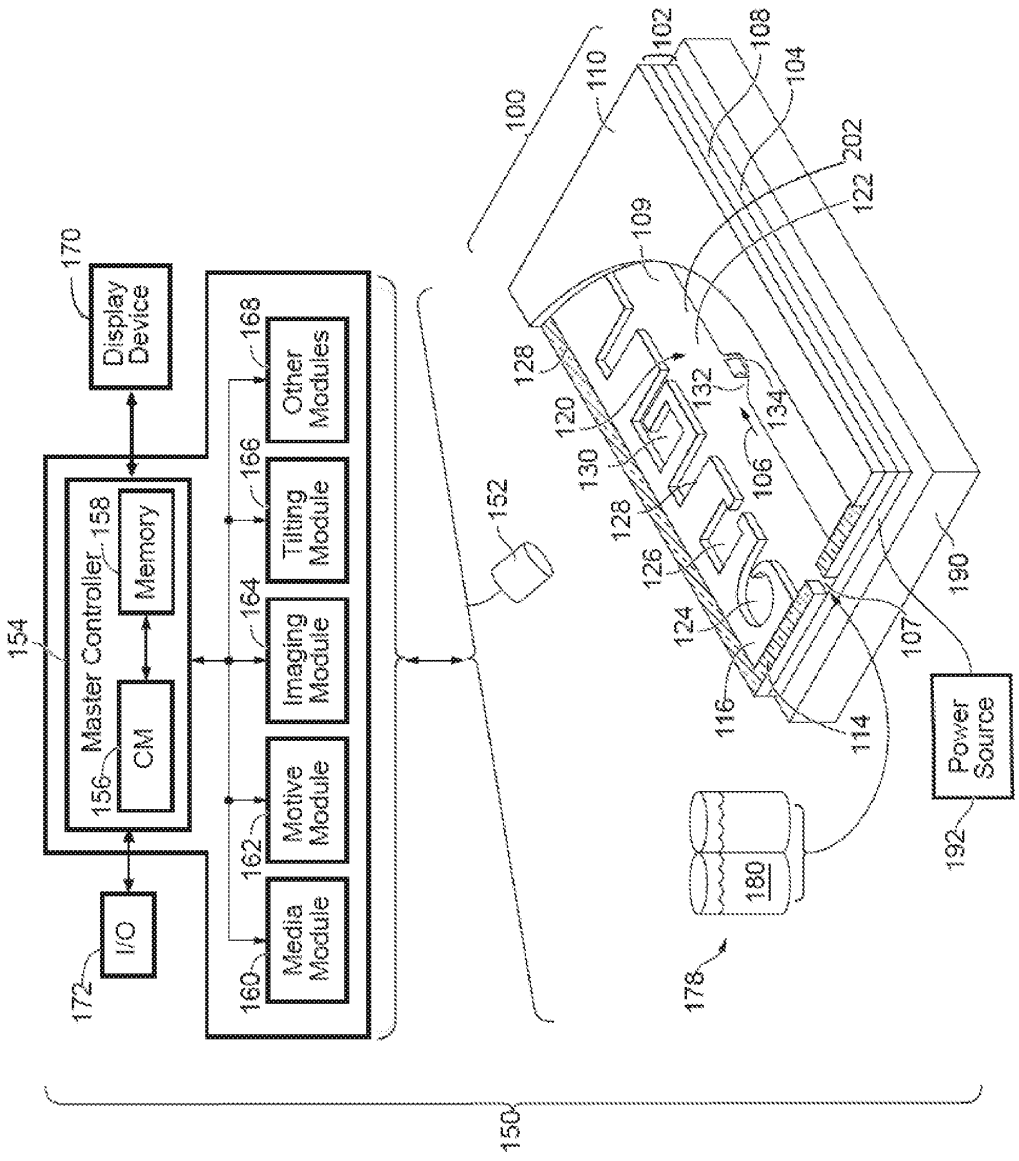

150
154
Master Controller
156
CM
158
Memory
160
Media Module
162
Motive Module
164
Imaging Module
166
Tilting Module
168
Other Modules
170
Display Device
172
I/O
152
100
102
104
106
107
108
109
110
114
116
120
122
124
126
128
130
132
134
178
180
190
192
Power Source
202

FIG. 1A

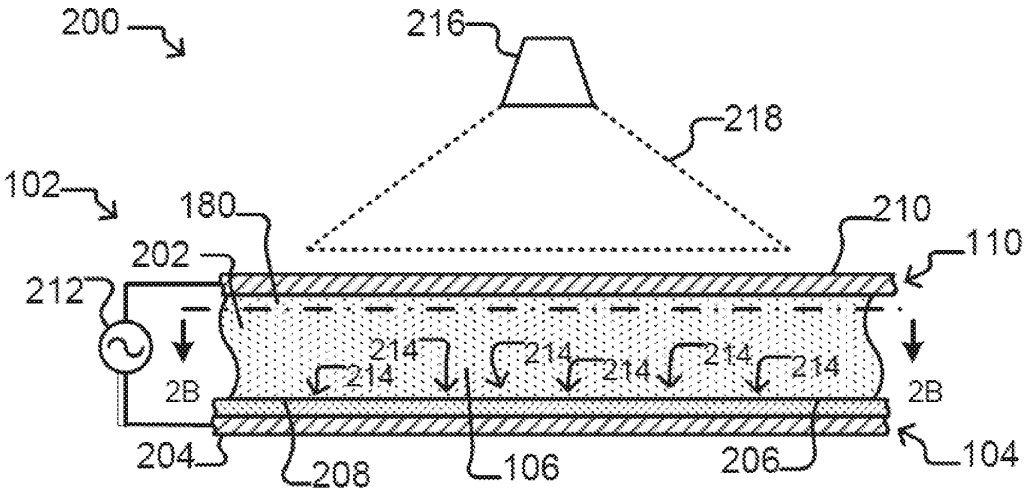

200
216
218
102
180
210
110
202
212
214
214
214
214
214
214
2B
2B
204
208
106
206
104

FIG. 1B

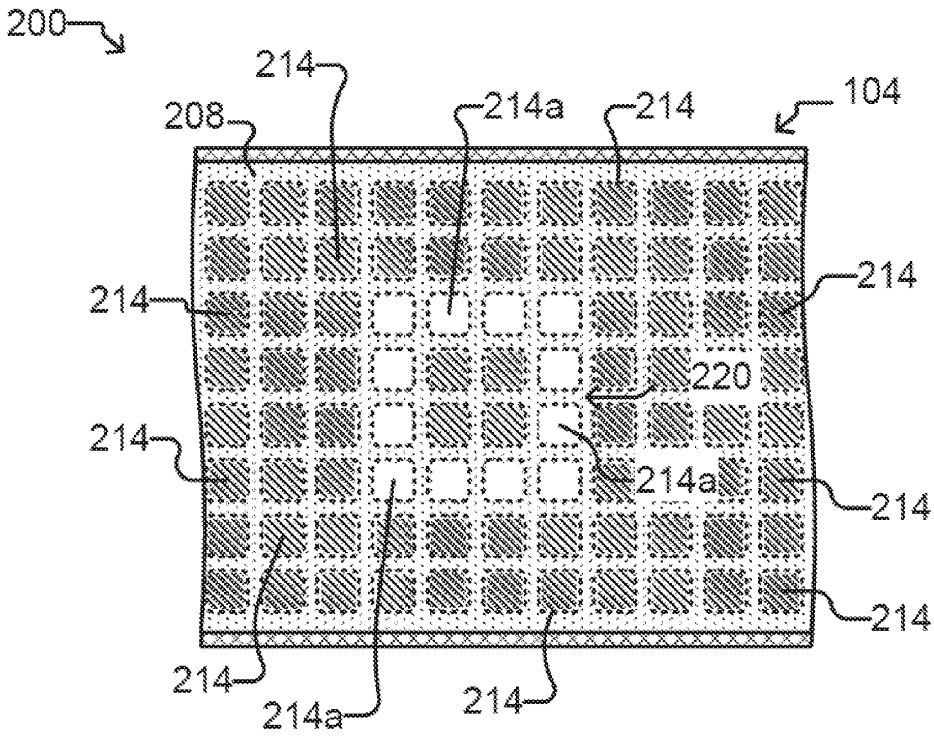

200
214
208
214a
214
104
214
214
220
214
214a
214
214
214
214a
214

FIG. 1C

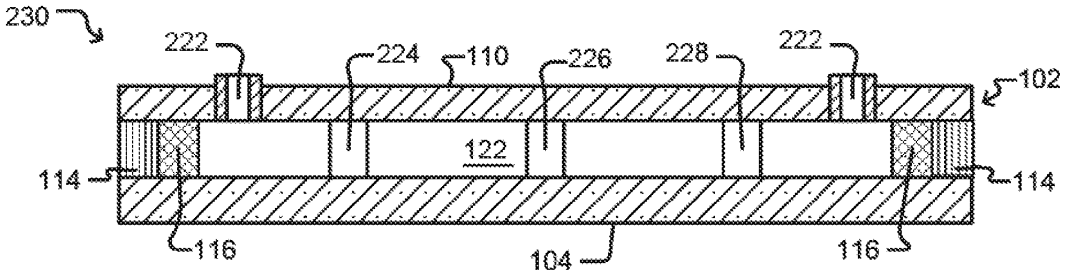

230
222
224
110
226
228
222
102
122
114
114
116
104
116

FIG. 2A

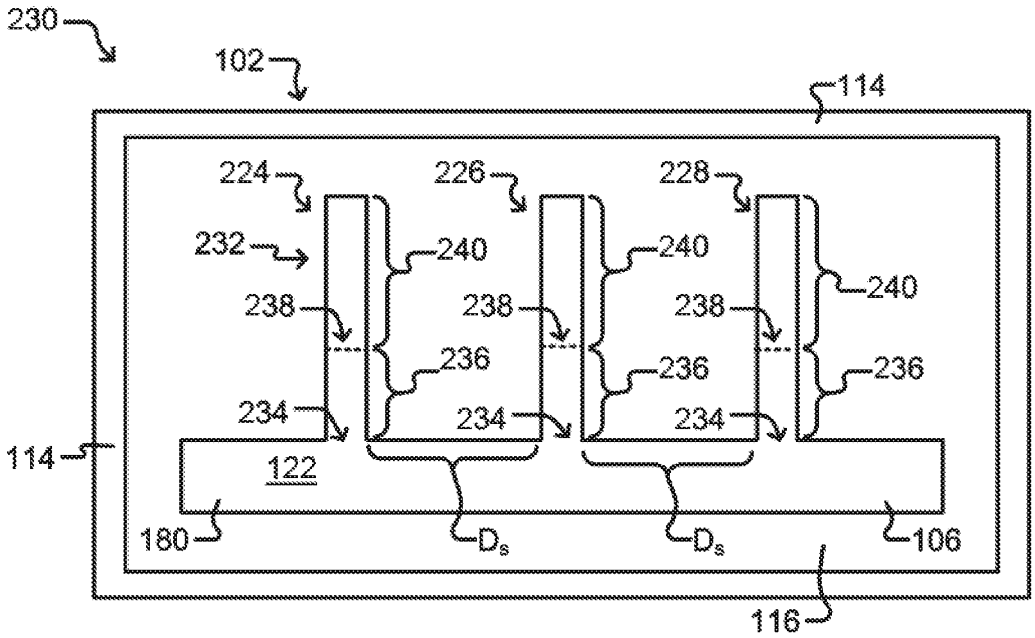

230
102
114
224
226
228
232
240
240
240
238
238
238
236
236
236
234
234
234
114
122
180
D_s
D_s
106
116

FIG. 2B

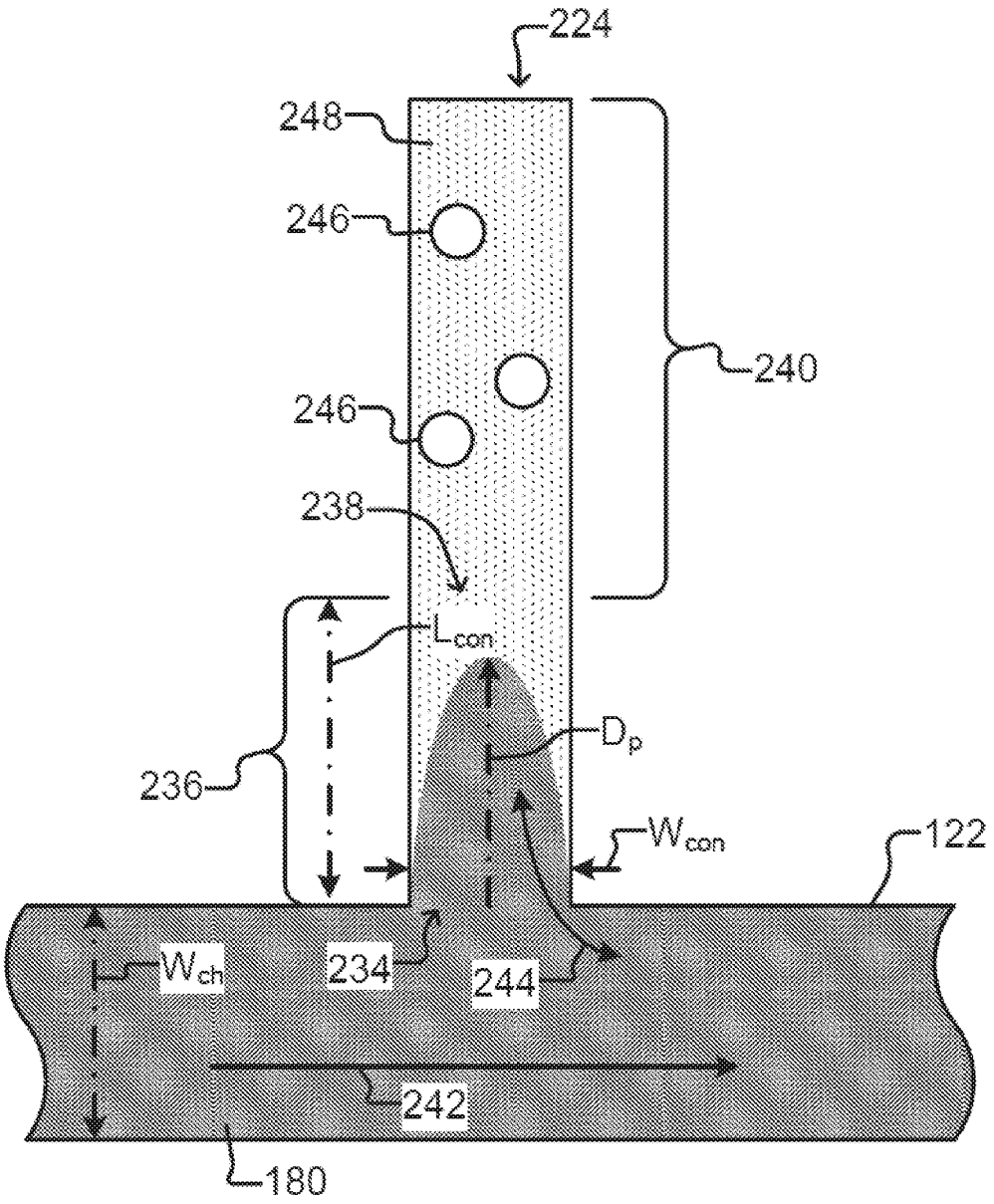


FIG. 2C

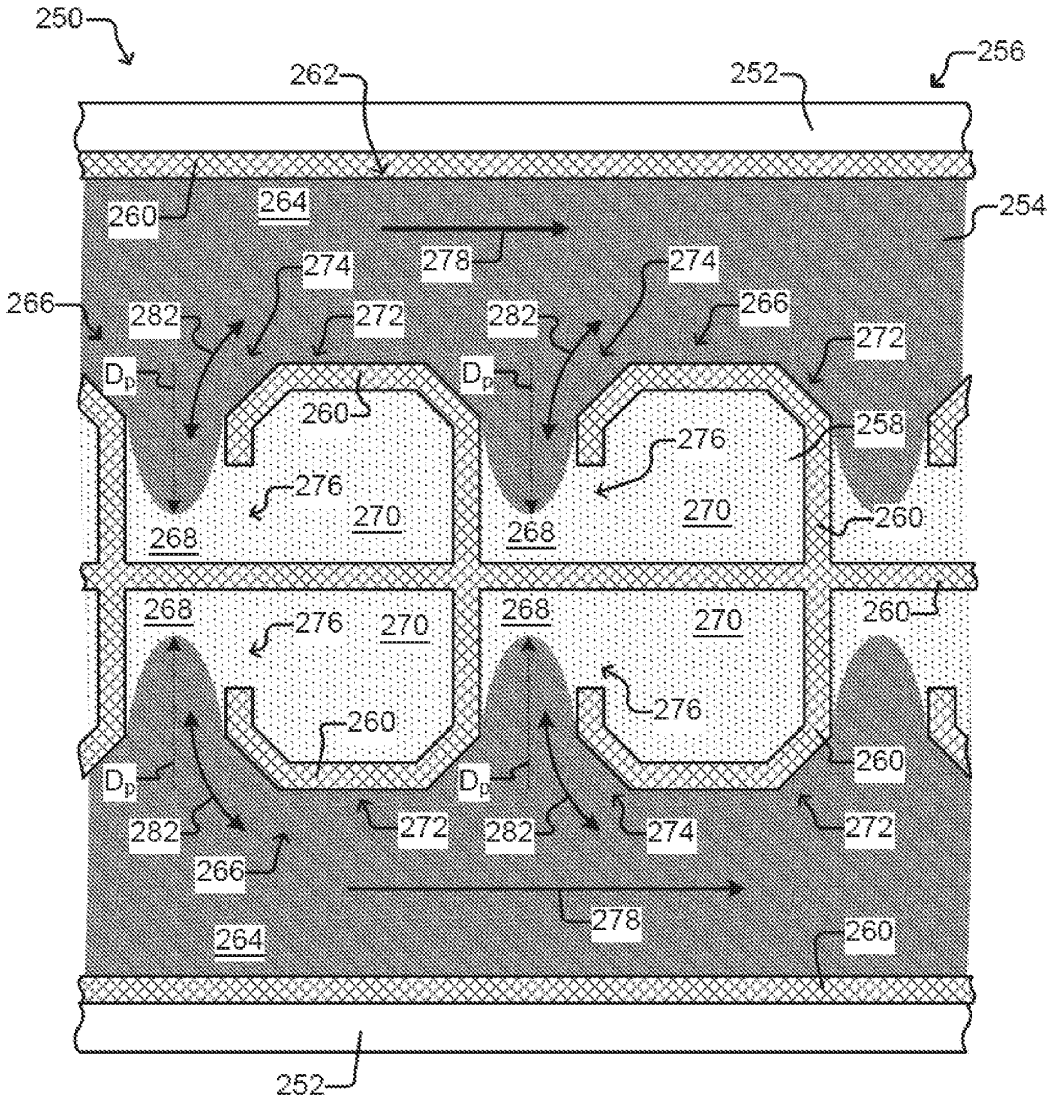

250
262
252
256
260
264
254
278
274
266
282
272
D_p
276
270
268
258

FIG. 2D

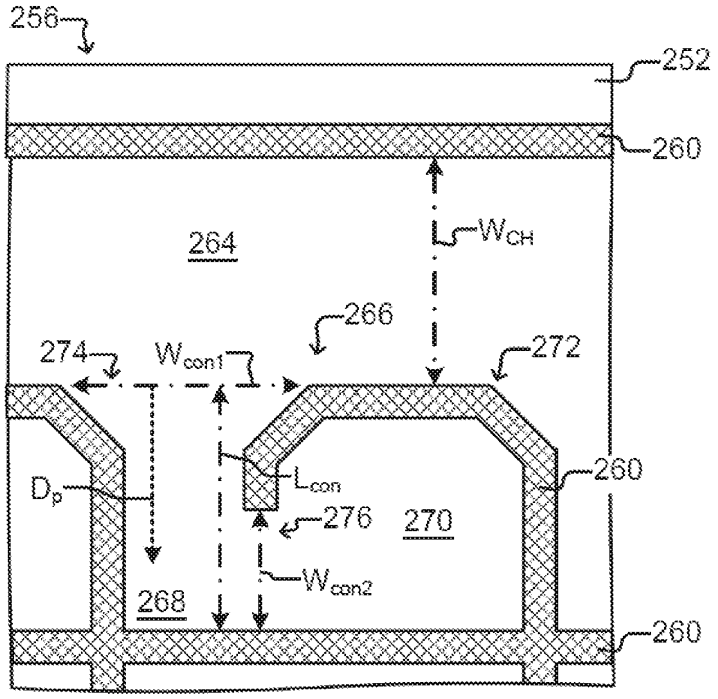

256
252
260
264
W_{CH}
266
274
W_{con1}
272
D_p
L_{con}
260
276
270
W_{con2}
268
260

FIG. 2E

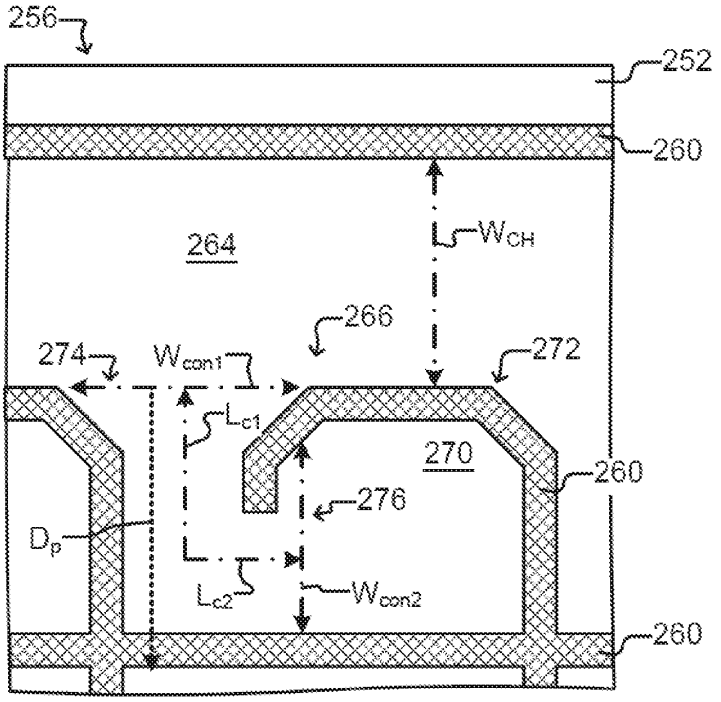

256
252
260
264
W_{CH}
266
274
W_{con1}
272
L_{c1}
270
260
276
D_p
L_{c2}
W_{con2}
260

FIG. 2F

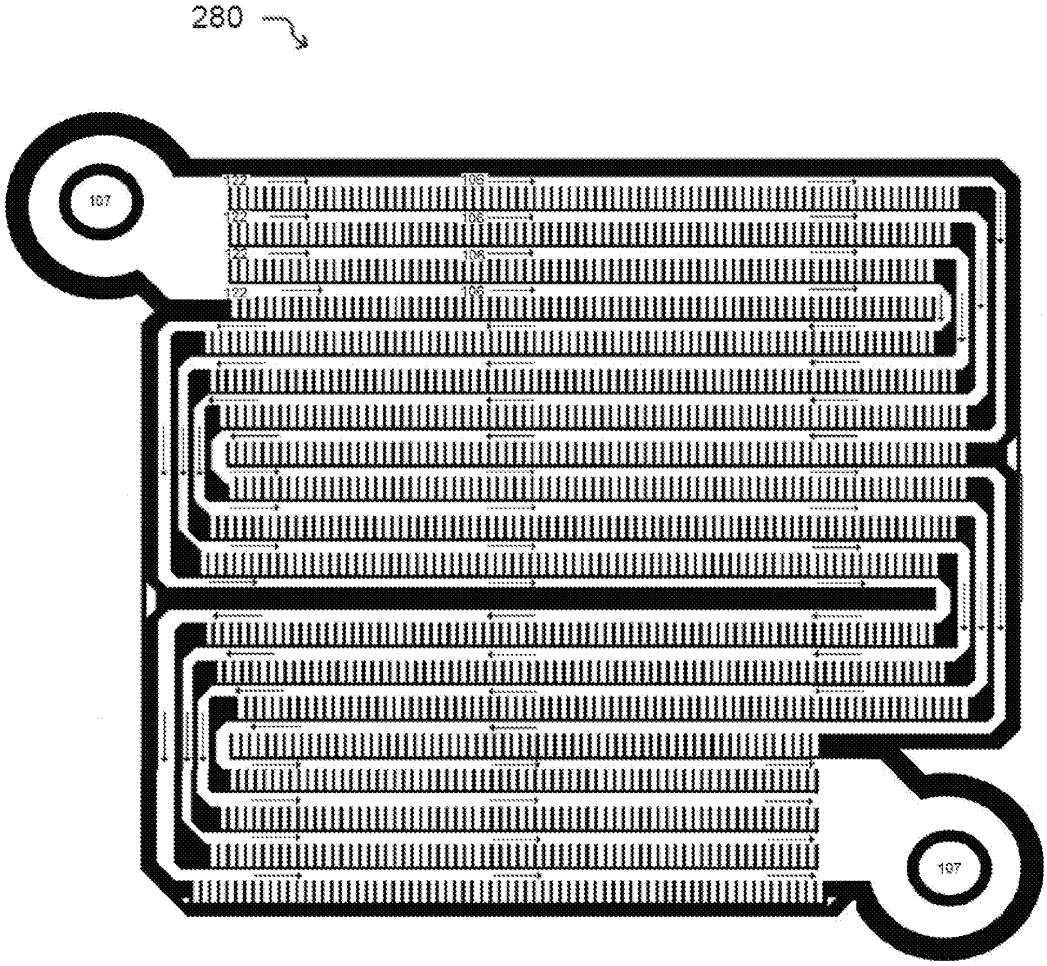


FIG. 2G

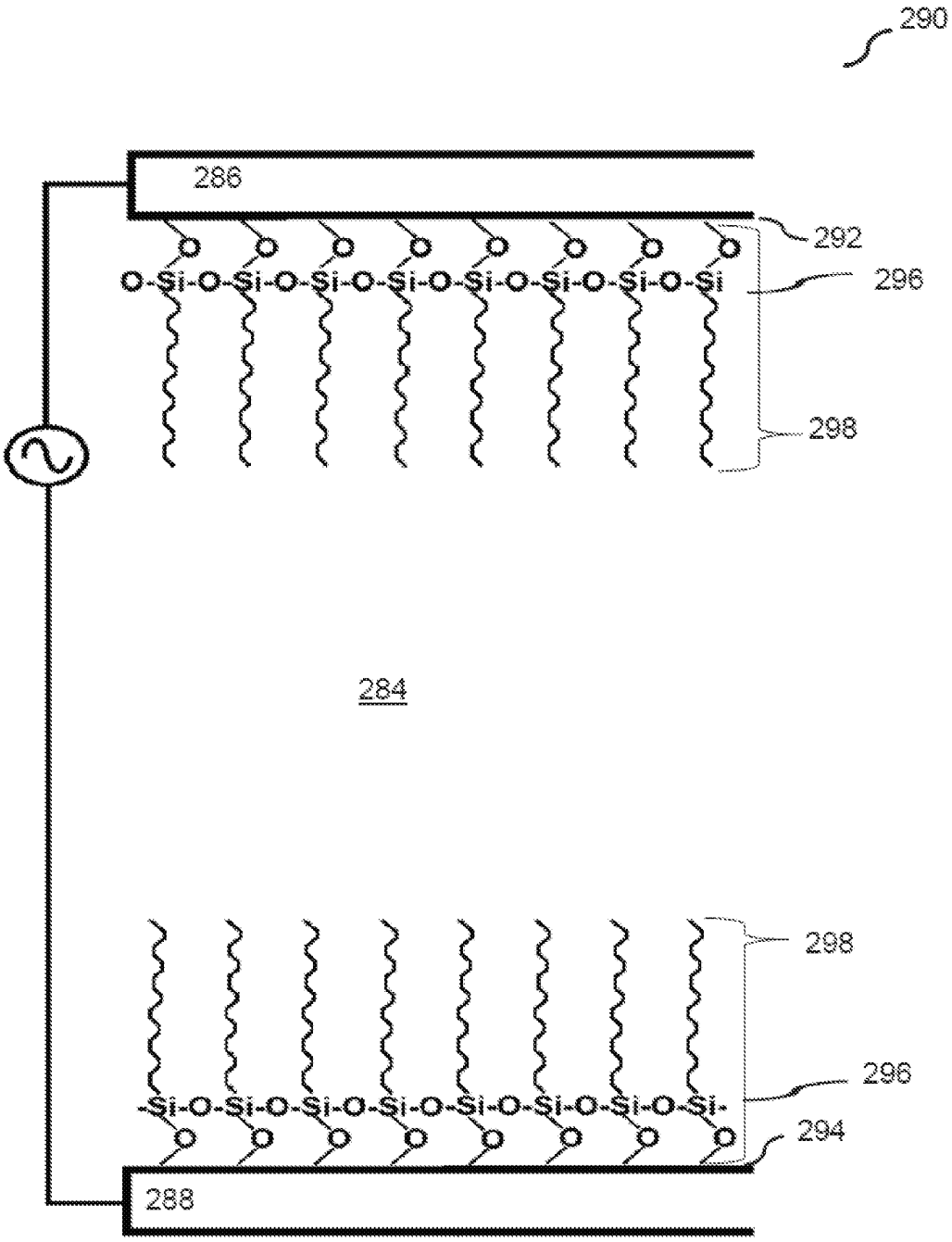

290
286
292
O-Si-O-Si-O-Si-O-Si-O-Si-O-Si-O-Si-O-Si
296
298
284
298
296
-Si-O-Si-O-Si-O-Si-O-Si-O-Si-O-Si-O-Si-
294
288

FIG. 2H

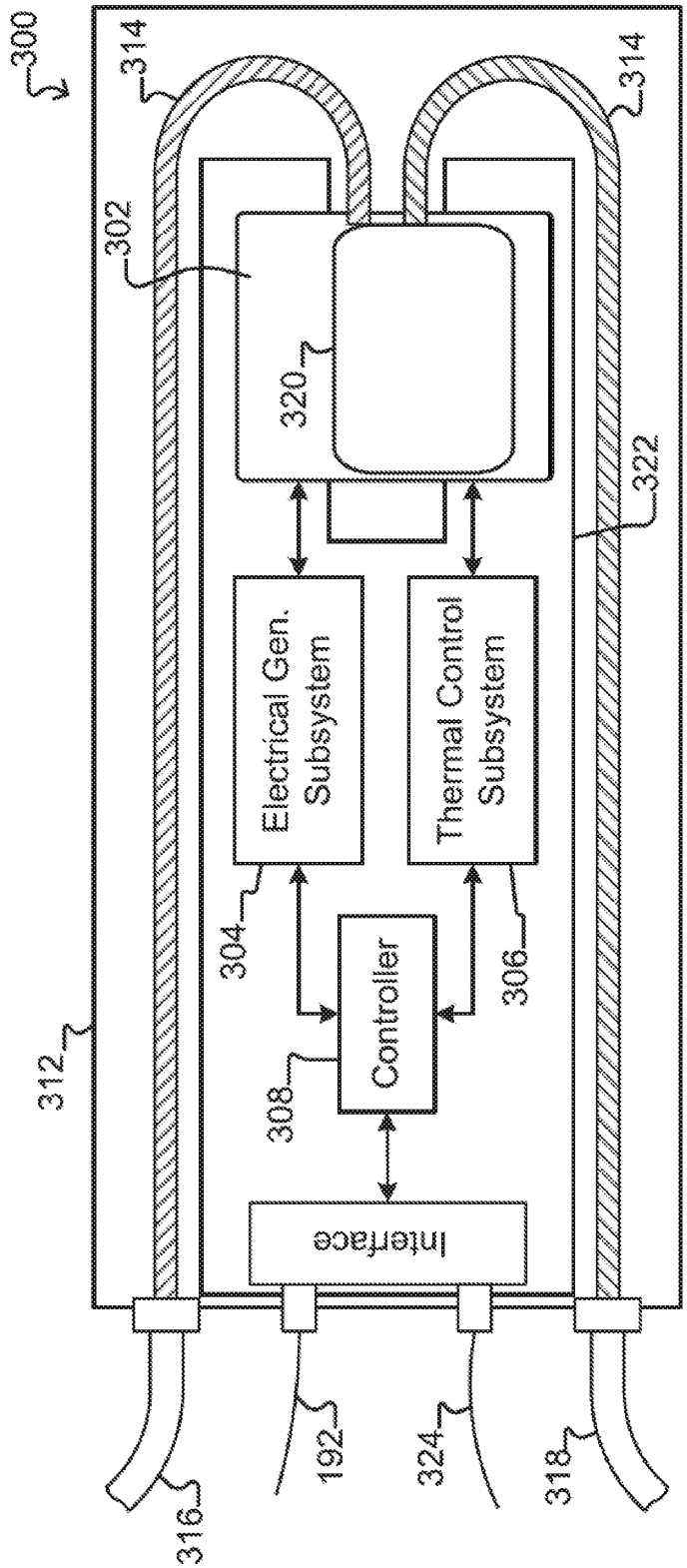

300
314
314
302
320
322
Electrical Gen. Subsystem
Thermal Control Subsystem
304
306
312
Controller
308
Interface
316
192
324
318

FIG. 3A

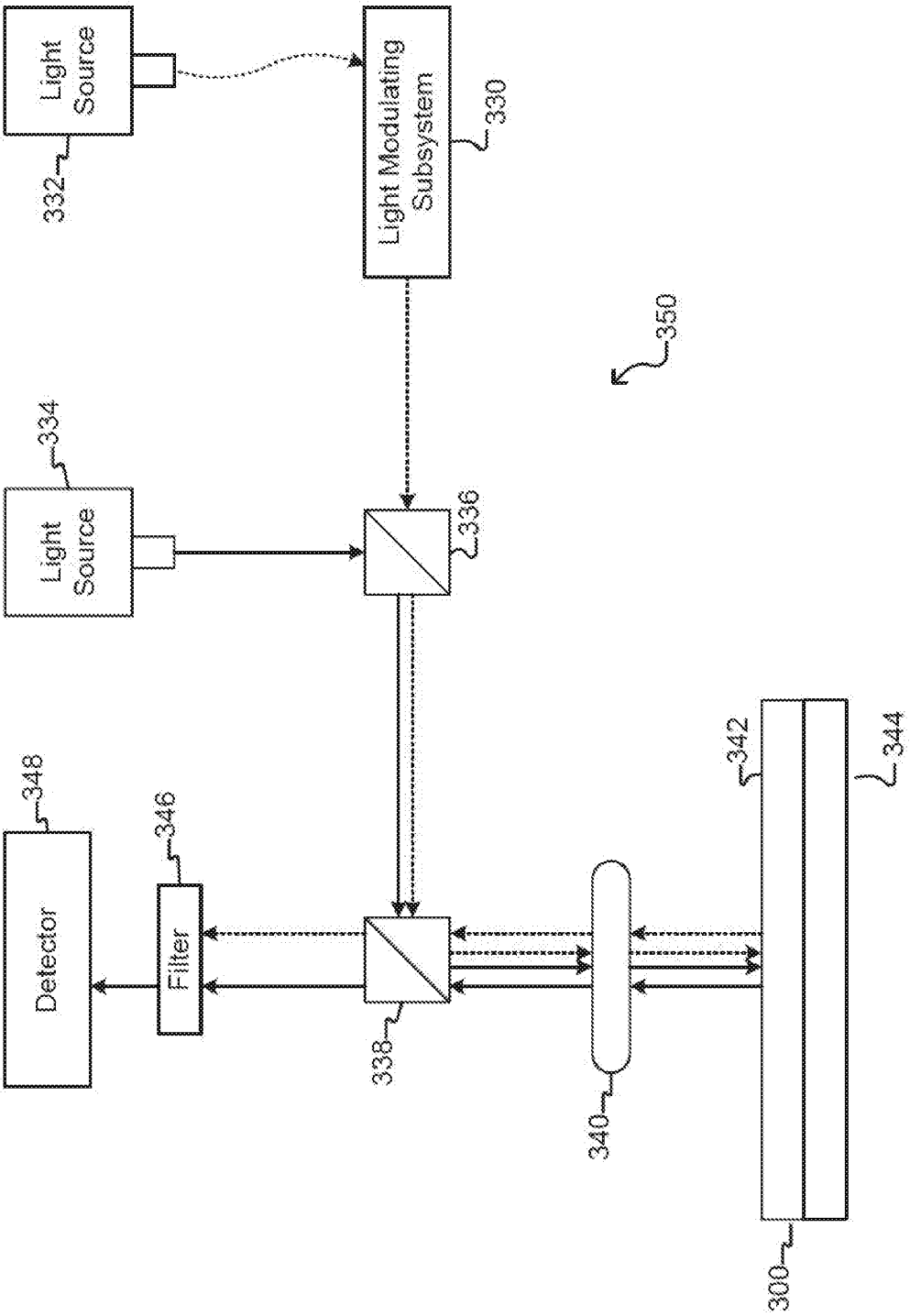

Light Source
332
Light Modulating Subsystem
330
350
Light Source
334
336
Detector
348
Filter
346
338
340
342
344
300

FIG. 3B

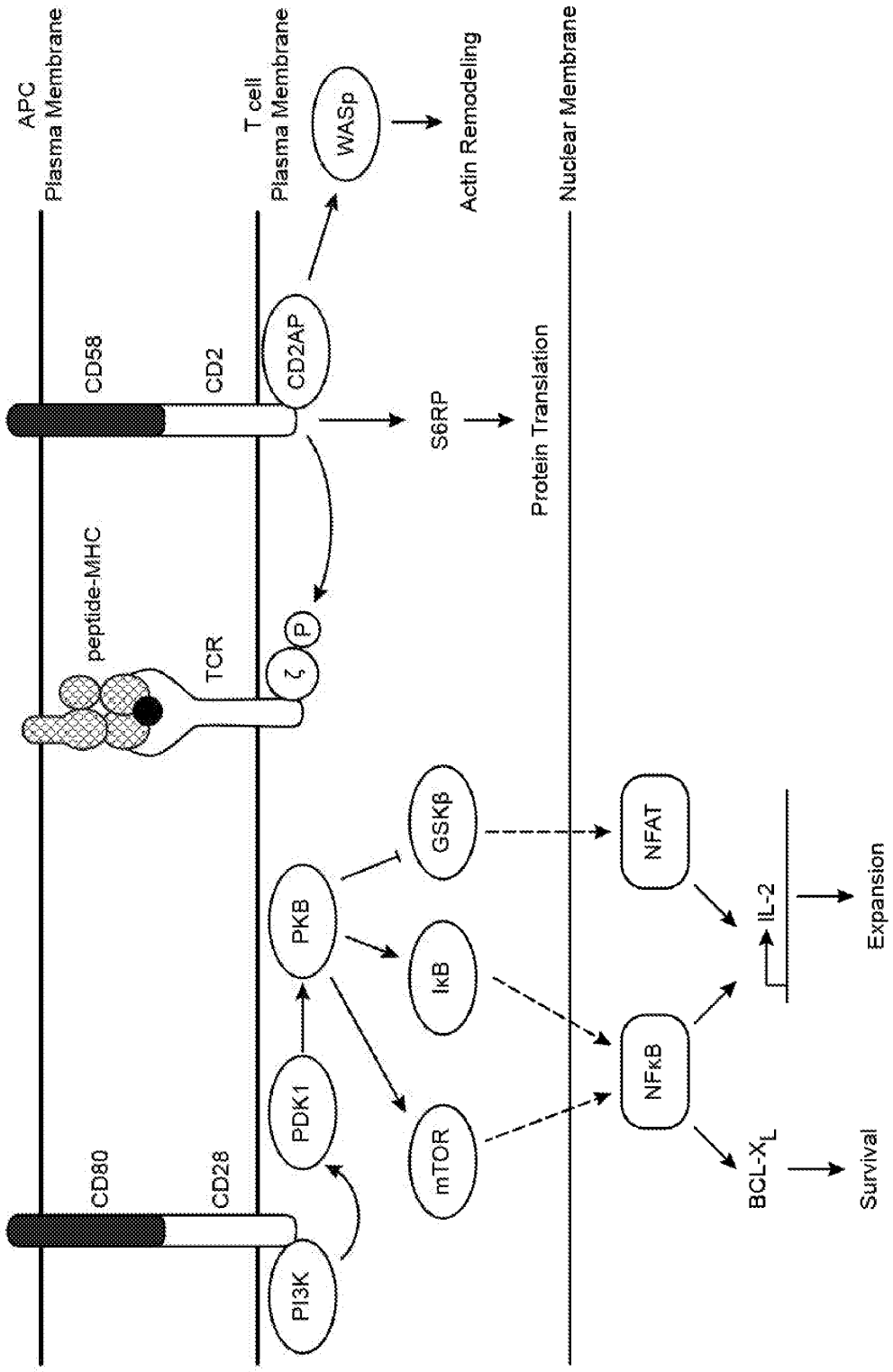
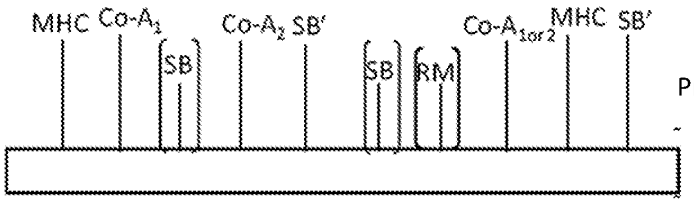
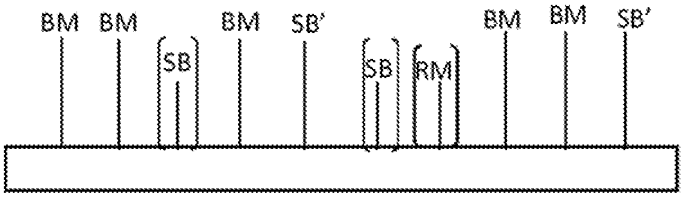

APC
Plasma Membrane
T cell
Plasma Membrane
Nuclear Membrane
CD58
CD2
CD2AP
WASp
Actin Remodeling
S6RP
Protein Translation
peptide-MHC
TCR
ζ
P
CD80
CD28
PI3K
PDK1
PKB
GSKβ
IκB
mTOR
NFAT
NFκB
IL-2
Expansion
BCL-XL
Survival

FIG. 4



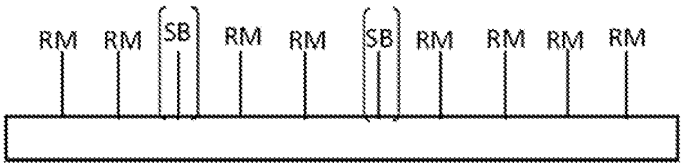
Proto-antigen-presenting surface
- MHC is primary activating ligand bound to exchange factor
- $Co\text{-}A_1$ Co-Activating ligand
- $Co\text{-}A_2$ Co-Activating ligand
- $Co\text{-}A_1 =/\neq Co\text{-}A_2$
- Co-Activating ligand
  - TCR co-activating
  - TCR adjunct activating

Activating Ligand Reagent(s)



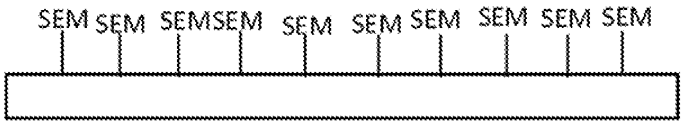
Covalently functionalized surface
- BM binding moiety
- SB surface blocking molecule
- SB =/≠ SB'

Functionalizing Reagent(s)



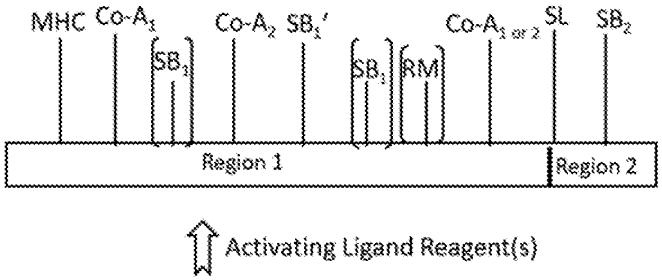
Intermediate reactive surface
- RM reactive moiety
- SB surface blocking molecule

Preparing Reagent(s)



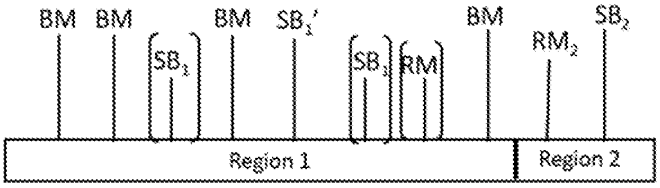
Synthetic reactive surface
- SEM = Surface exposed moiety

FIG. 5A



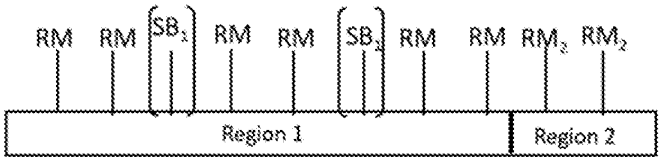
Activating Ligand Reagent(s)

Proto-antigen-presenting surface
- MHC is primary activating ligand bound to exchange factor
- $Co\text{-}A_1$ is Co-Activating ligand
- $Co\text{-}A_2$ is Co-Activating ligand
- $Co\text{-}A_1 =/\neq Co\text{-}A_2$
- Co-Activating ligand
  - TCR co-activating
  - TCR adjunct activating
- SL is Secondary ligand
- $SB_1 =/\neq SB_1' =/\neq SB_2$



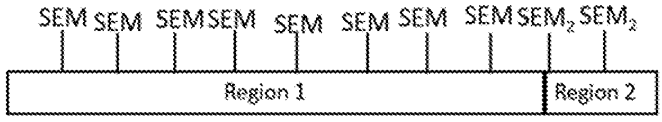
Functionalizing Reagent(s)

Covalently functionalized surface
- BM binding moiety
- SB surface blocking molecule
- $SB_1 =/\neq SB_1' =/\neq SB_2$



Preparing Reagent(s)

Intermediate reactive surface
- RM reactive moiety
- SB_1 surface blocking molecule



Synthetic reactive surface
- SEM = Surface exposed moiety

FIG. 5B

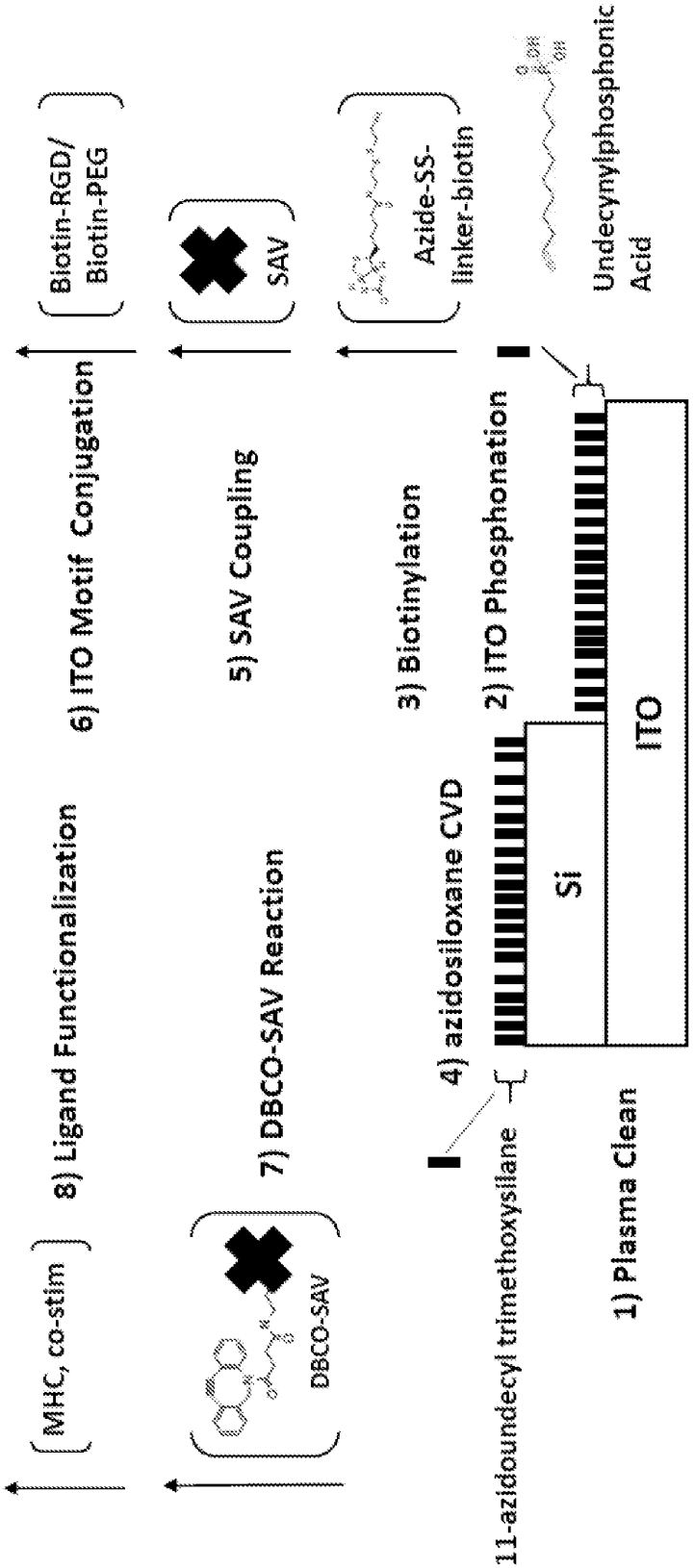

1) Plasma Clean
11-azidoundecyl trimethoxysilane
4) azidosiloxane CVD
2) ITO Phosphonation
3) Biotinylation
Undecynylphosphonic Acid
Azide-SS-linker-biotin
5) SAV Coupling
SAV
6) ITO Motif Conjugation
Biotin-RGD/ Biotin-PEG
7) DBCO-SAV Reaction
DBCO-SAV
8) Ligand Functionalization
MHC, co-stim
Si
ITO

FIG. 6

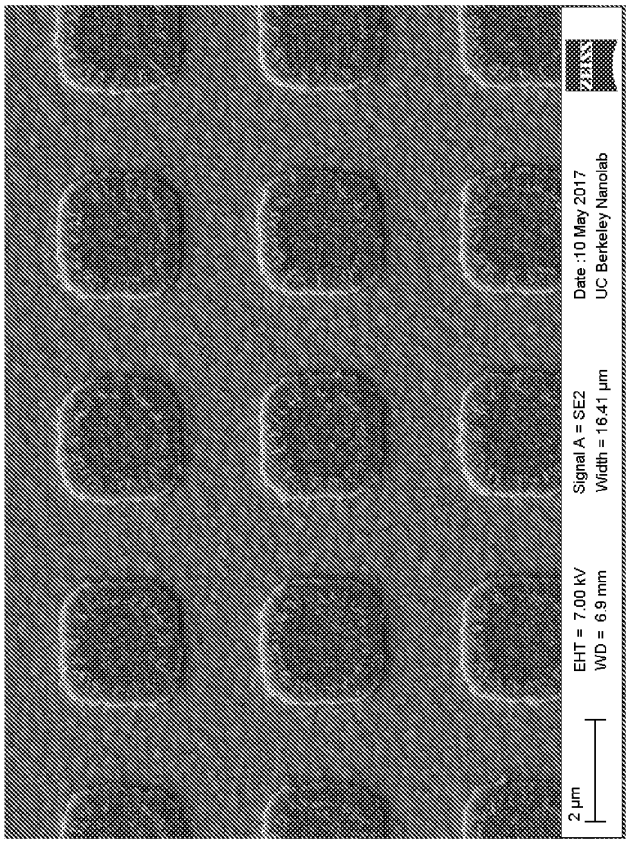

2 µm
EHT = 7.00 kV
WD = 6.9 mm
Signal A = SE2
Width = 16.41 µm
Date :10 May 2017
UC Berkeley Nanolab

FIG. 7B

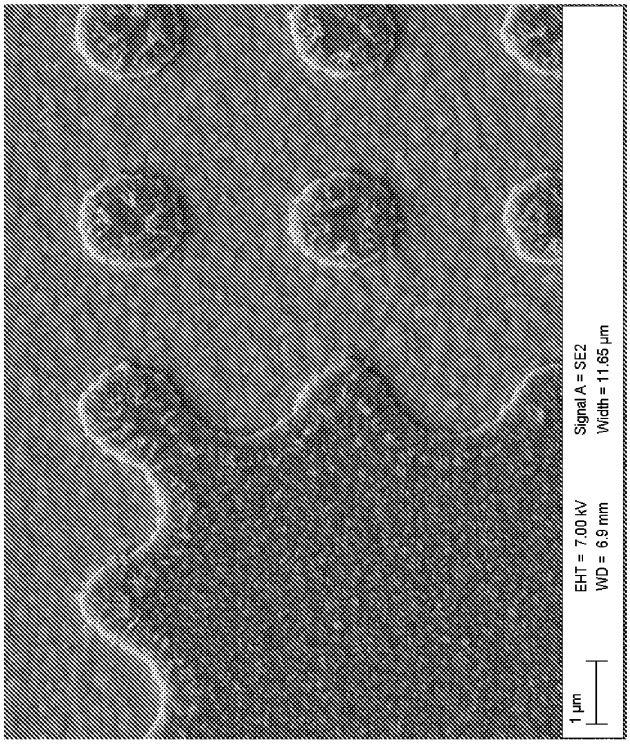

1 µm
EHT = 7.00 kV
WD = 6.9 mm
Signal A = SE2
Width = 11.65 µm

FIG. 7A

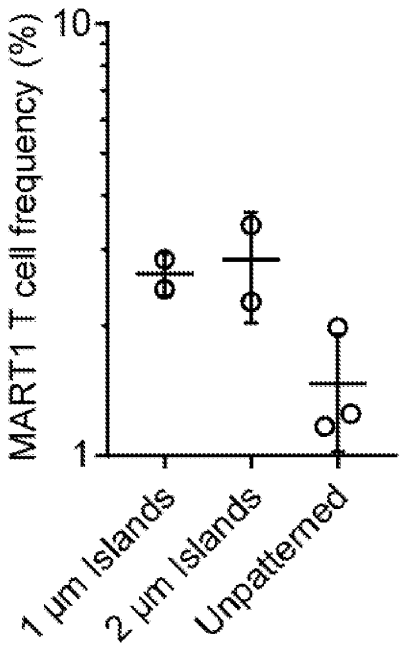


FIG. 8A

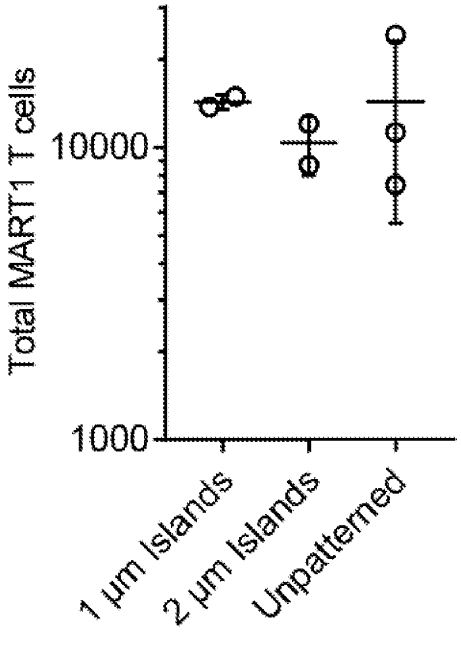


FIG. 8B

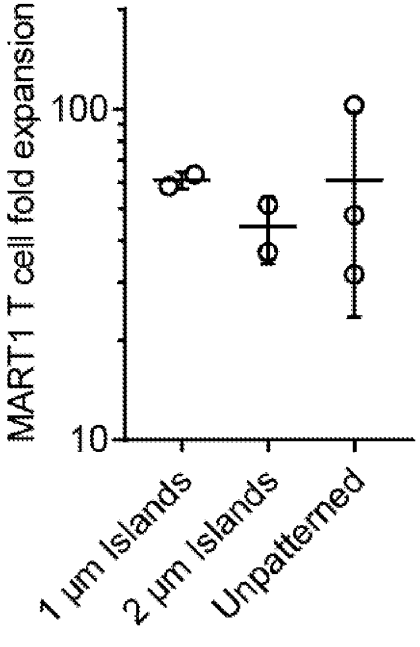


FIG. 8C

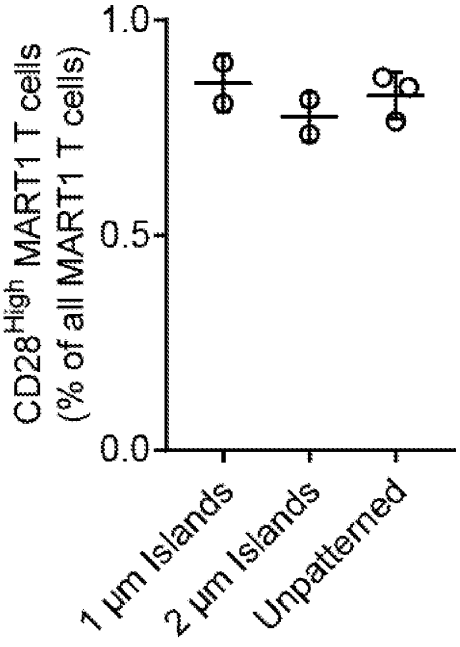


FIG. 8D

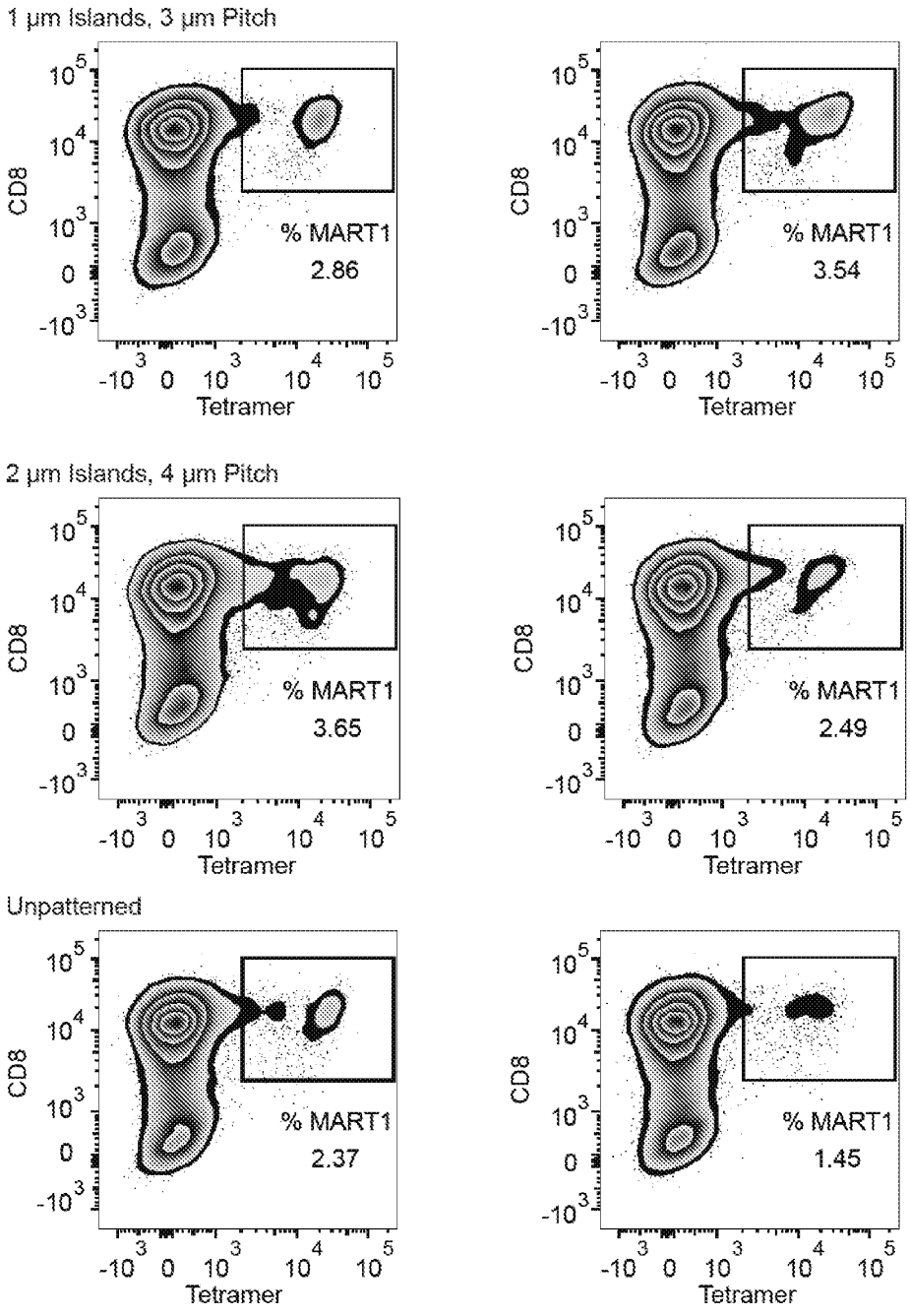

1 µm Islands, 3 µm Pitch
% MART1
2.86
% MART1
3.54
2 µm Islands, 4 µm Pitch
% MART1
3.65
% MART1
2.49
Unpatterned
% MART1
2.37
% MART1
1.45
CD8
Tetramer

FIG. 9

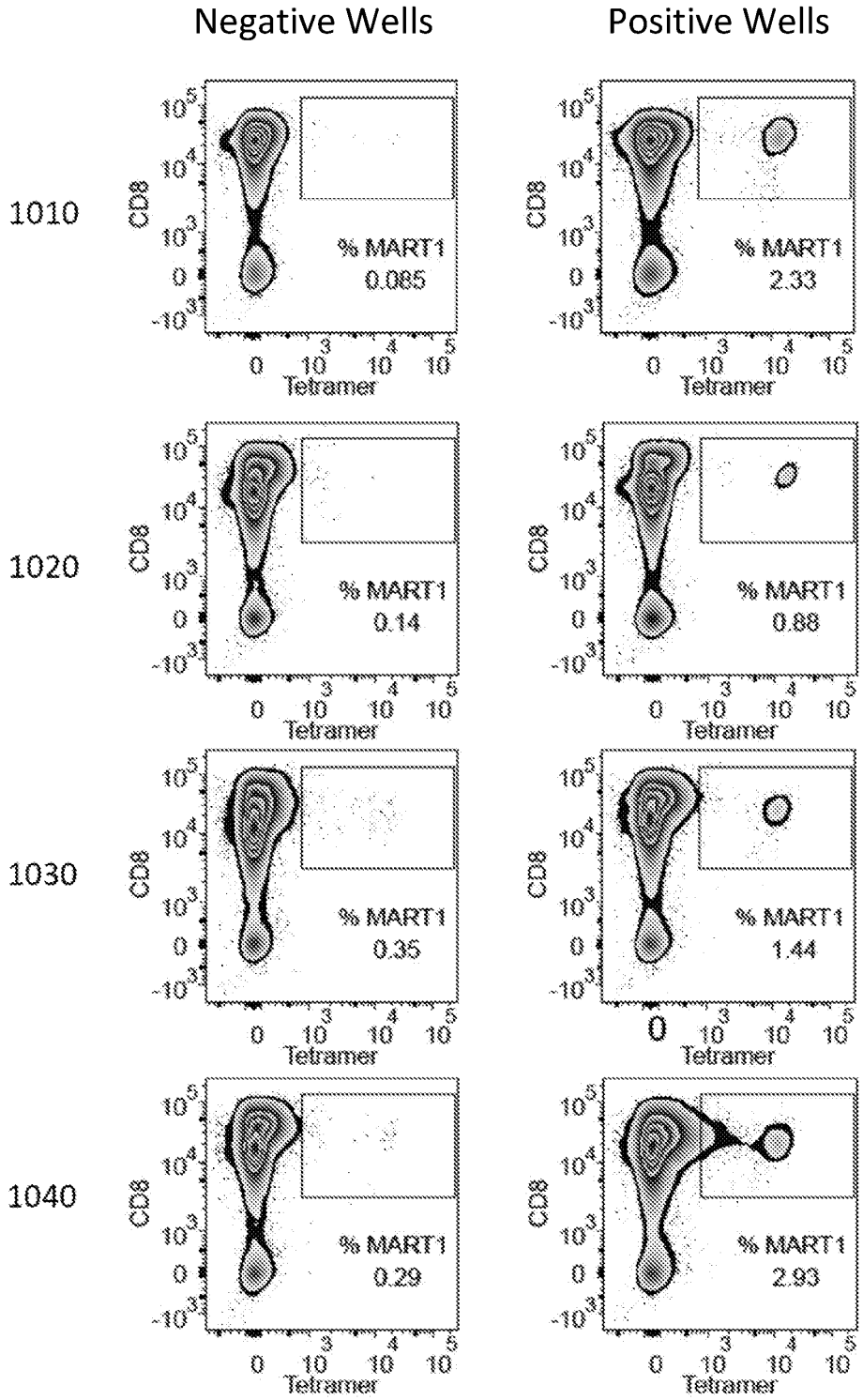

Negative Wells
Positive Wells
1010
1020
1030
1040
CD8
Tetramer
% MART1
0.085
2.33
0.14
0.88
0.35
1.44
0.29
2.93

FIG.10

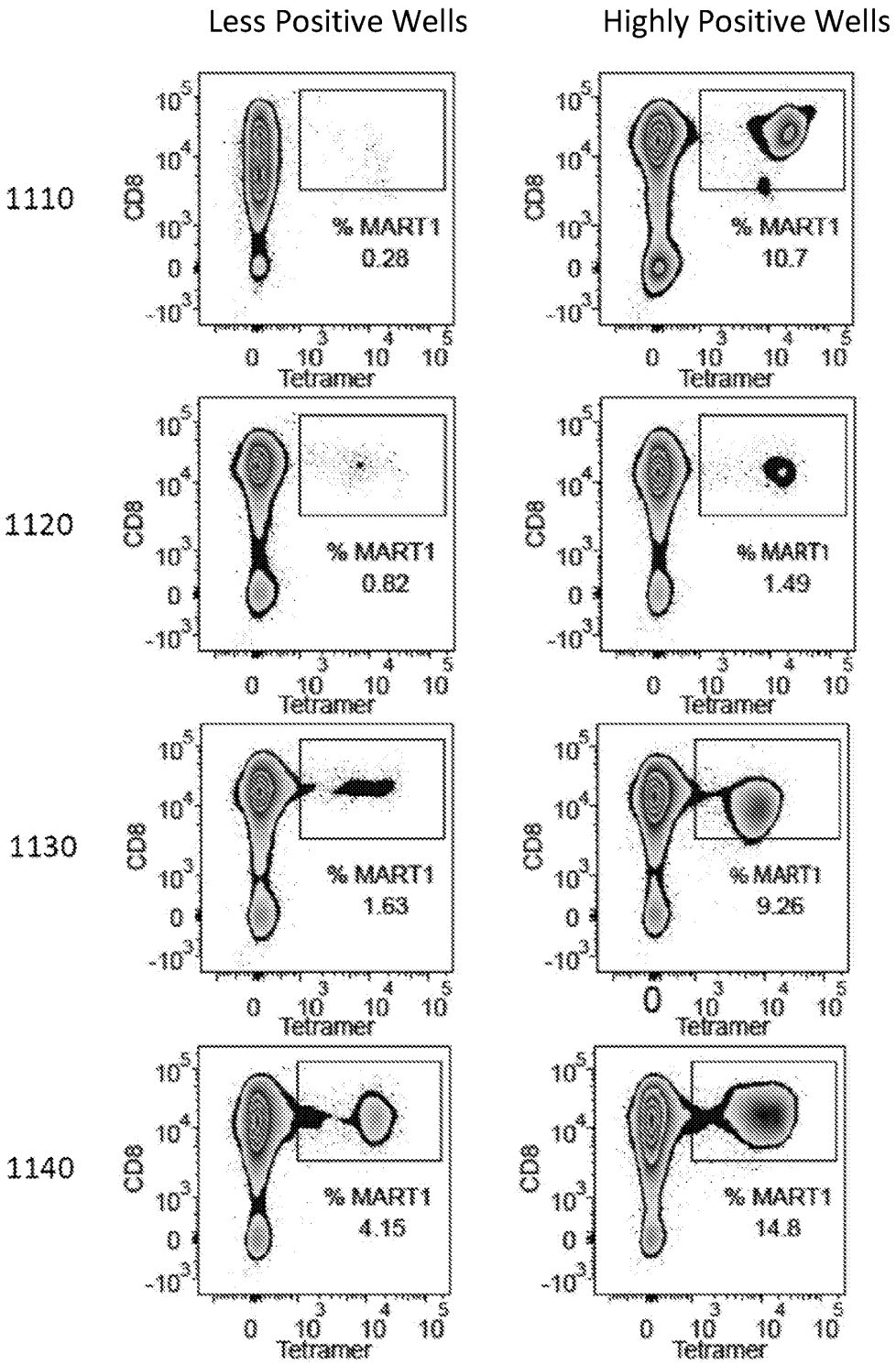
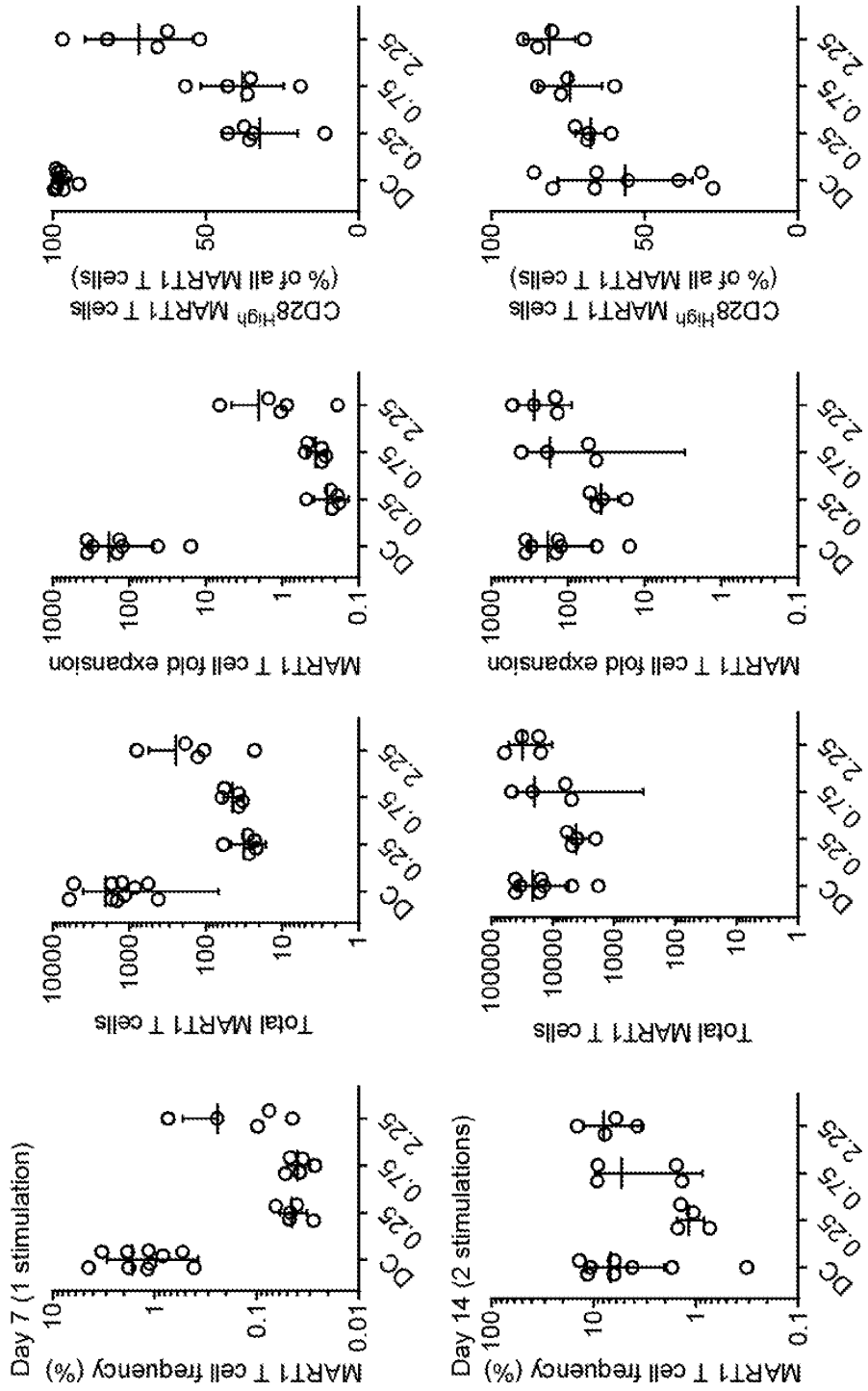

Less Positive Wells
Highly Positive Wells
1110
1120
1130
1140
CD8
Tetramer
% MART1
0.28
10.7
0.82
1.49
1.63
9.26
4.15
14.8

FIG. 11



DC Dendritic cell stimulation
0.25 aAPC stimulation - 0.25 µg costimulation antibody / 1e7 beads
0.75 aAPC stimulation - 0.75 µg costimulation antibody / 1e7 beads
2.25 aAPC stimulation - 2.25 µg costimulation antibody / 1e7 beads

FIG. 12

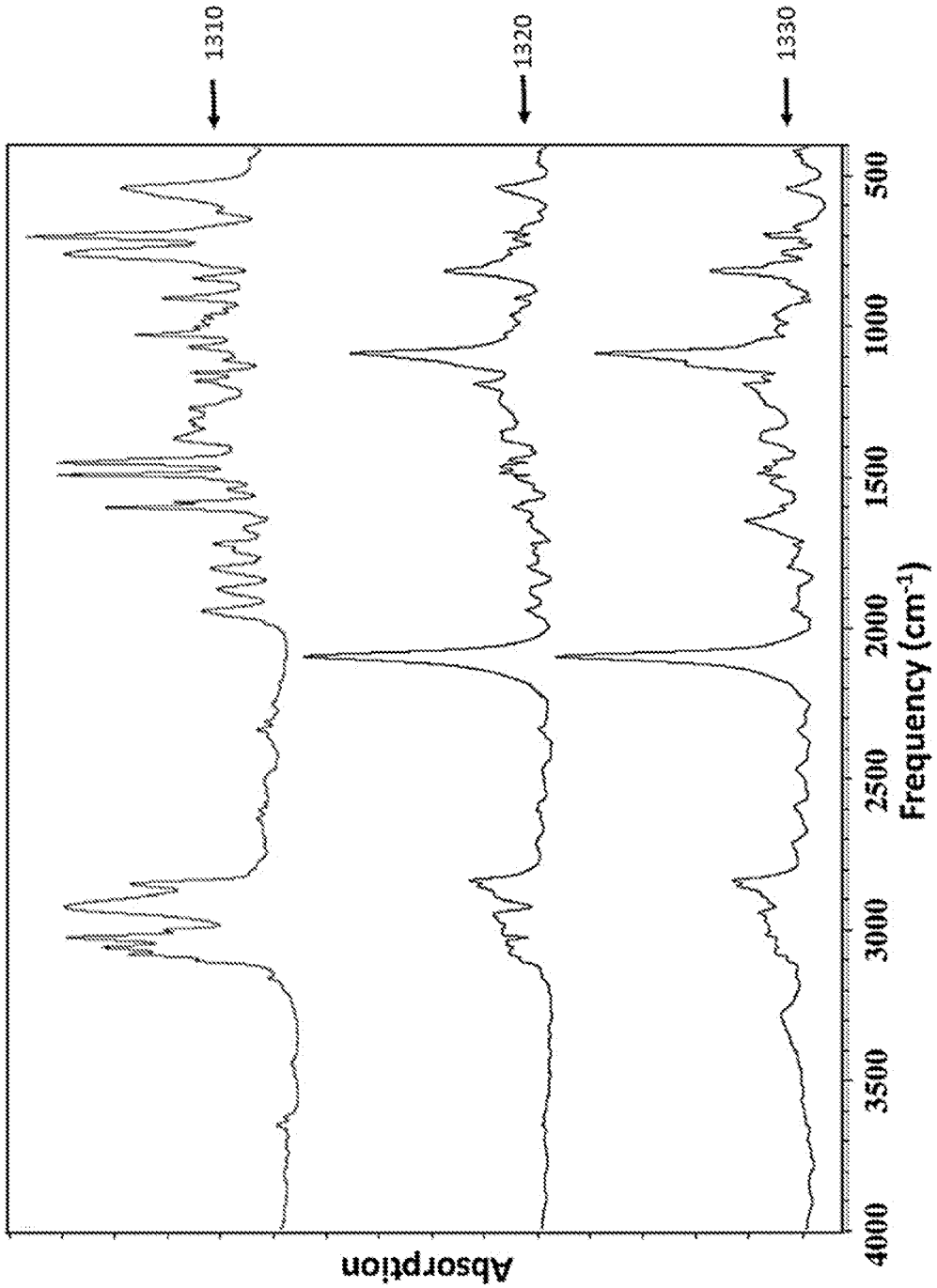

1310
1320
1330
Absorption
4000
3500
3000
2500
2000
1500
1000
500
Frequency (cm-1)

FIG. 13

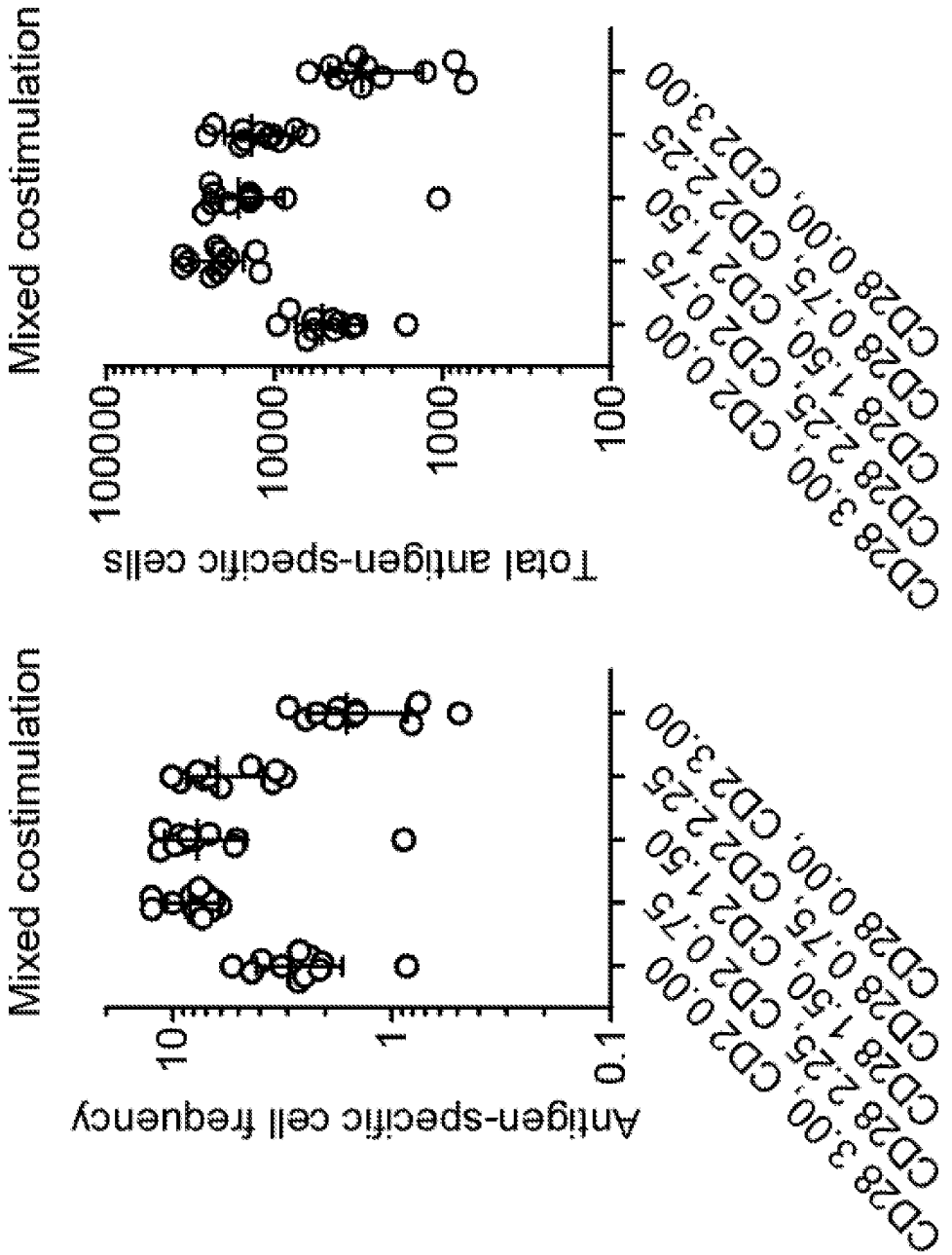


FIG. 14A

FIG. 14B

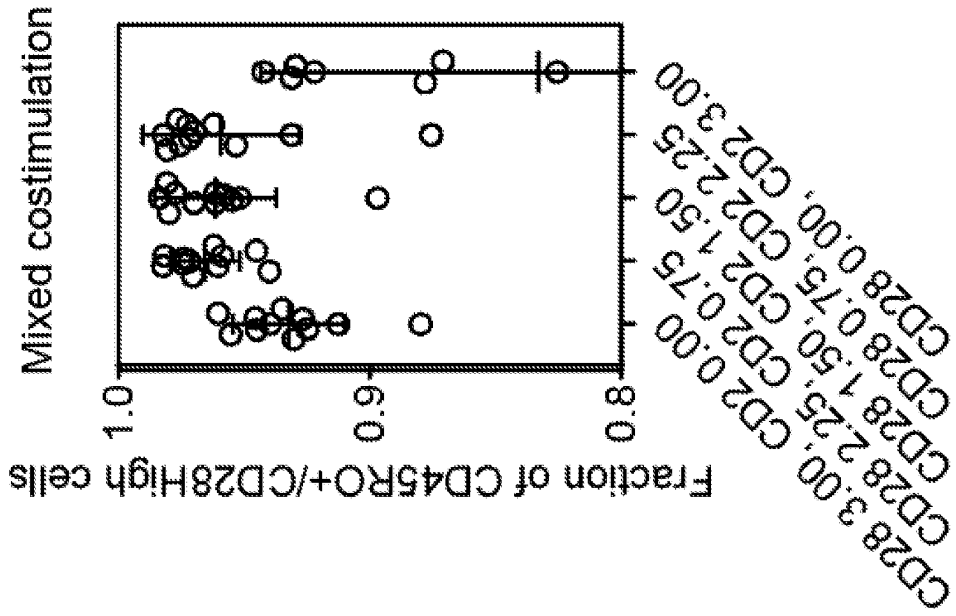


FIG. 14D

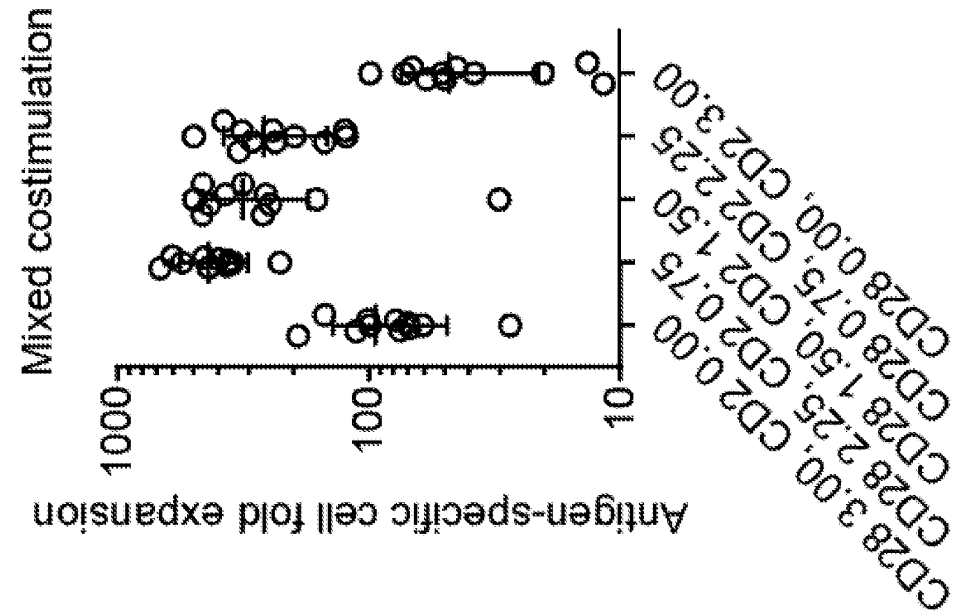


FIG. 14C

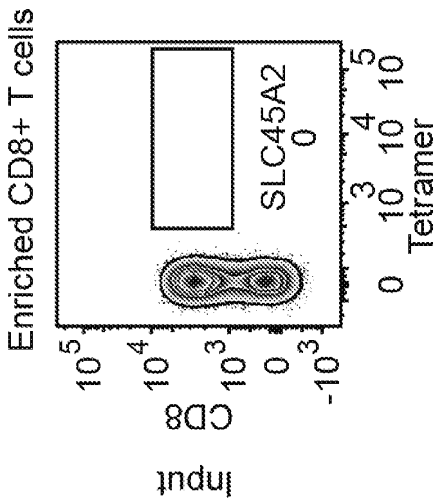


FIG. 15A

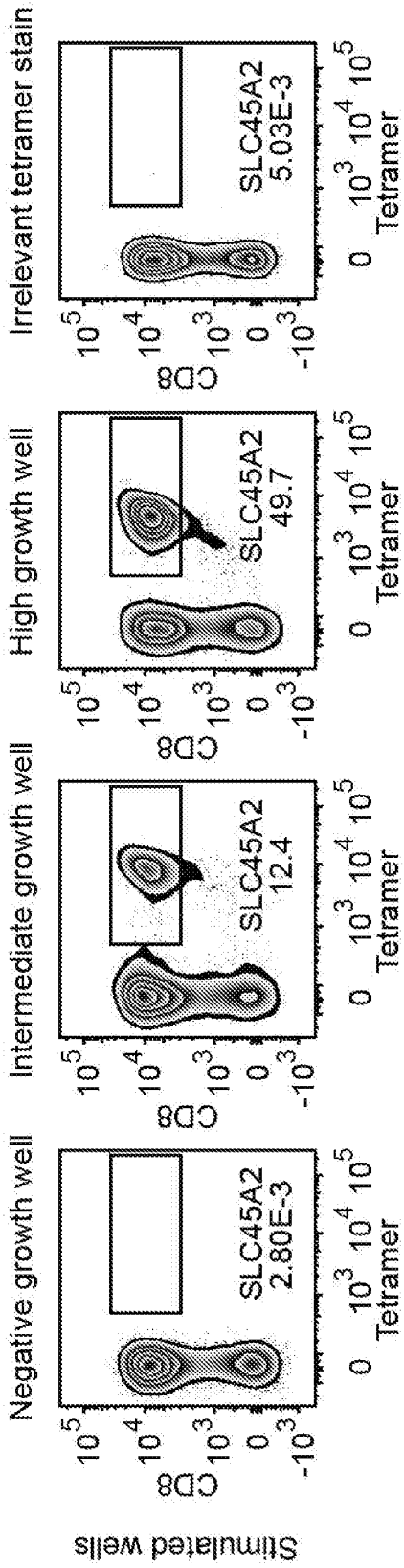


FIG. 15B FIG. 15C FIG. 15D FIG. 15E

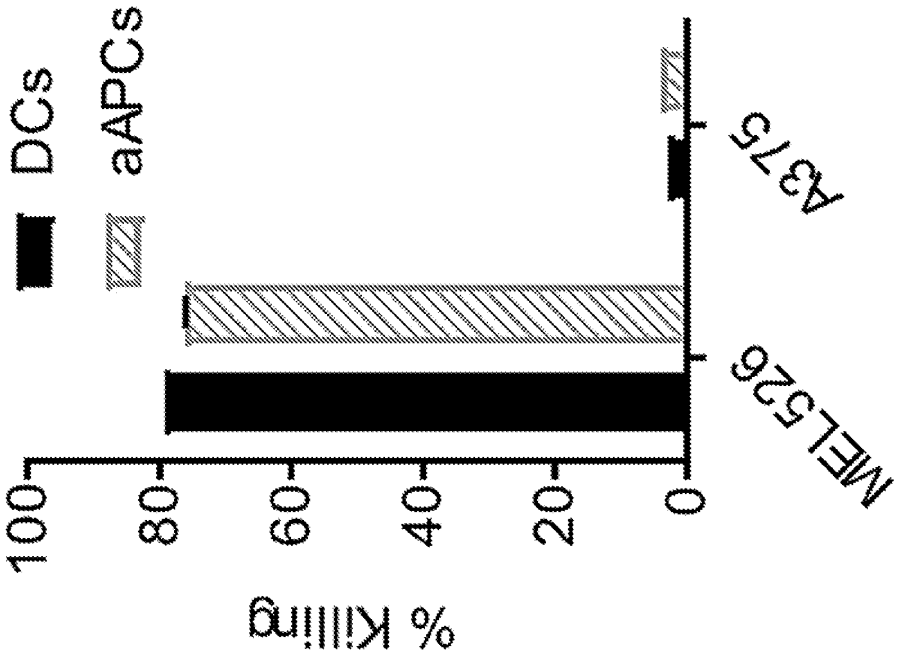

DCs
aAPCs
% Killing
100
80
60
40
20
0
MEL526
A375

FIG. 17

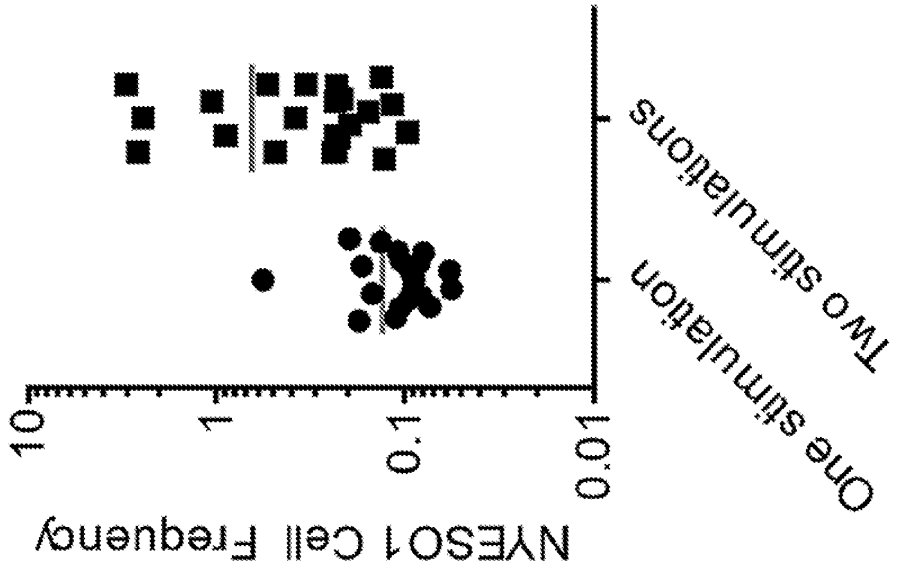

NYESO1 Cell Frequency
10
1
0.1
0.01
One stimulation
Two stimulations

FIG. 16

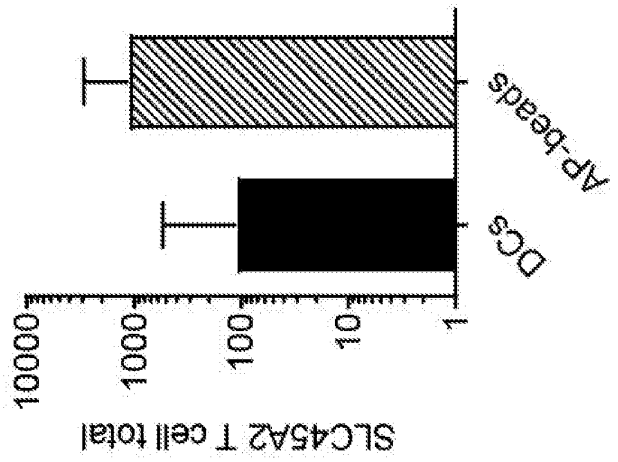


FIG. 18C

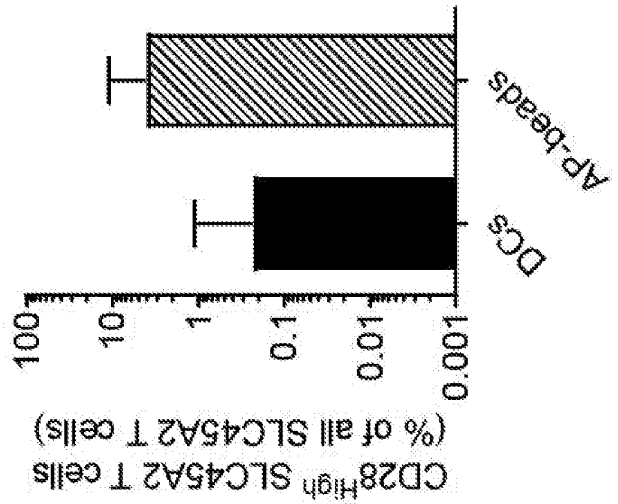


FIG. 18B

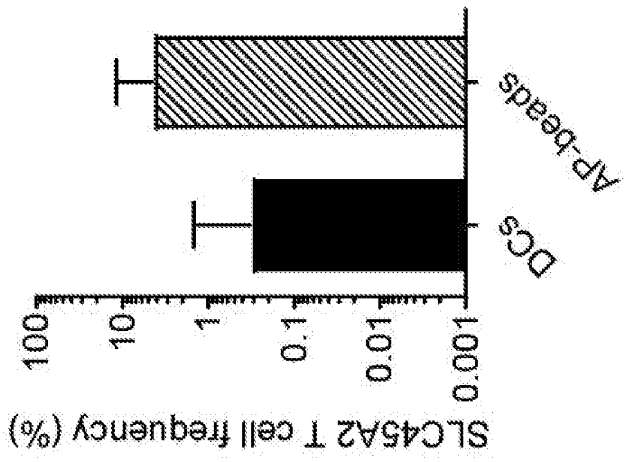


FIG. 18A

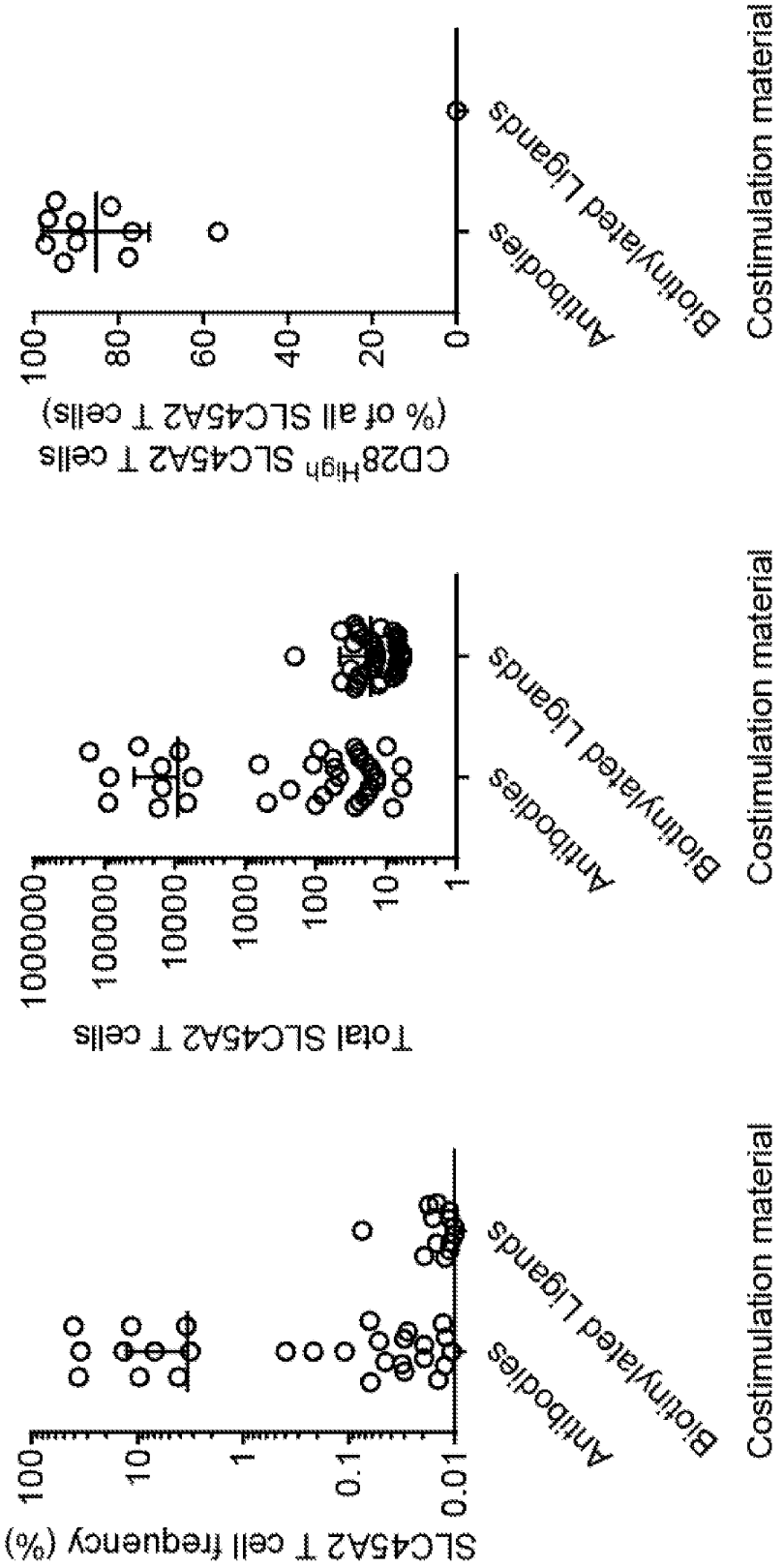


FIG. 19A

FIG. 19B

FIG. 19C

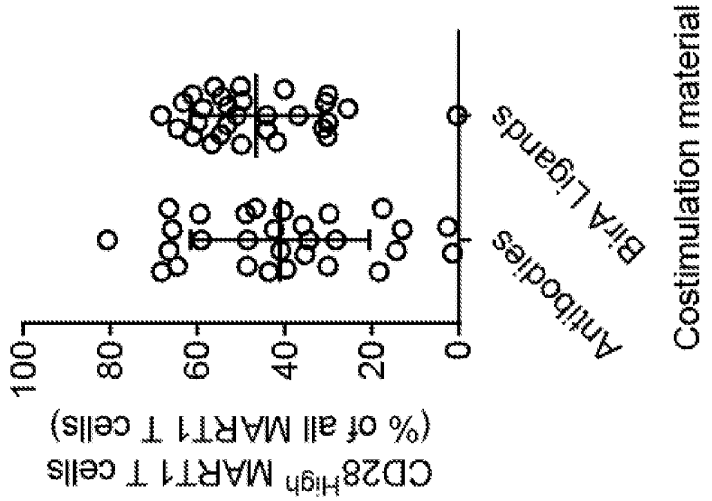


FIG. 19D

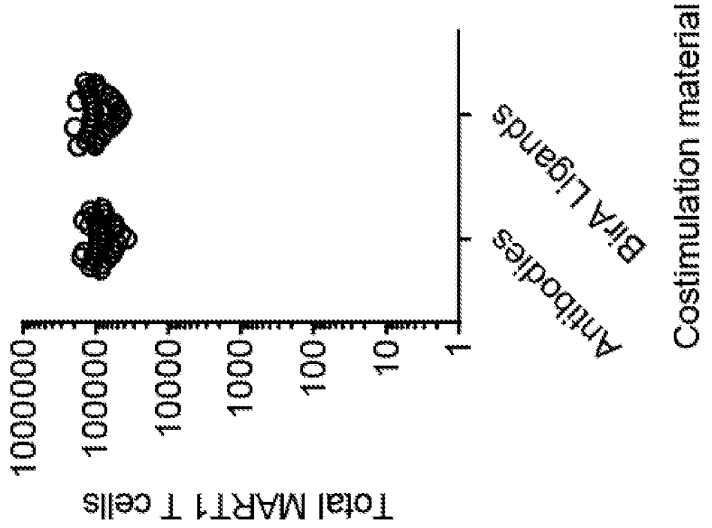


FIG. 19E

FIG. 19F

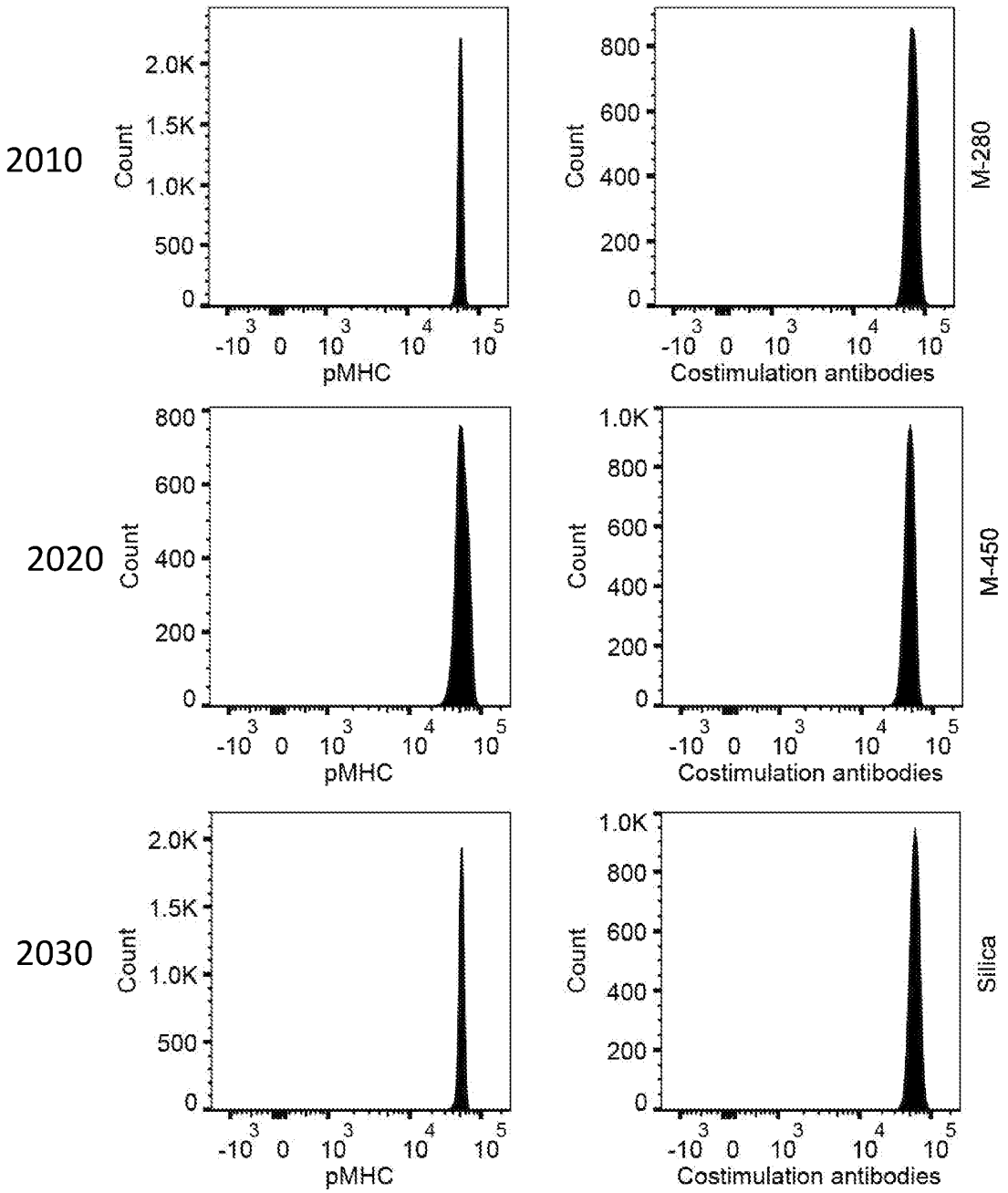
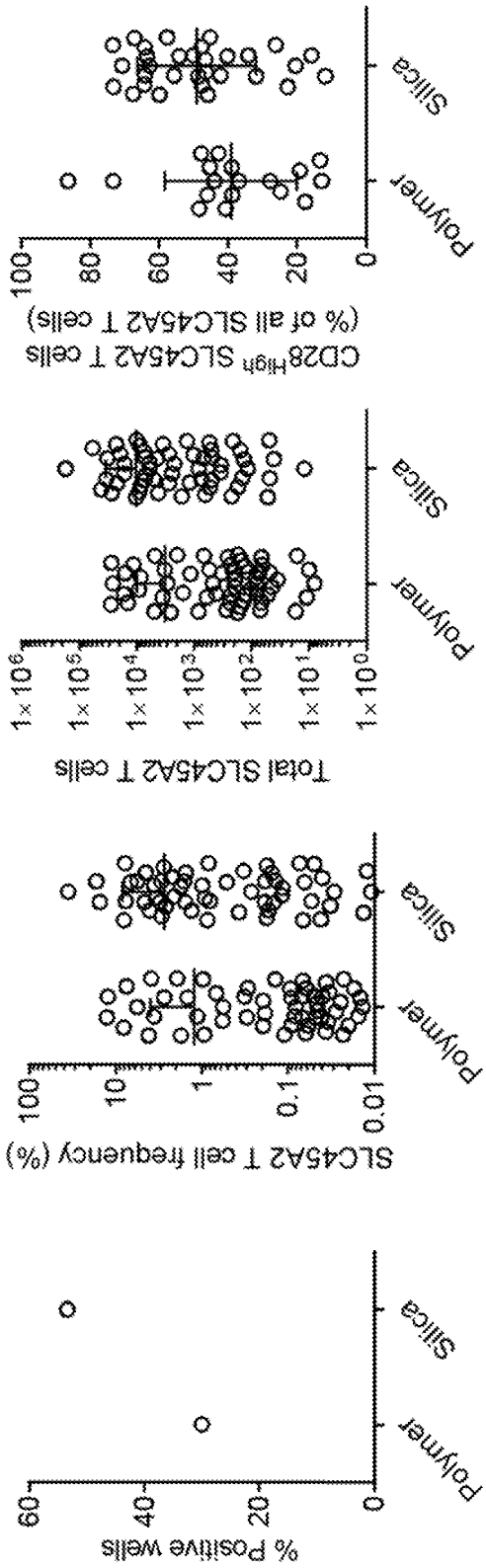

2010
2020
2030
Count
pMHC
Costimulation antibodies
M-280
M-450
Silica
2.0K
1.5K
1.0K
500
800
600
400
200
0
-10^3 0 10^3 10^4 10^5

FIG. 20A



Polymer = convoluted 2.8 micron polymeric bead

FIG. 20B FIG. 20C FIG. 20D FIG. 20E

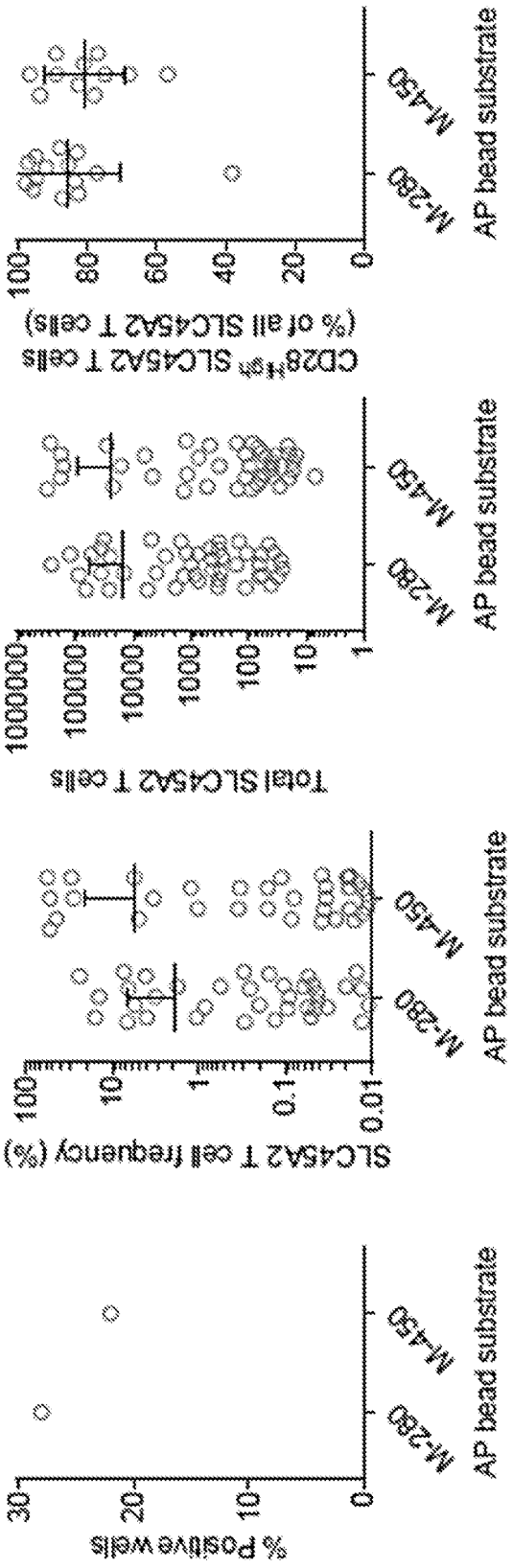


FIG. 20F

FIG. 20G

FIG. 20H

FIG. 20I

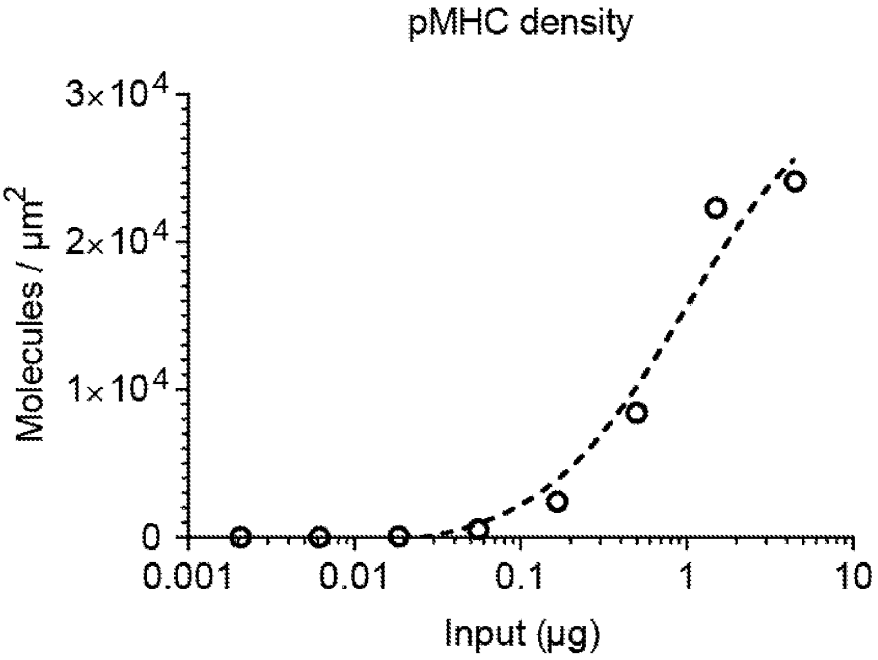


FIG. 21A

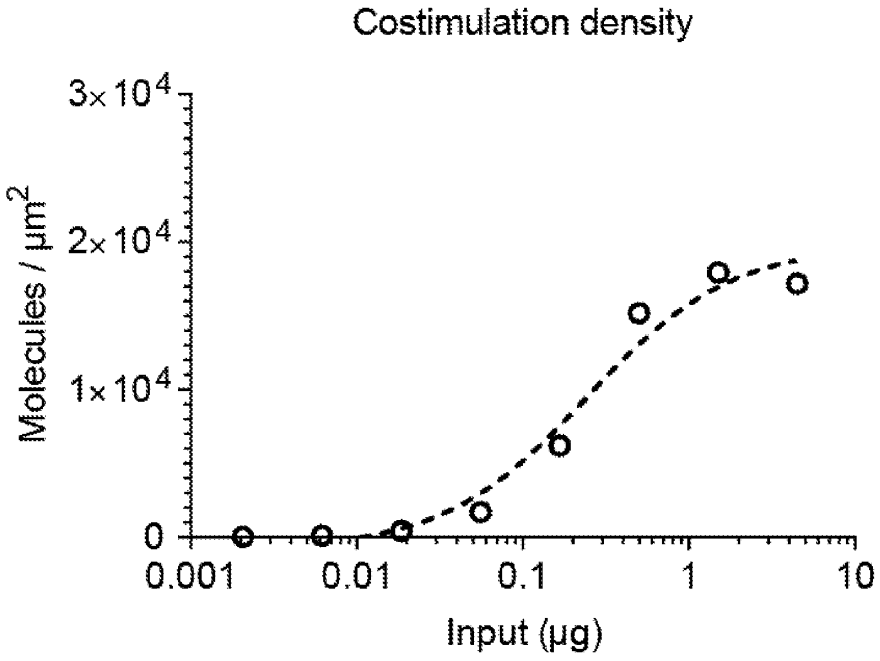


FIG. 21B

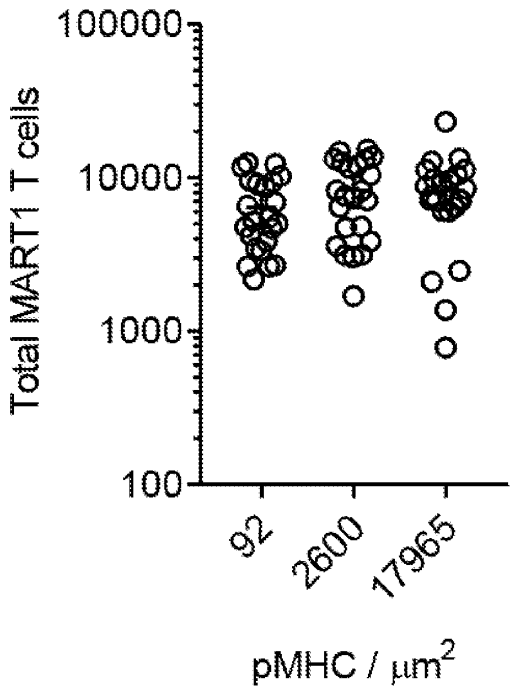


FIG. 21C

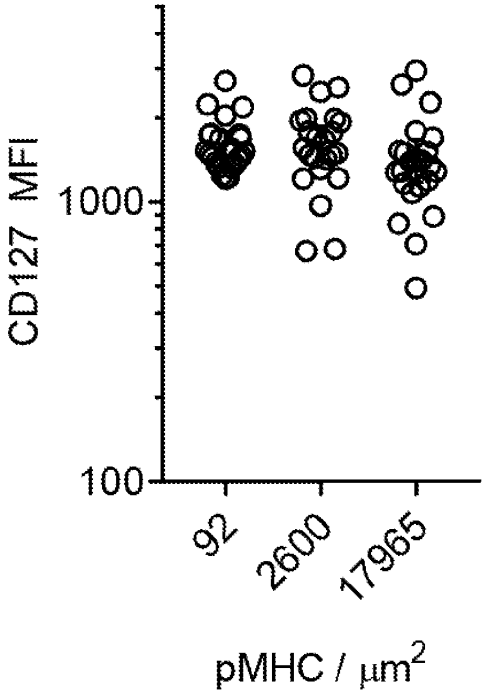


FIG. 21D

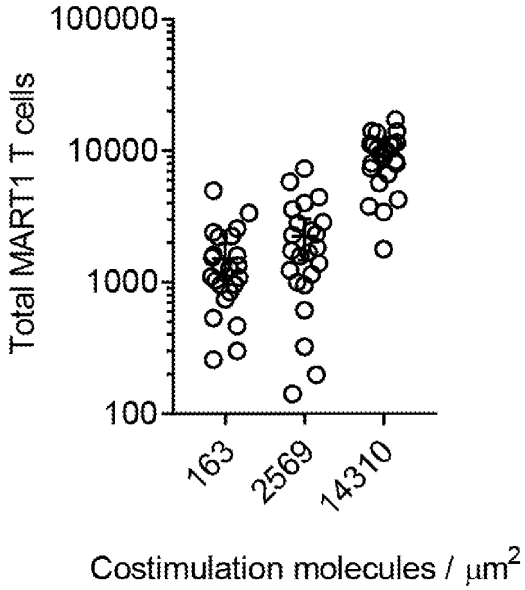


FIG. 21E

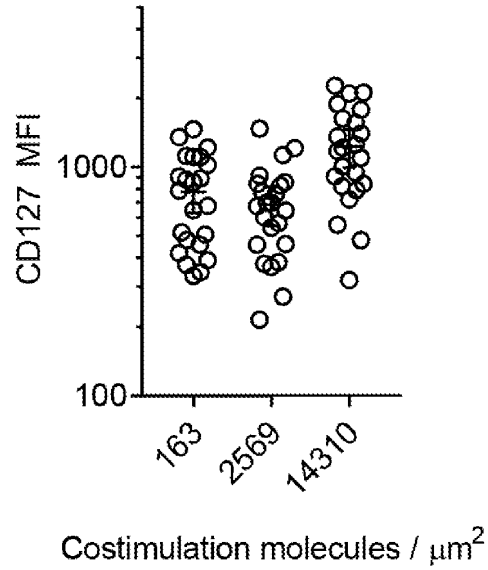


FIG. 21F

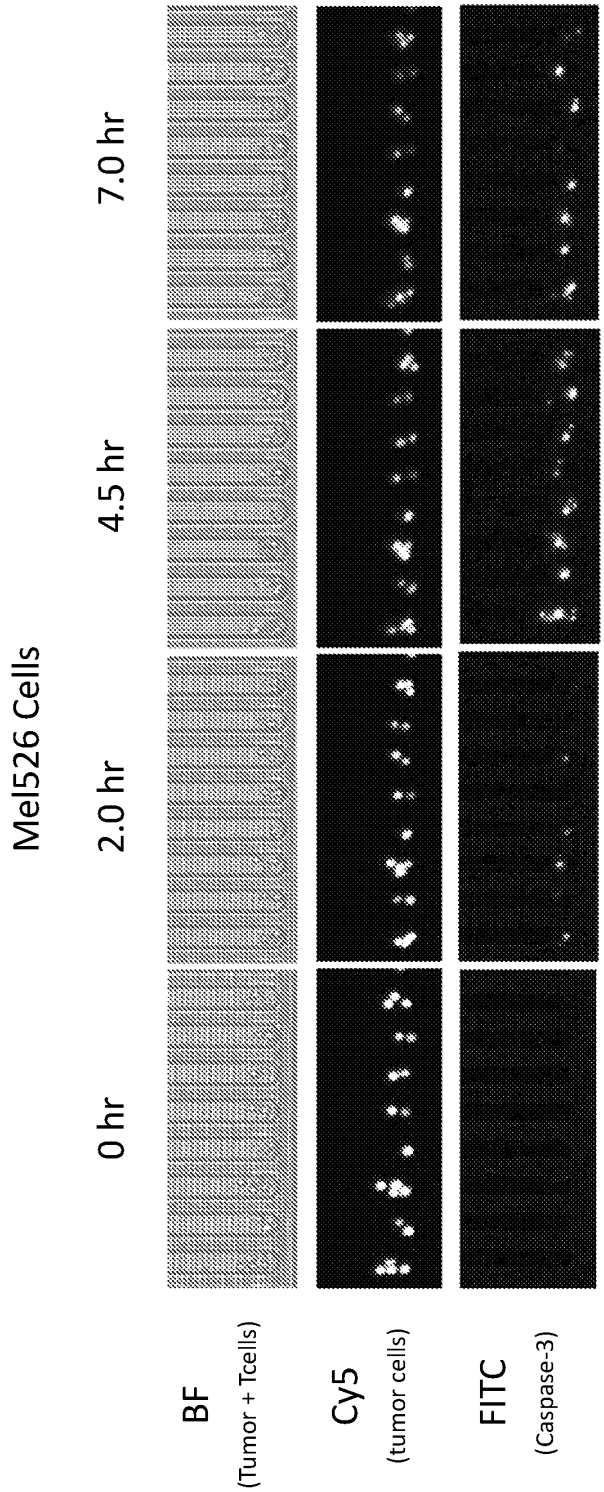

Mel526 Cells
0 hr
2.0 hr
4.5 hr
7.0 hr
BF
(Tumor + Tcells)
Cy5
(tumor cells)
FITC
(Caspase-3)

FIG. 22A

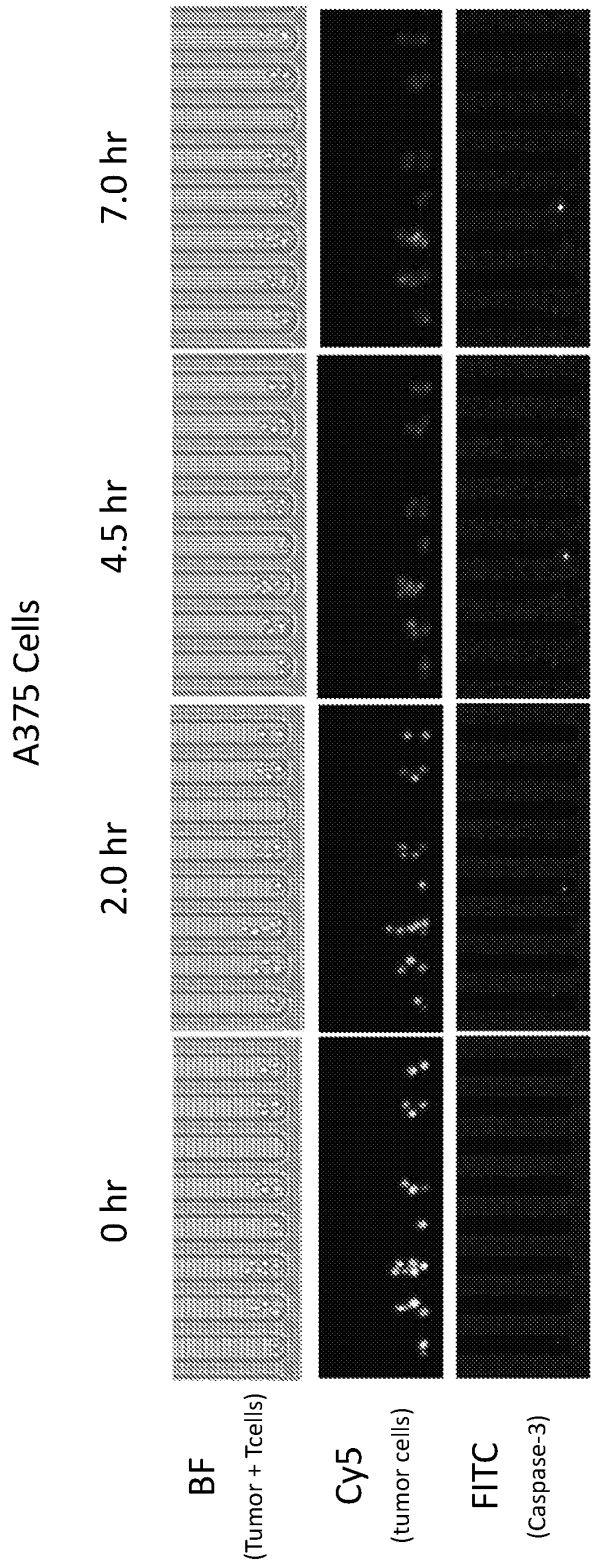

A375 Cells
0 hr
2.0 hr
4.5 hr
7.0 hr
BF
(Tumor + Tcells)
Cy5
(tumor cells)
FITC
(Caspase-3)

FIG. 22B

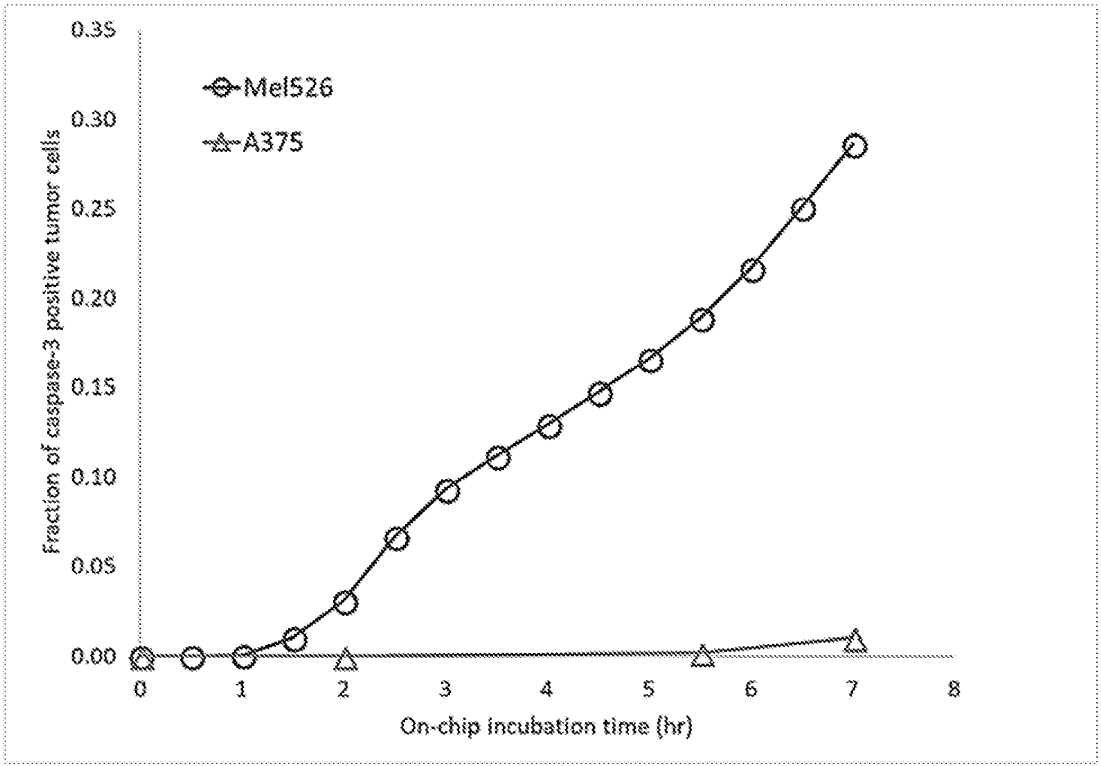


FIG. 22C

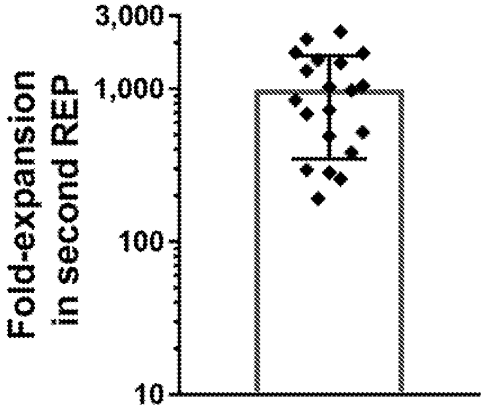


FIG. 23A

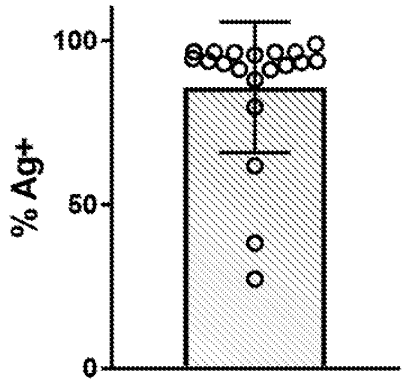


FIG. 23B

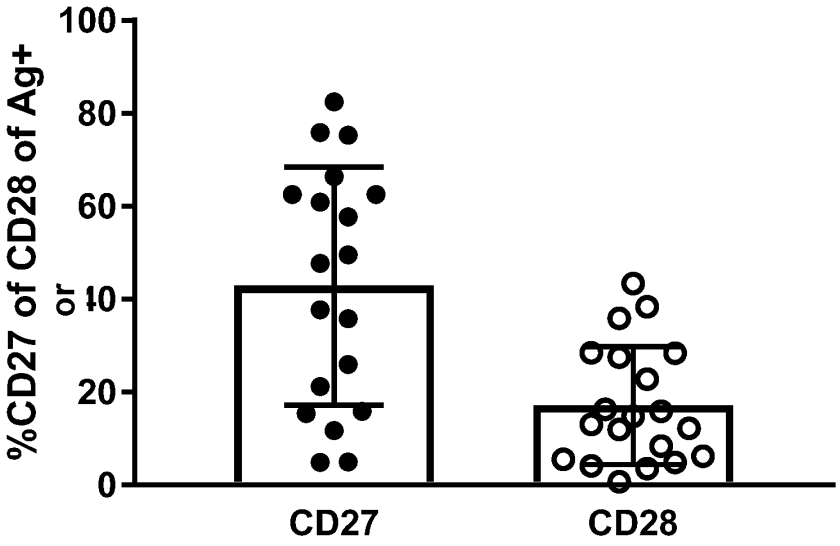


FIG. 23C

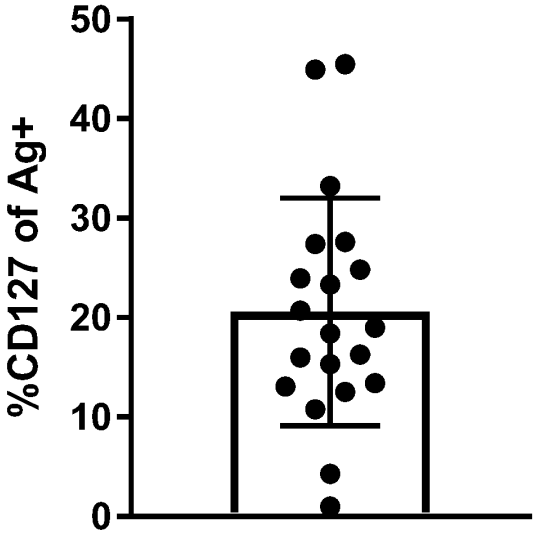


FIG. 23D

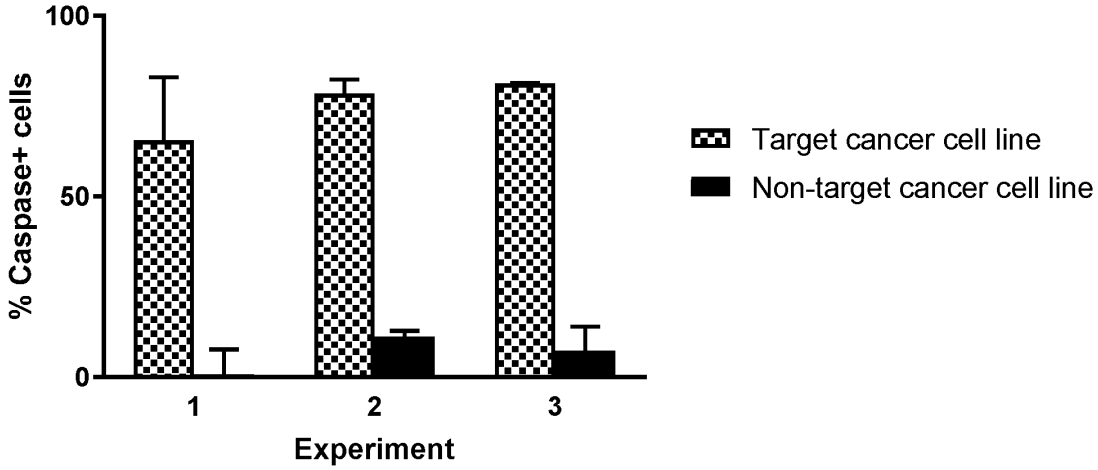

100
50
0
% Caspase+ cells
1
2
3
Experiment
Target cancer cell line
Non-target cancer cell line

FIG. 23E

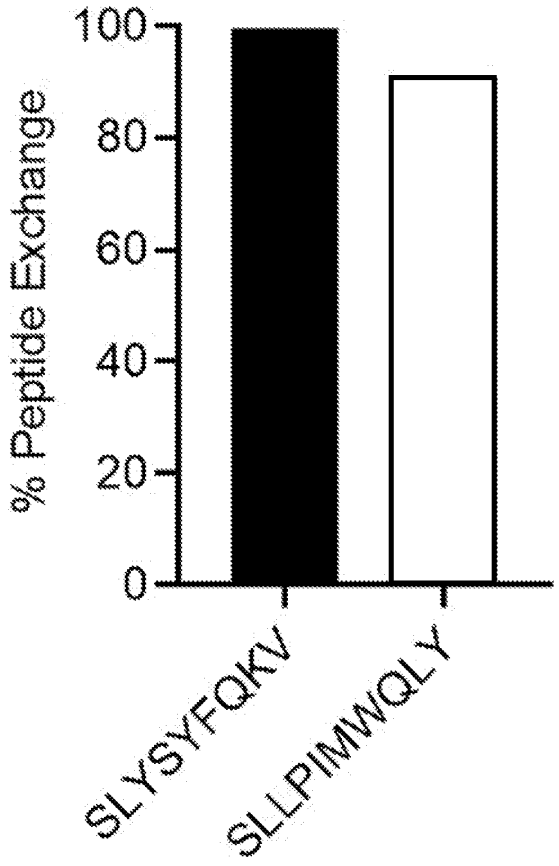


FIG. 24

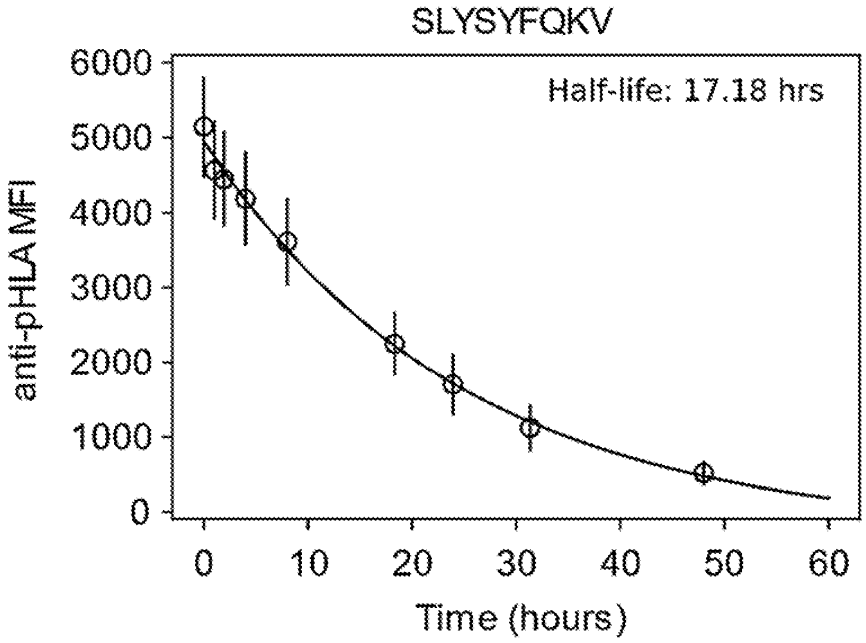


FIG. 25A

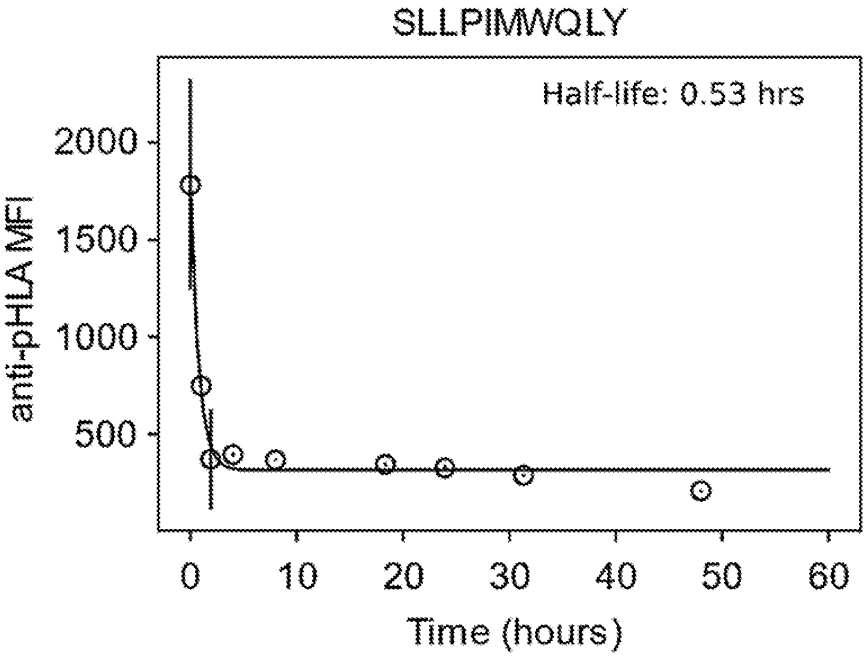


FIG. 25B

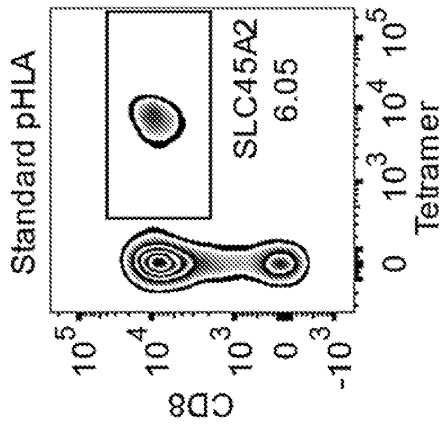


FIG. 26A

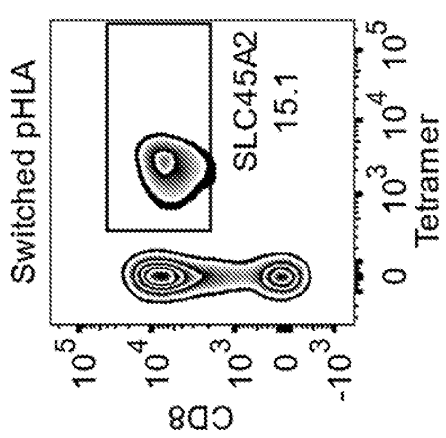


FIG. 26B

FIG. 26C

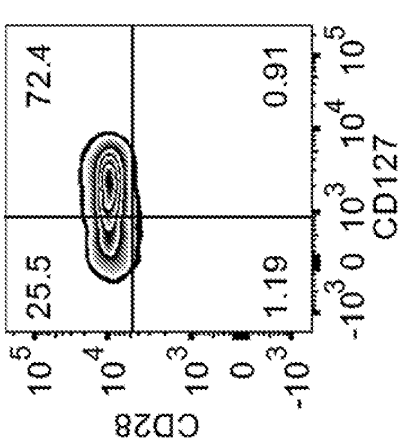


FIG. 26D

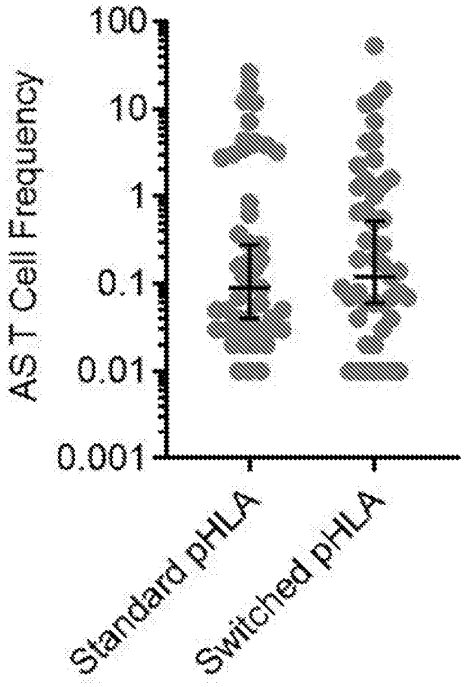

100
10
1
0.1
0.01
0.001
AS T Cell Frequency
Standard pHLA
Switched pHLA

FIG. 27A

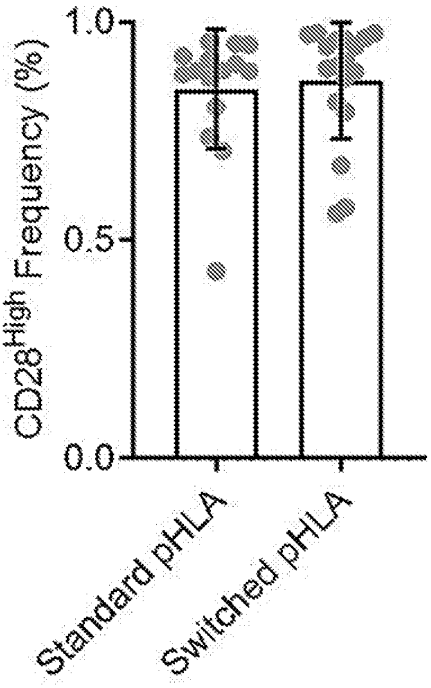


FIG. 27B

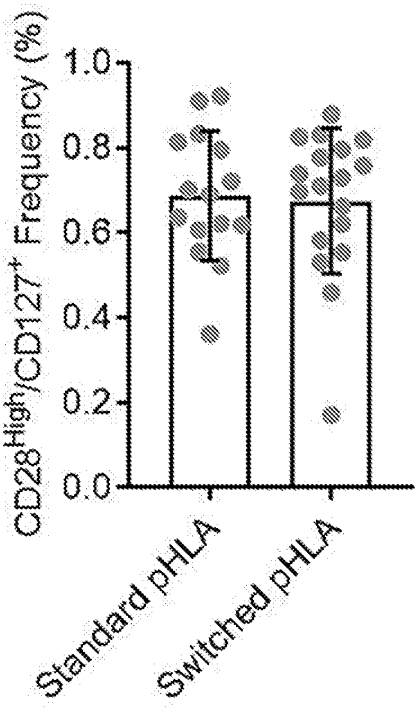

CD28High/CD127+ Frequency (%)
1.0
0.8
0.6
0.4
0.2
0.0
Standard pHLA
Switched pHLA

FIG. 27C