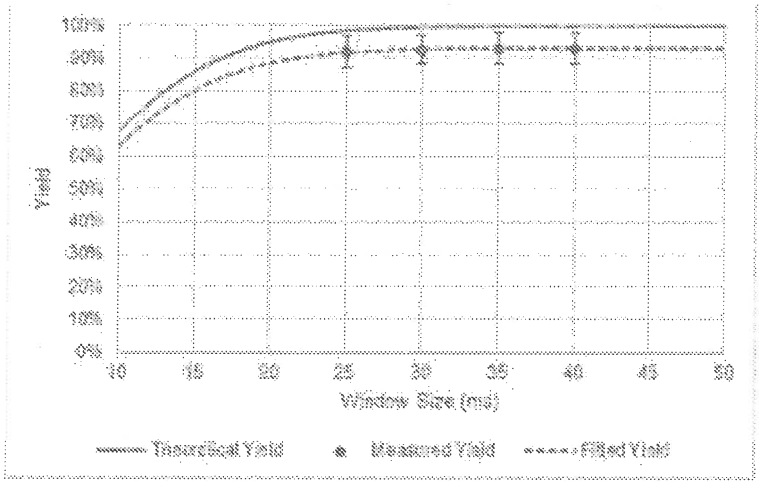
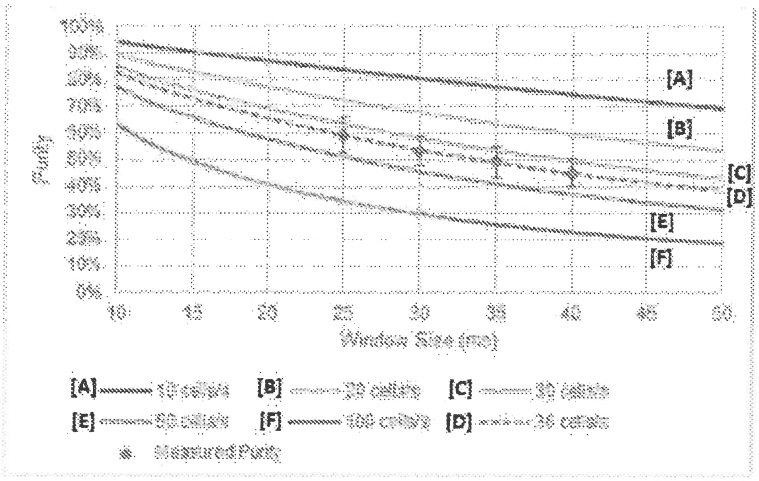

Pixels supporting NSCLC
Pixels opposing WBC
Pixels opposing fnRBC
Pixels opposing Liver

FIG. 13


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Yield
10
15
20
25
30
35
40
45
50
Window Size (ms)
Theoretical Yield
Measured Yield
Fitted Yield

(a)


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Purity
10
15
20
25
30
35
40
45
50
Window Size (ms)
[A]
[B]
[C]
[D]
[E]
[F]
[A] 10 cells/s
[B] 20 cells/s
[C] 30 cells/s
[E] 50 cells/s
[F] 100 cells/s
[D] 36 cells/s
Measured Purity

(b)

FIG. 14

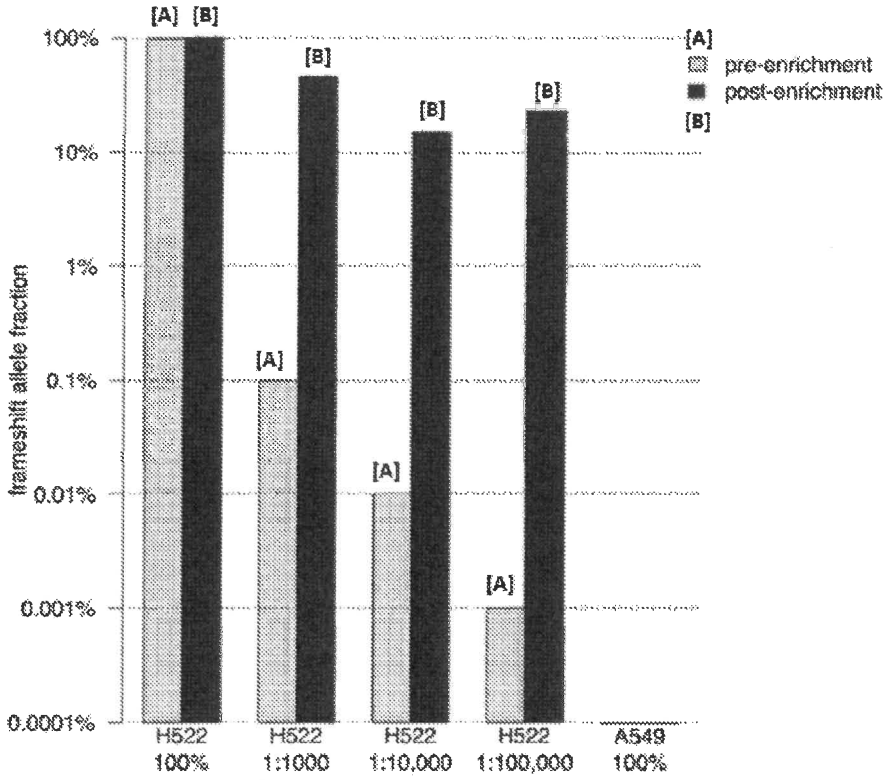

[A] [B]
100%
10%
1%
0.1%
0.01%
0.001%
0.0001%
frameshift allele fraction
[A]
[B]
[B]
[A]
[B]
[A]
[B]
[A]
[A]
pre-enrichment
post-enrichment
[B]
H522
100%
H522
1:1000
H522
1:10,000
H522
1:100,000
A549
100%

FIG. 15

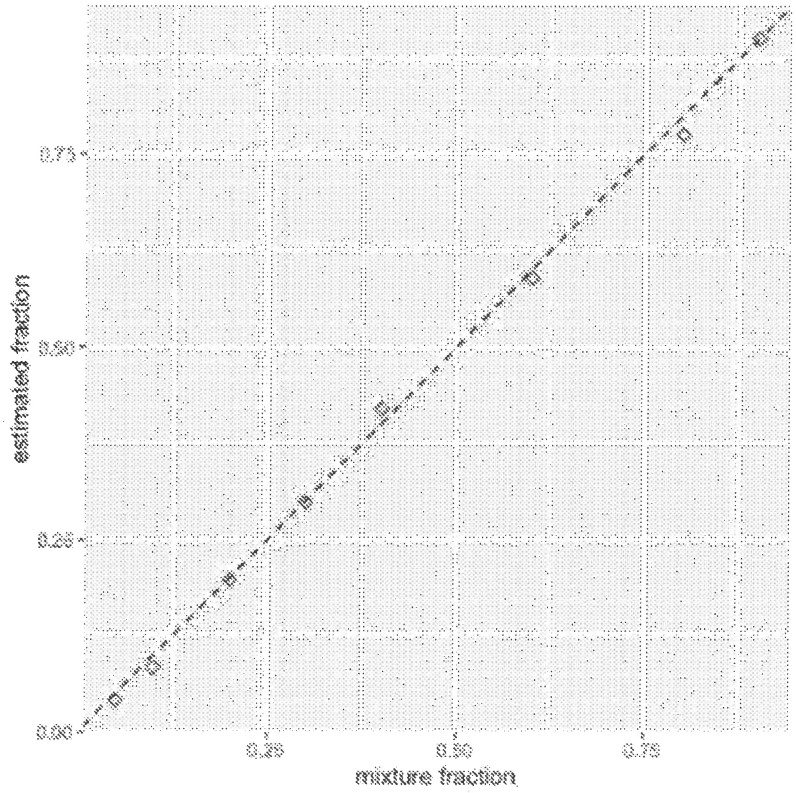

estimated fraction
0.75
0.50
0.25
0.00
0.25
0.50
0.75
mixture fraction

FIG. 16

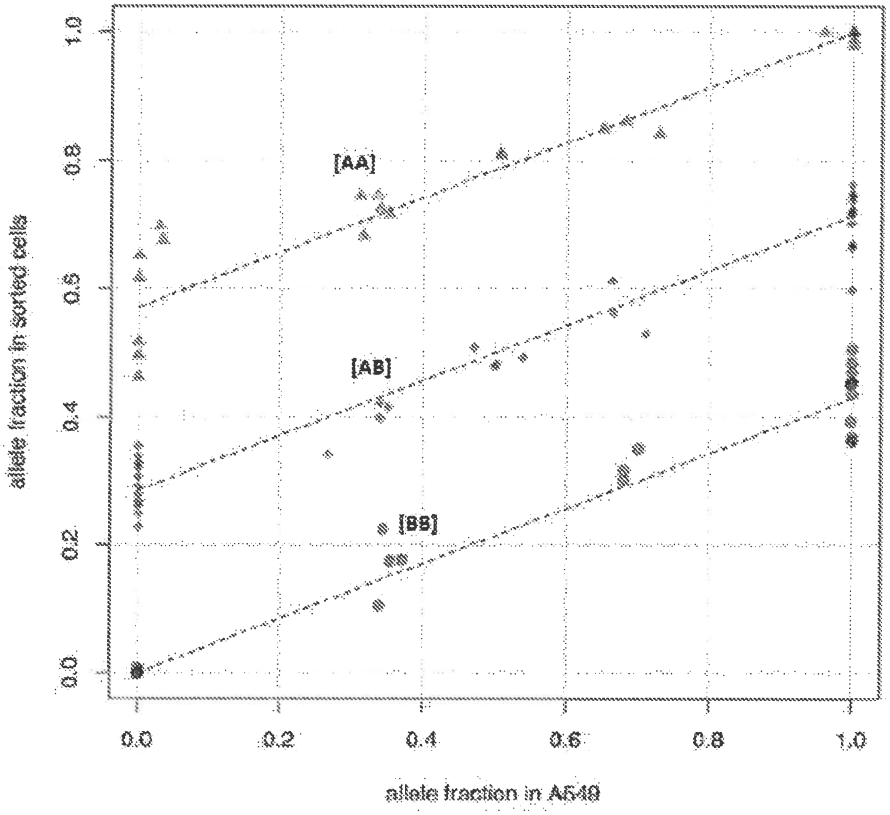

allele fraction in sorted cells
allele fraction in A549
[AA]
[AB]
[BB]
0.0
0.2
0.4
0.6
0.8
1.0

FIG. 17