FIGURE 1

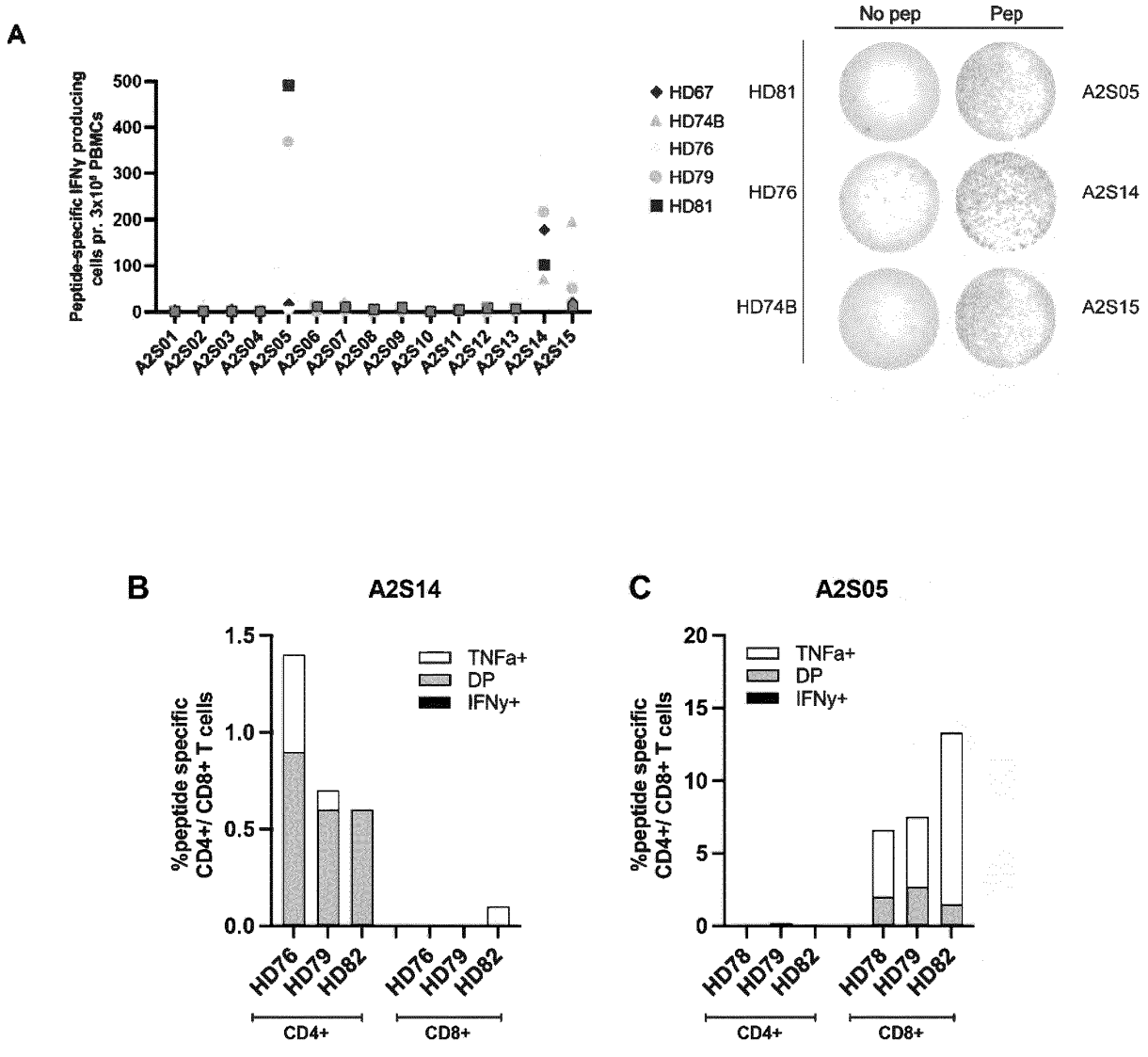
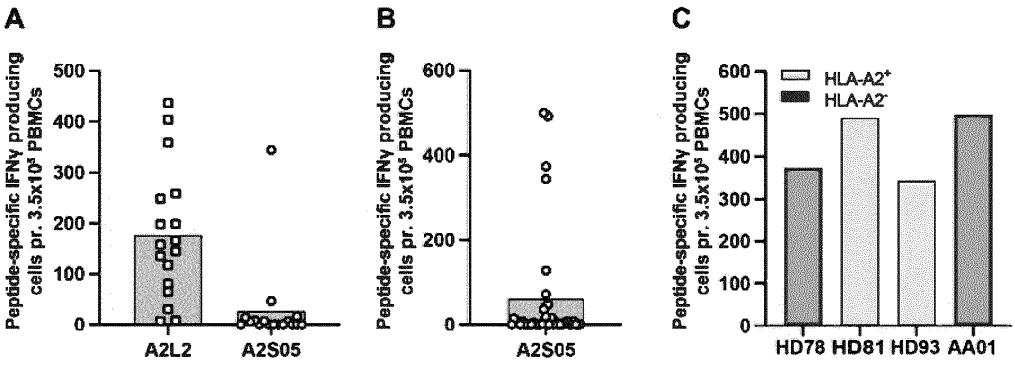

A
Peptide-specific IFNγ producing cells pr. 3x10⁵ PBMCs
500
400
300
200
100
0
A2S01
A2S02
A2S03
A2S04
A2S05
A2S06
A2S07
A2S08
A2S09
A2S10
A2S11
A2S12
A2S13
A2S14
A2S15
HD67
HD74B
HD76
HD79
HD81
No pep
Pep
HD81
HD76
HD74B
A2S05
A2S14
A2S15
B
A2S14
%peptide specific CD4+/ CD8+ T cells
1.5
1.0
0.5
0.0
TNFa+
DP
IFNγ+
HD76
HD79
HD82
HD76
HD79
HD82
CD4+
CD8+
C
A2S05
%peptide specific CD4+/ CD8+ T cells
20
15
10
5
0
TNFa+
DP
IFNγ+
HD78
HD79
HD82
HD78
HD79
HD82
CD4+
CD8+

FIGURE 2



D

DONOR	HLA-A		HLA-B		HLA-C	
HD78	01:01:01	29:02:01	08:01:01	44:03:01	16:01:01	07:01:01
HD81	01:01:01	02:01:01	08:01:01	44:02:01	05:01:01	07:01:01
HD93	01:01:01	02:01:01	08:01:01	57:01:01	06:02:01	07:01:01
AA01	01:01:01	11:01:01	08:01:01	15:24:01	03:03:01	07:01:01

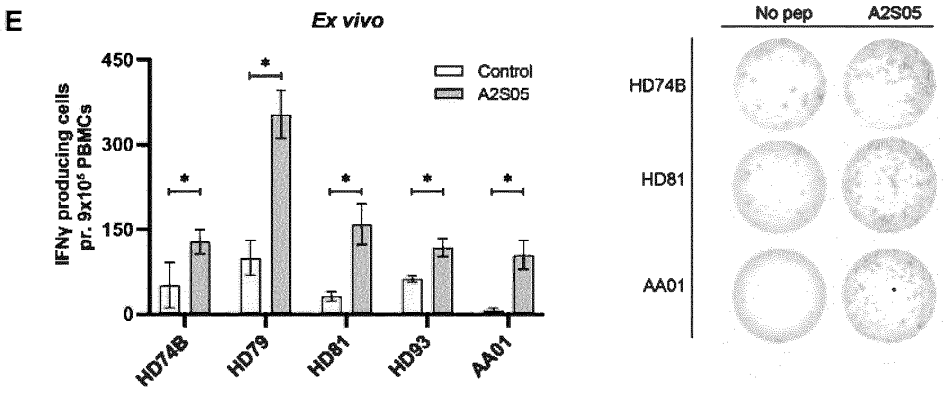


FIGURE 3

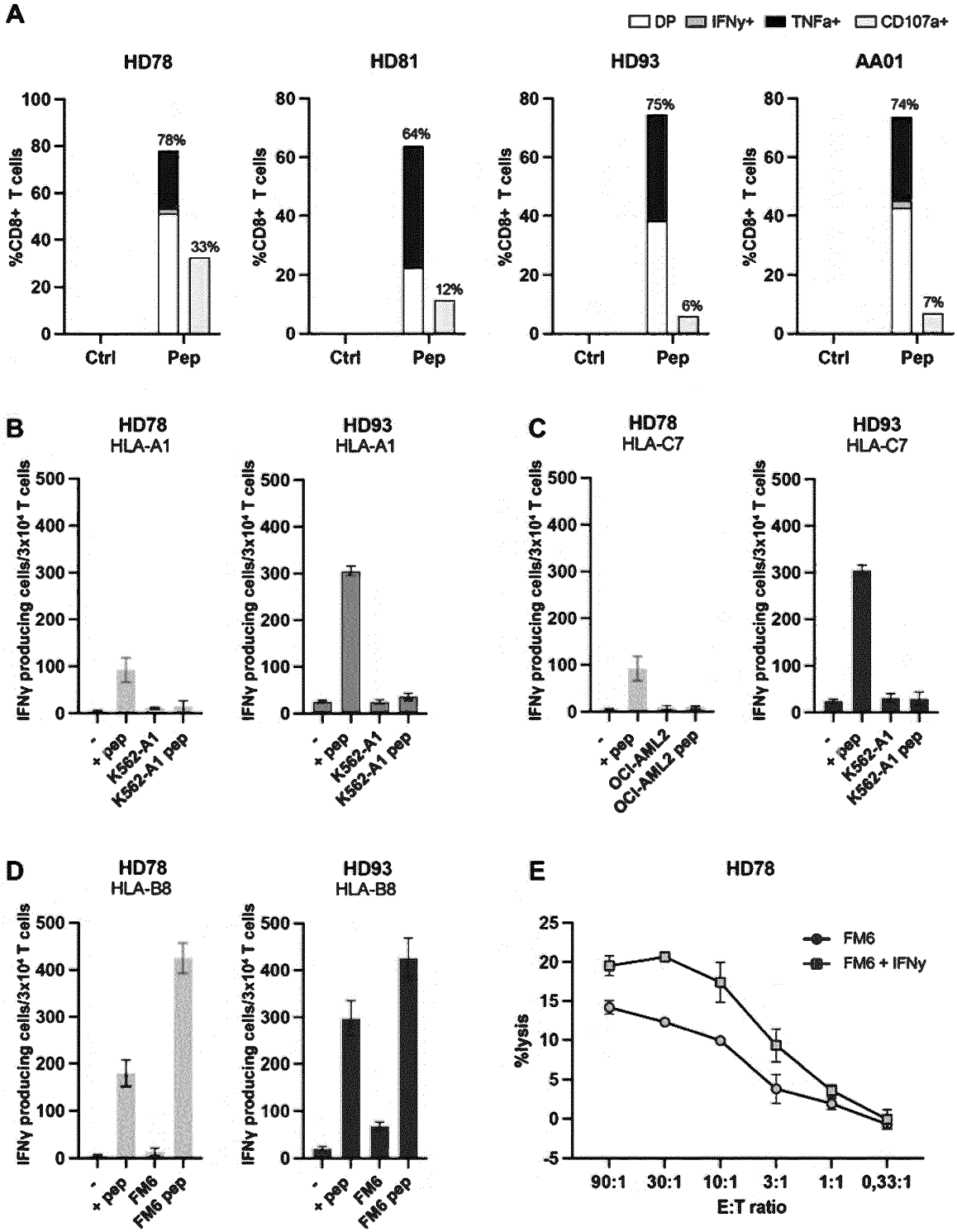

A
DP
IFNγ+
TNFa+
CD107a+
HD78
HD81
HD93
AA01
%CD8+ T cells
78%
33%
64%
12%
75%
6%
74%
7%
Ctrl
Pep
B
HD78
HLA-A1
HD93
HLA-A1
IFNγ producing cells/3x10⁴ T cells
-
+ pep
K562-A1
K562-A1 pep
C
HD78
HLA-C7
HD93
HLA-C7
OCI-AML2
OCI-AML2 pep
D
HD78
HLA-B8
HD93
HLA-B8
FM6
FM6 pep
E
HD78
FM6
FM6 + IFNγ
%lysis
90:1
30:1
10:1
3:1
1:1
0,33:1
E:T ratio

FIGURE 4

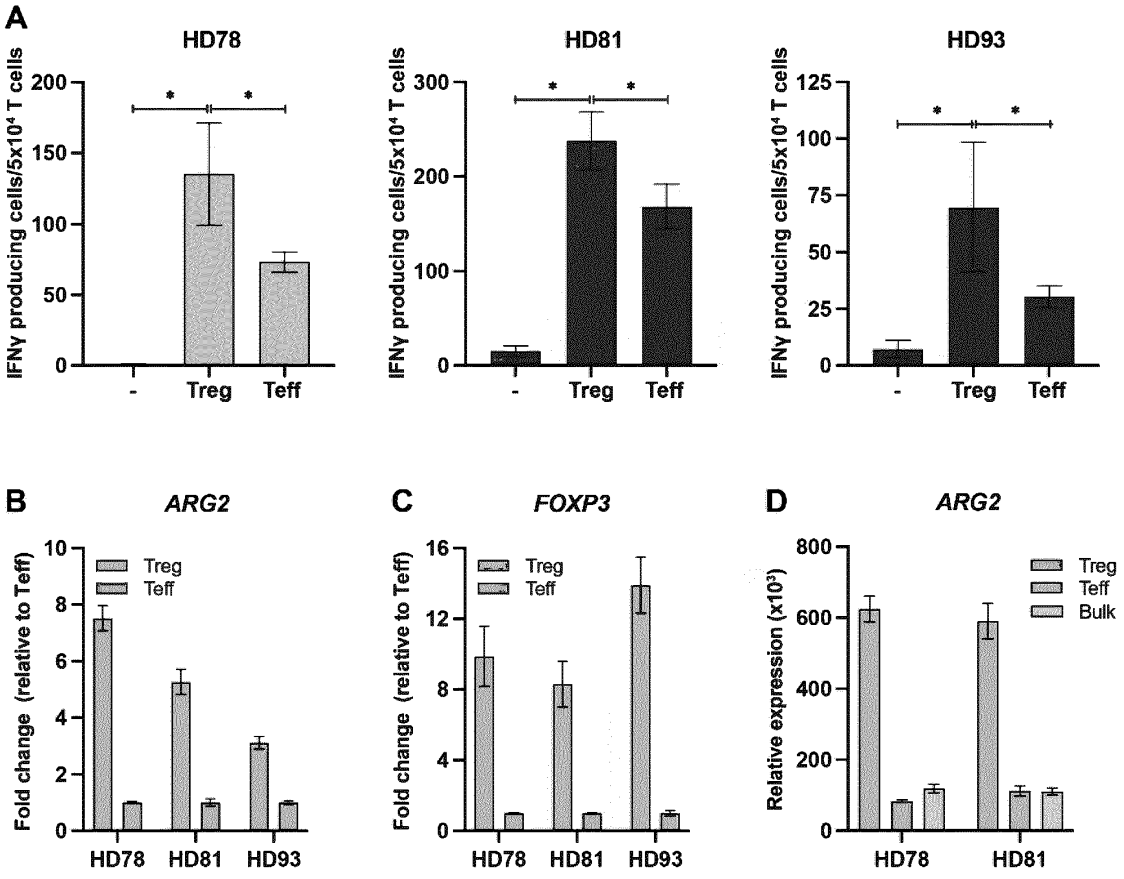

A
HD78
HD81
HD93
IFNγ producing cells/5x10⁴ T cells
200
150
100
50
0
300
125
75
25
*
-
Treg
Teff
B
ARG2
Fold change (relative to Teff)
10
8
6
4
2
Treg
Teff
HD78
HD81
HD93
C
FOXP3
16
12
D
ARG2
Relative expression (x10³)
800
600
400
Bulk

FIGURE 5

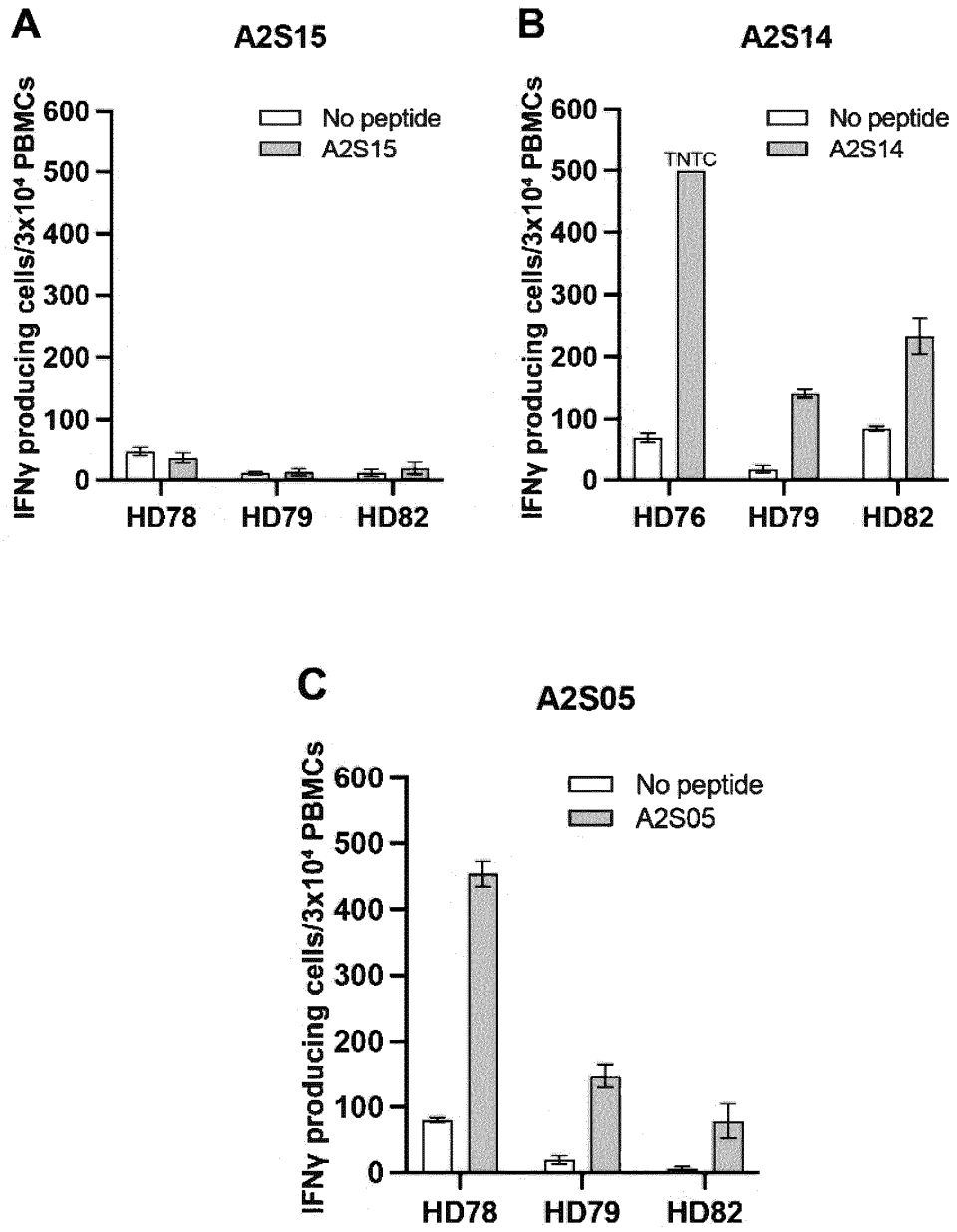

A
A2S15
IFNγ producing cells/3x10⁴ PBMCs
600
500
400
300
200
100
0
No peptide
A2S15
HD78
HD79
HD82
B
A2S14
TNTC
No peptide
A2S14
HD76
HD79
HD82
C
A2S05
No peptide
A2S05
HD78
HD79
HD82

FIGURE 6

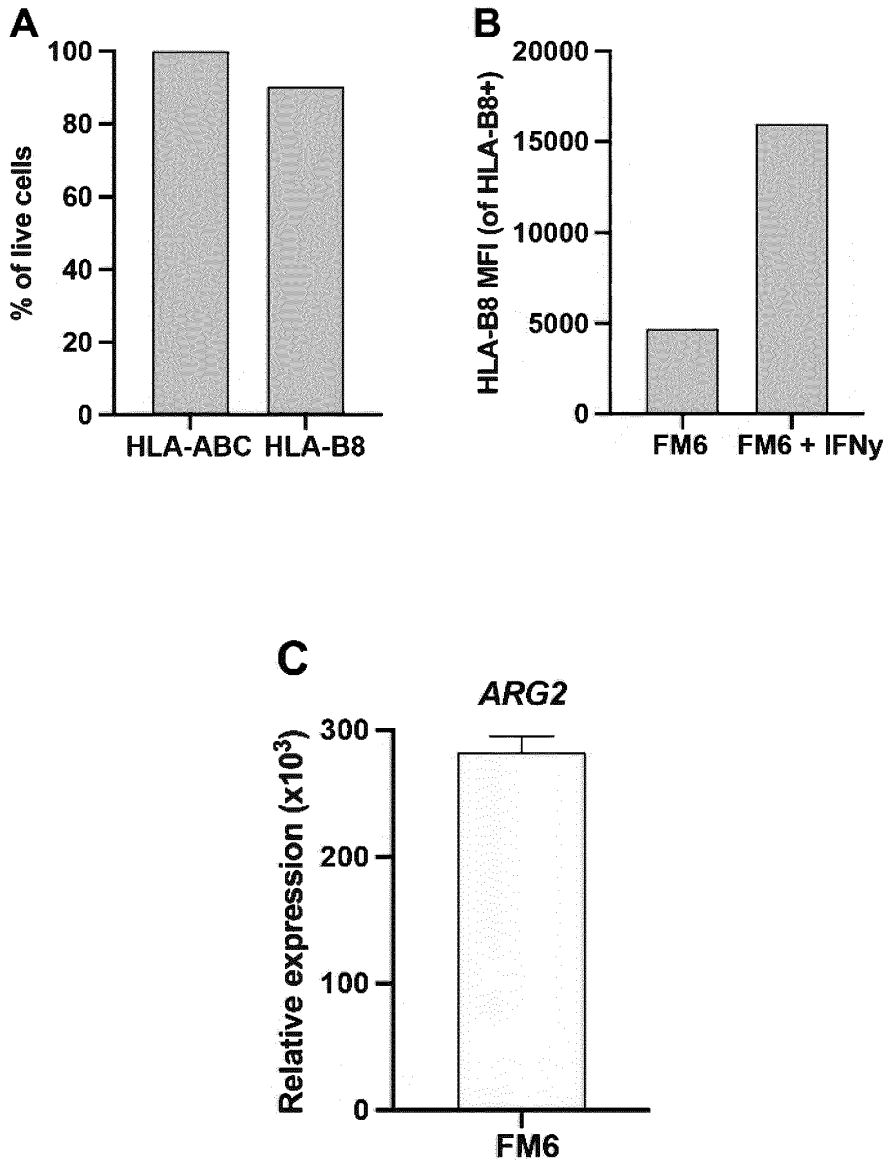

A
% of live cells
100
80
60
40
20
0
HLA-ABC
HLA-B8
B
HLA-B8 MFI (of HLA-B8+)
20000
15000
10000
5000
0
FM6
FM6 + IFNy
C
ARG2
Relative expression (x10³)
300
200
100
0
FM6

FIGURE 7

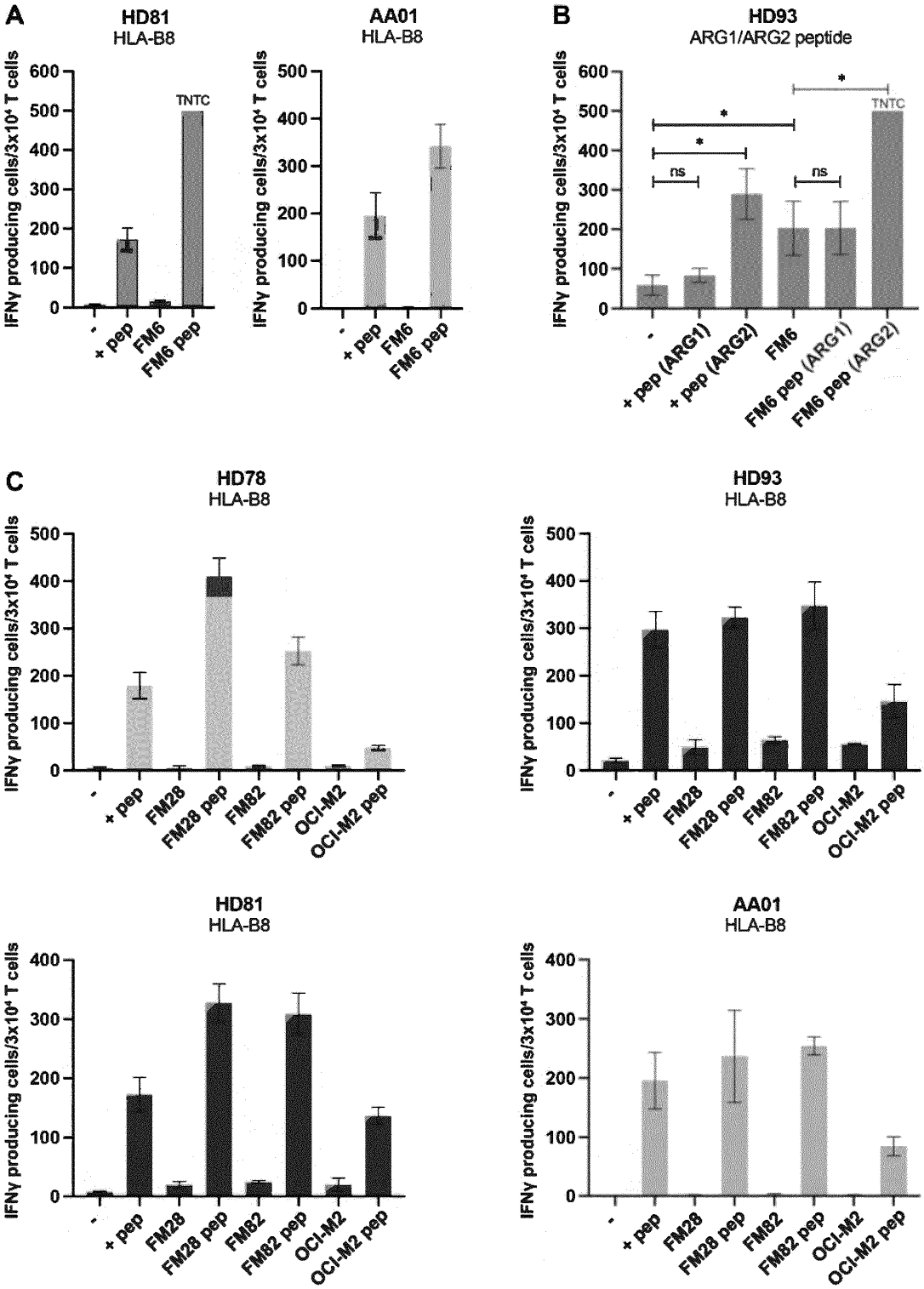

A
HD81
HLA-B8
AA01
HLA-B8
IFNγ producing cells/3x10⁴ T cells
TNTC
- + pep FM6 FM6 pep
B
HD93
ARG1/ARG2 peptide
ns
*
- + pep (ARG1) + pep (ARG2) FM6 FM6 pep (ARG1) FM6 pep (ARG2)
C
HD78
HLA-B8
HD93
HLA-B8
HD81
HLA-B8
AA01
HLA-B8
- + pep FM28 FM28 pep FM82 FM82 pep OCI-M2 OCI-M2 pep

FIGURE 8

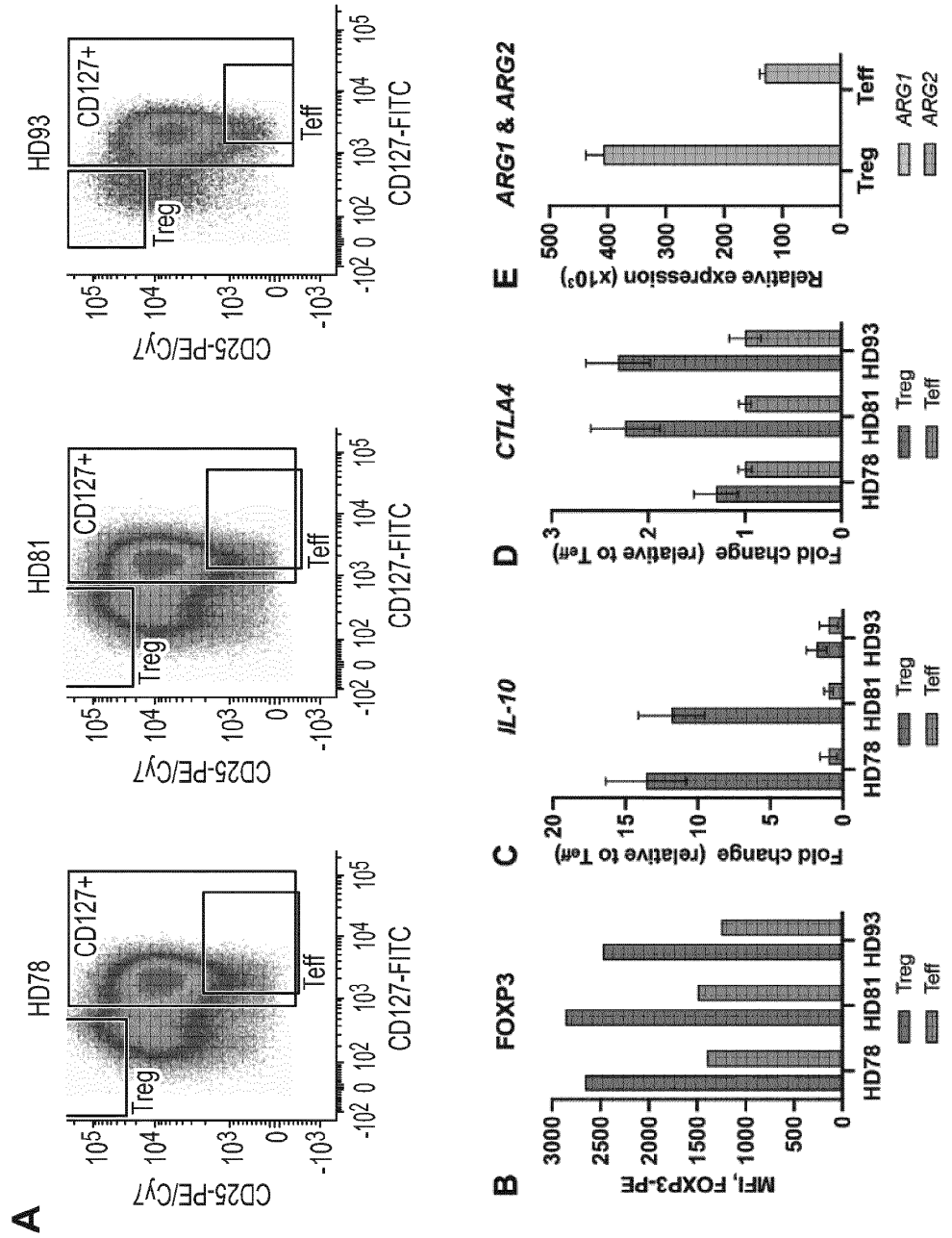

A
HD78
HD81
HD93
CD127+
Treg
Teff
CD25-PE/Cy7
CD127-FITC
B
FOXP3
MFI, FOXP3-PE
C
IL-10
Fold change (relative to Teff)
D
CTLA4
E
ARG1 & ARG2
Relative expression (x10³)
HD78 HD81 HD93
Treg
Teff
ARG1
ARG2

FIGURE 9

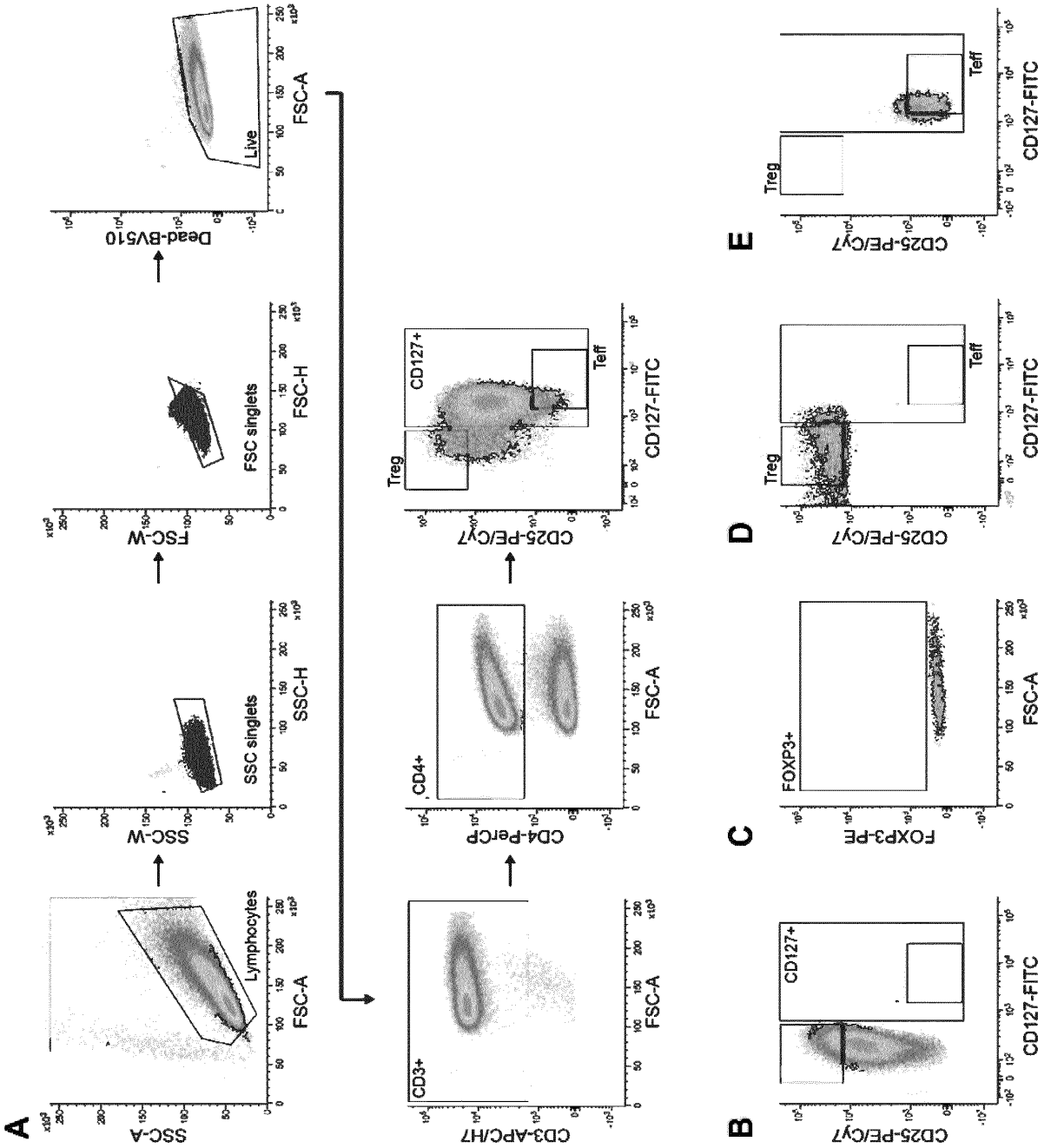

A
SSC-A
FSC-A
Lymphocytes
SSC-W
SSC-H
SSC singlets
FSC-W
FSC-H
FSC singlets
Dead-BV510
Live
CD3-APC/H7
CD4-PerCP
CD4+
CD25-PE/Cy7
CD127-FITC
CD127+
Treg
Teff
B
C
FOXP3-PE
FOXP3+
D
E

FIGURE 10

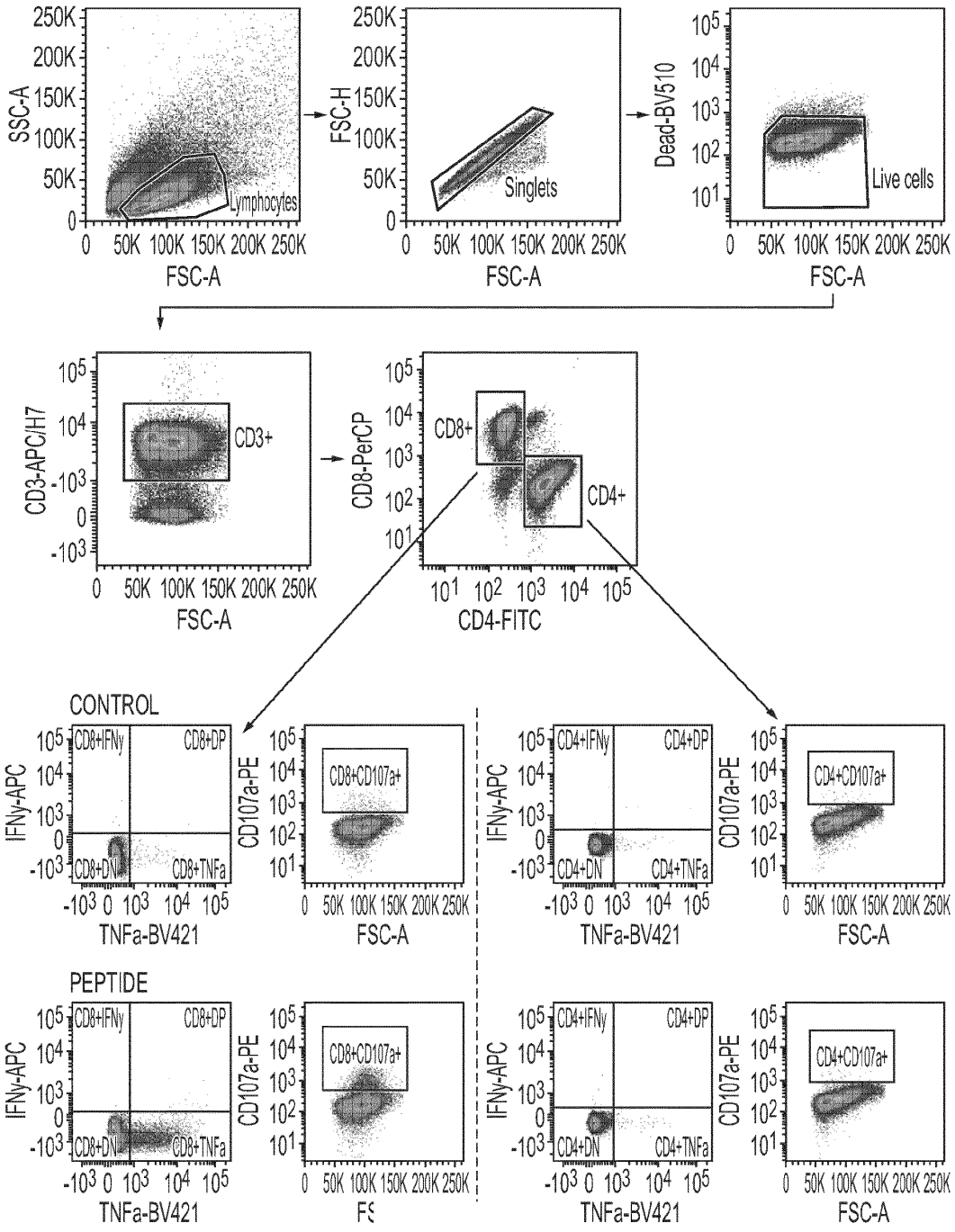

SSC-A
FSC-A
Lymphocytes
FSC-H
Singlets
Dead-BV510
Live cells
CD3-APC/H7
CD3+
CD8-PerCP
CD8+
CD4+
CD4-FITC
CONTROL
PEPTIDE
IFNγ-APC
TNFa-BV421
CD107a-PE
CD8+IFNγ
CD8+DP
CD8+DN
CD8+TNFa
CD8+CD107a+
CD4+IFNγ
CD4+DP
CD4+DN
CD4+TNFa
CD4+CD107a+

FIGURE 11

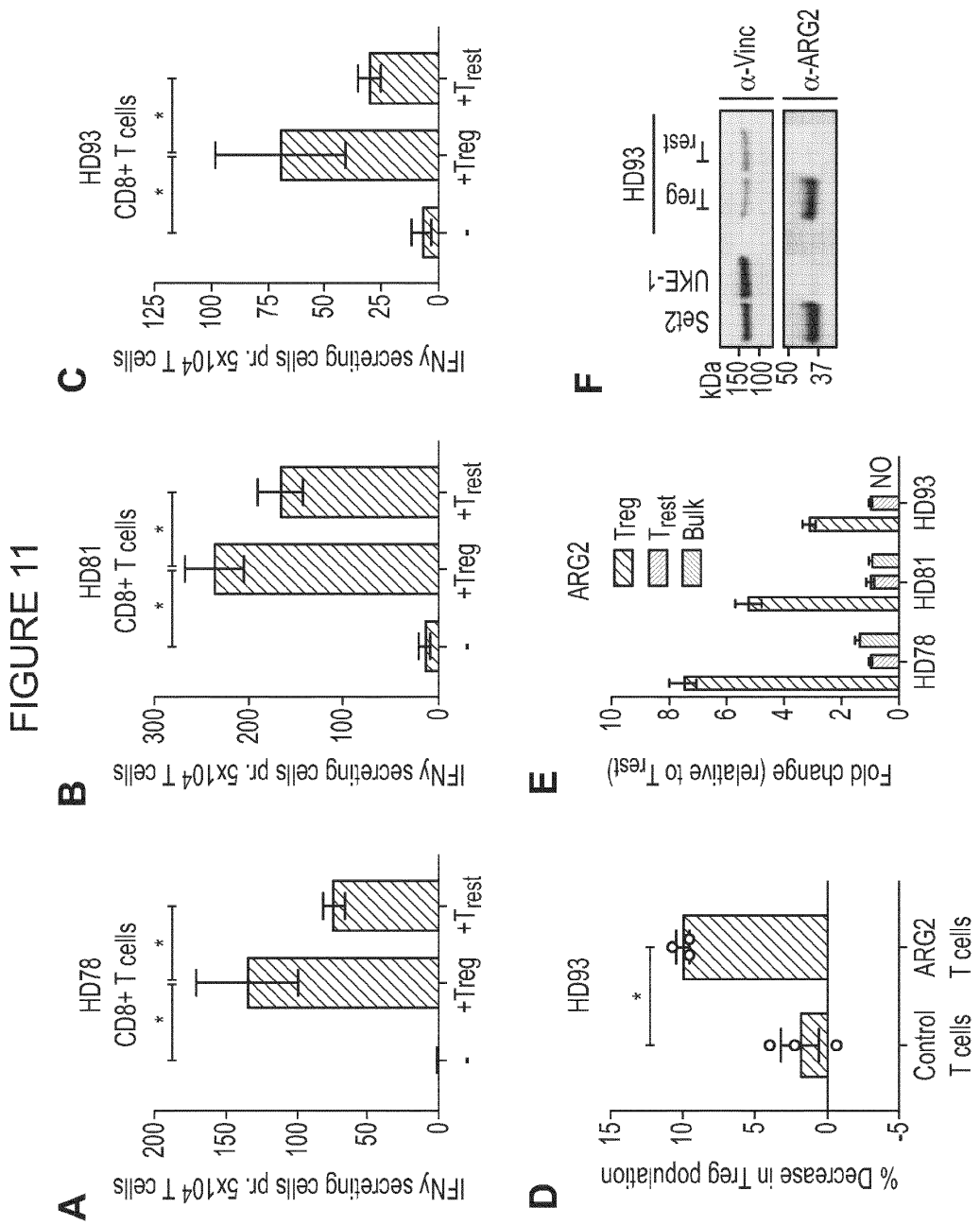

A
HD78
CD8+ T cells
IFNγ secreting cells pr. 5x10⁴ T cells
200
150
100
50
0
*
*
-
+Treg
+Trest
B
HD81
CD8+ T cells
IFNγ secreting cells pr. 5x10⁴ T cells
300
200
100
0
*
*
-
+Treg
+Trest
C
HD93
CD8+ T cells
IFNγ secreting cells pr. 5x10⁴ T cells
125
100
75
50
25
0
*
*
-
+Treg
+Trest
D
HD93
*
% Decrease in Treg population
15
10
5
0
-5
Control
T cells
ARG2
T cells
E
ARG2
Treg
Trest
Bulk
Fold change (relative to Trest)
10
8
6
4
2
0
HD78
HD81
HD93
NO
F
HD93
Treg
Trest
SeI2
UKE-1
kDa
150
100
50
37
α-Vinc
α-ARG2

FIGURE 11 (Cont.)

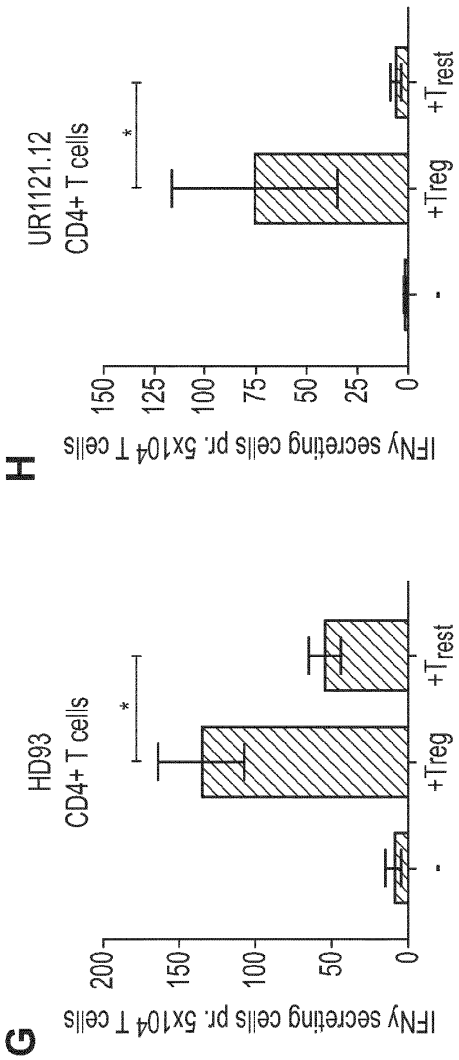


FIGURE 12

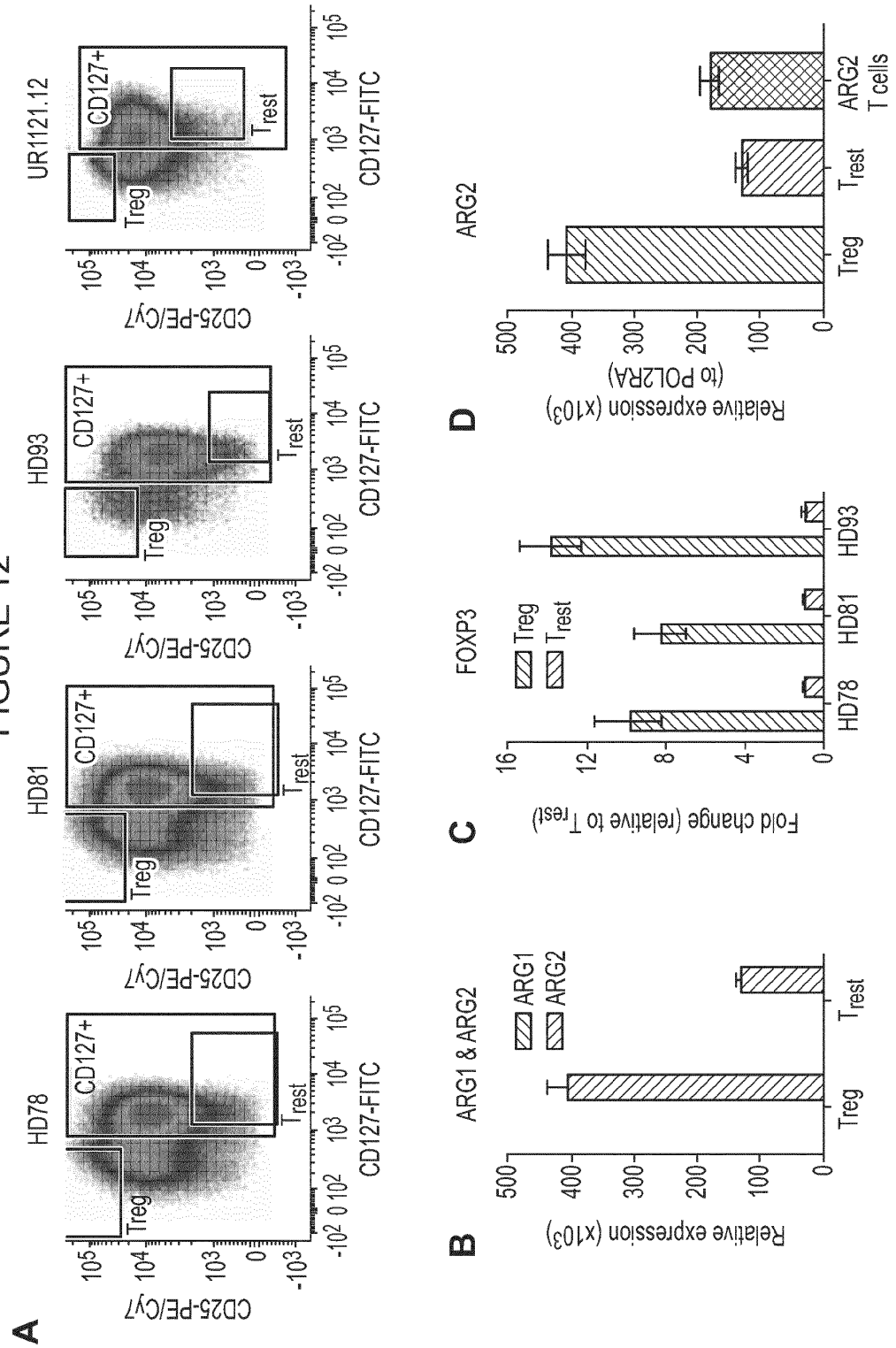

A
HD78
HD81
HD93
UR1121.12
CD127+
Treg
Trest
CD25-PE/Cy7
CD127-FITC
B
ARG1 & ARG2
ARG1
ARG2
Relative expression (x10³)
Treg
Trest
C
FOXP3
Treg
Trest
Fold change (relative to Trest)
HD78
HD81
HD93
D
ARG2
Relative expression (x10³)
(to POL2RA)
Treg
Trest
ARG2
T cells

FIGURE 12 (Cont.)

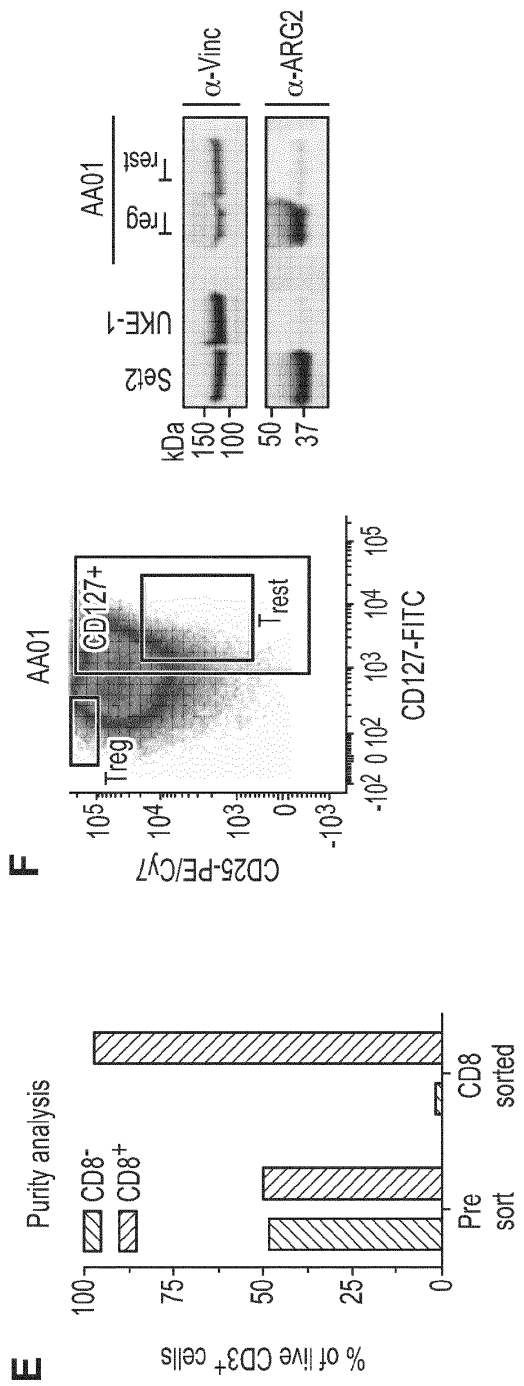


FIGURE 13

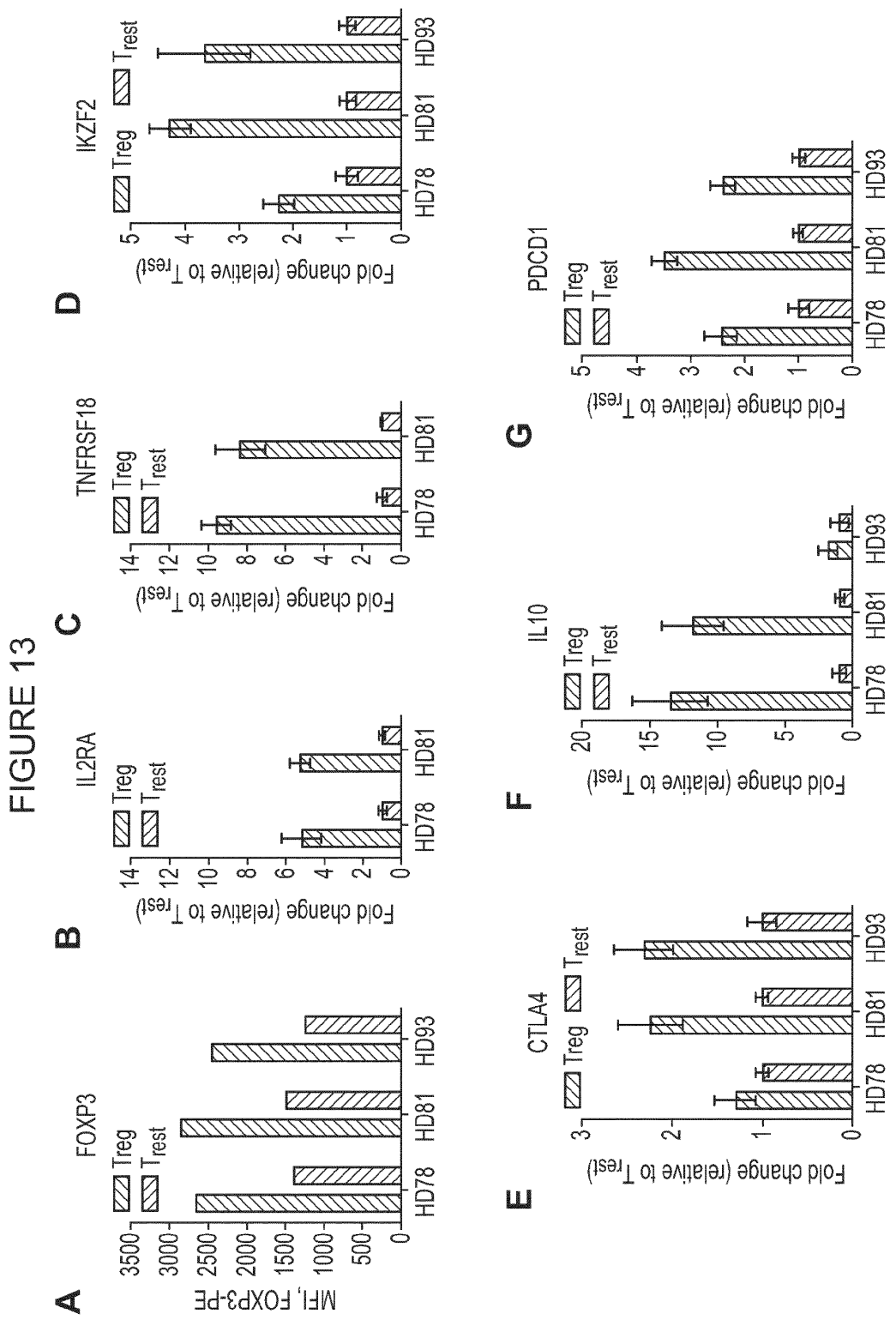

A
FOXP3
MFI, FOXP3-PE
B
IL2RA
C
TNFRSF18
D
IKZF2
E
CTLA4
F
IL10
G
PDCD1
Treg
Trest
Fold change (relative to Trest)
HD78
HD81
HD93

FIGURE 13 (Cont.)

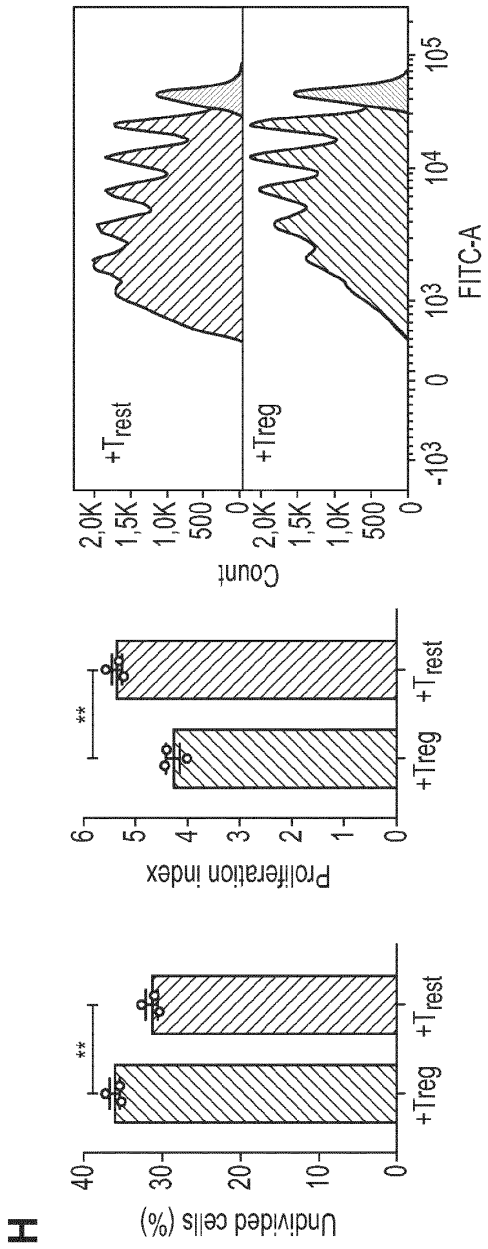


FIGURE 14

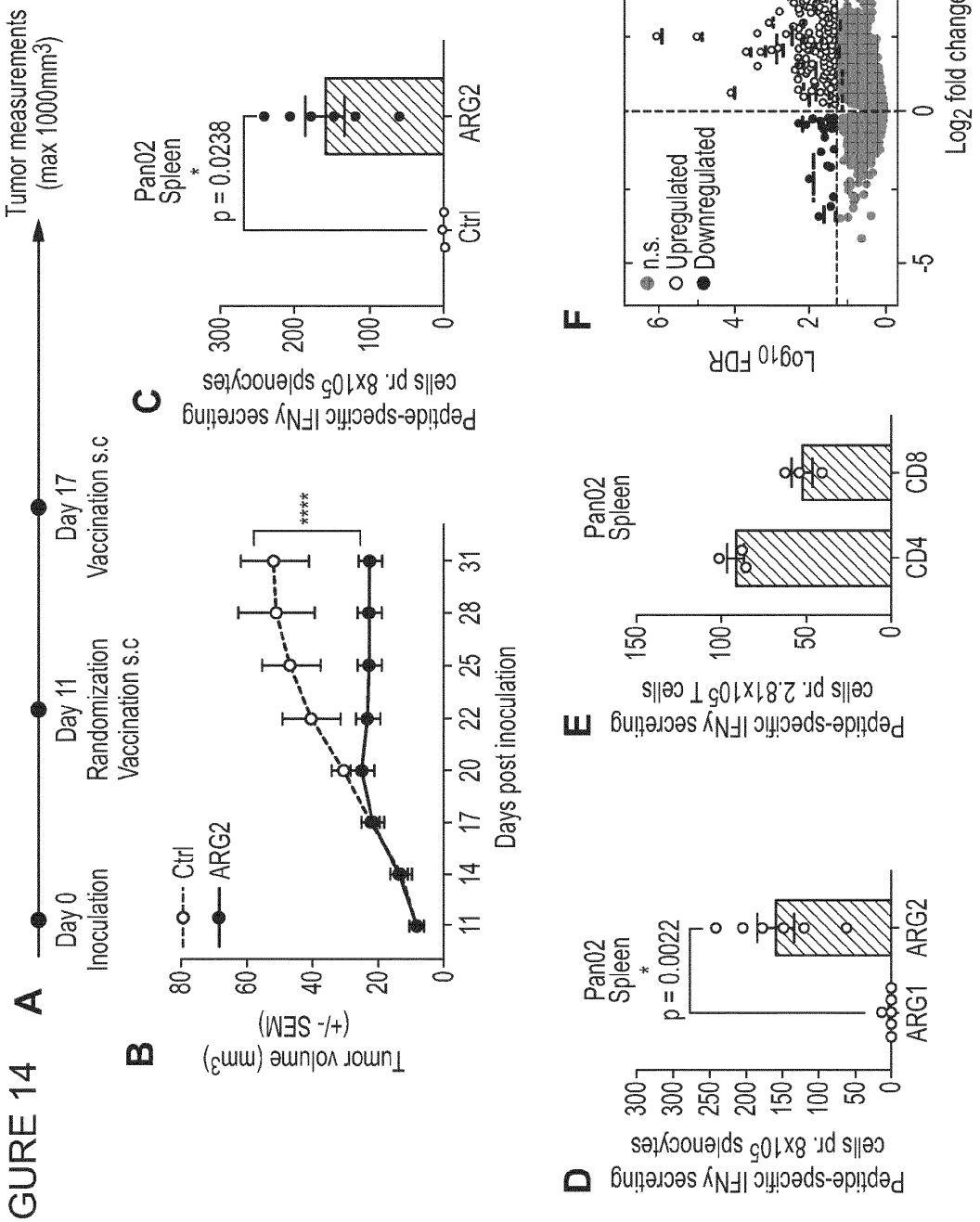

A
Day 0
Inoculation
Day 11
Randomization
Vaccination s.c
Day 17
Vaccination s.c
Tumor measurements
(max 1000mm3)
B
Ctrl
ARG2
Tumor volume (mm3)
(+/- SEM)
****
Days post inoculation
C
Pan02
Spleen
*
p = 0.0238
Peptide-specific IFNγ secreting
cells pr. 8x10^5 splenocytes
Ctrl
ARG2
D
Pan02
Spleen
*
p = 0.0022
Peptide-specific IFNγ secreting
cells pr. 8x10^5 splenocytes
ARG1
ARG2
E
Pan02
Spleen
Peptide-specific IFNγ secreting
cells pr. 2.81x10^5 T cells
CD4
CD8
F
n.s.
Upregulated
Downregulated
Log10 FDR
Log2 fold change

FIGURE 14 (Cont.)

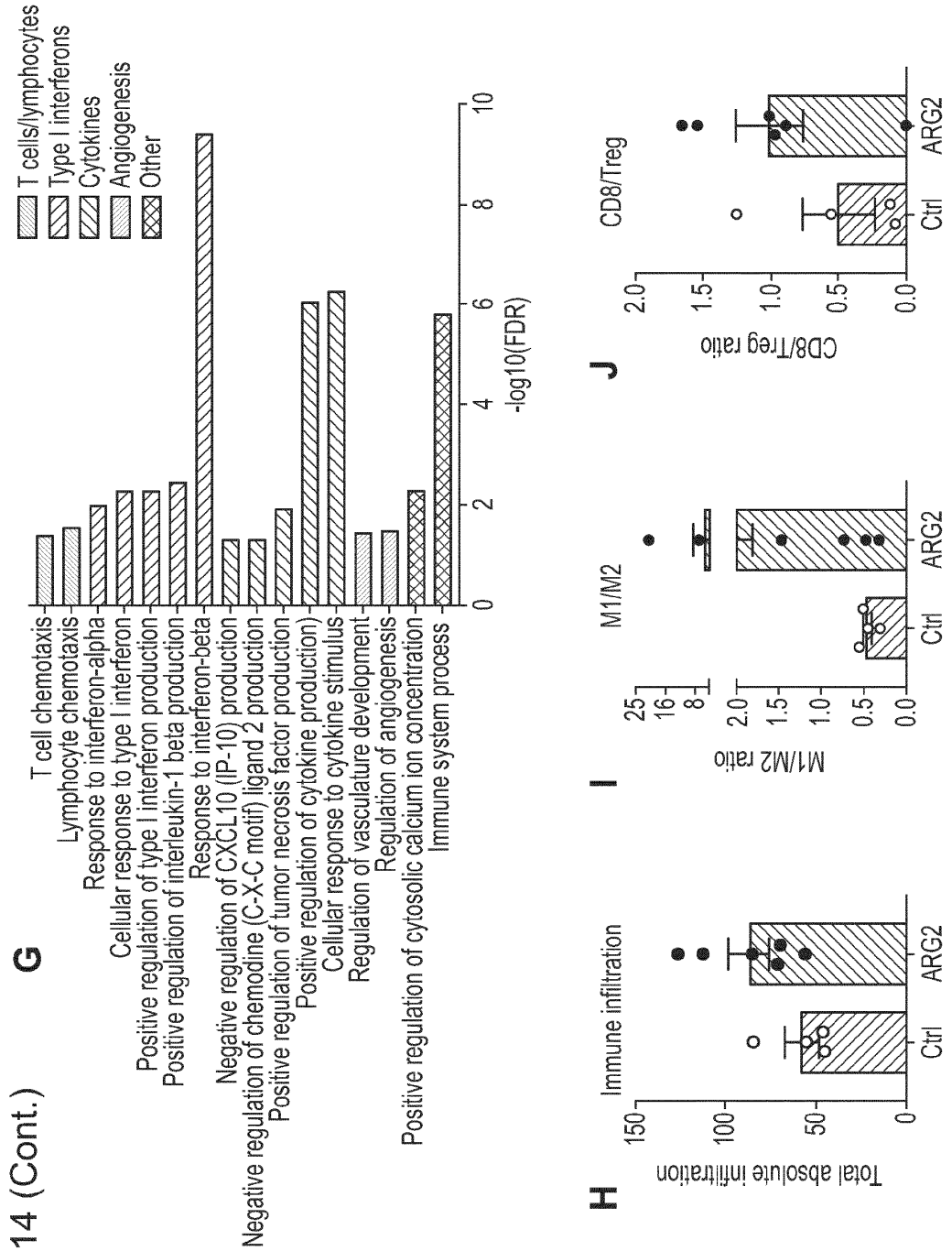


FIGURE 15

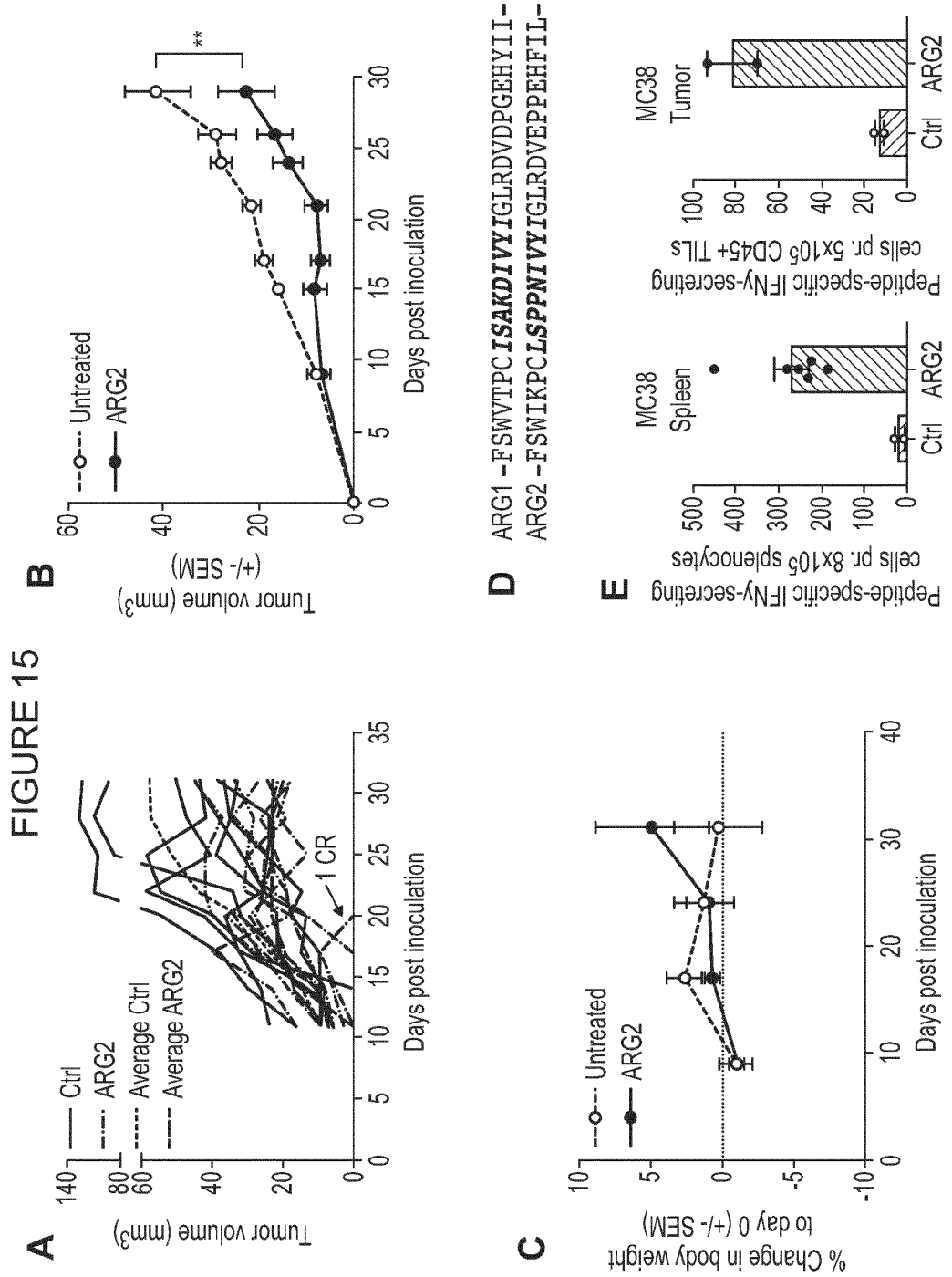

A
Tumor volume (mm3)
Ctrl
ARG2
Average Ctrl
Average ARG2
1 CR
Days post inoculation
B
Tumor volume (mm3) (+/- SEM)
Untreated
ARG2
**
Days post inoculation
C
% Change in body weight to day 0 (+/- SEM)
Untreated
ARG2
Days post inoculation
D
ARG1 -FSWVTPC*ISAKDIVYI*GLRDVDPGEHYII-
ARG2 -FSWIKPC*LSPPNIVYI*GLRDVEPPEHFIL-
E
Peptide-specific IFNγ-secreting cells pr. 8x10^5 splenocytes
MC38 Spleen
Ctrl
ARG2
Peptide-specific IFNγ-secreting cells pr. 5x10^5 CD45+ TILs
MC38 Tumor
Ctrl
ARG2

FIGURE 15 (Cont.)

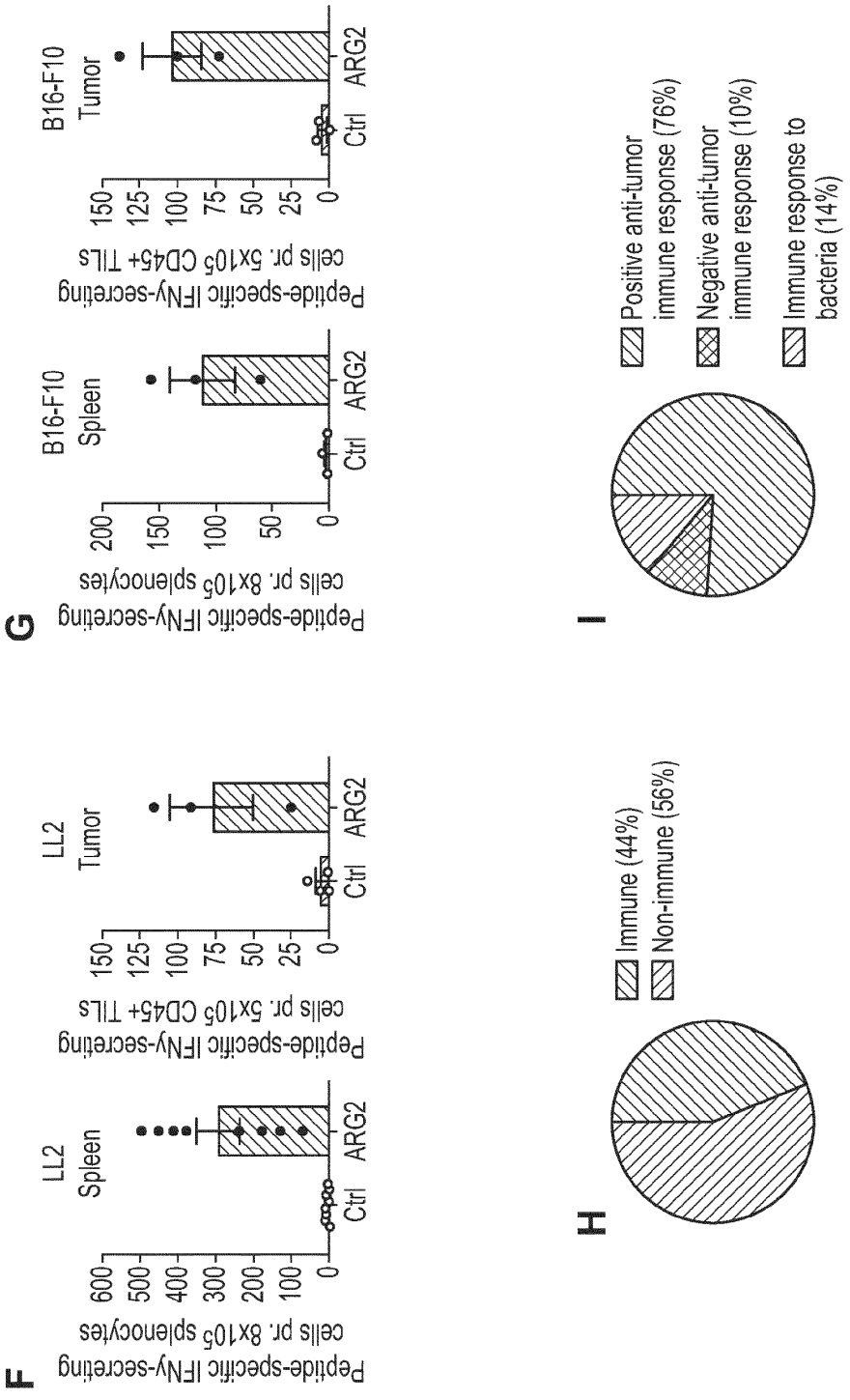


FIGURE 16

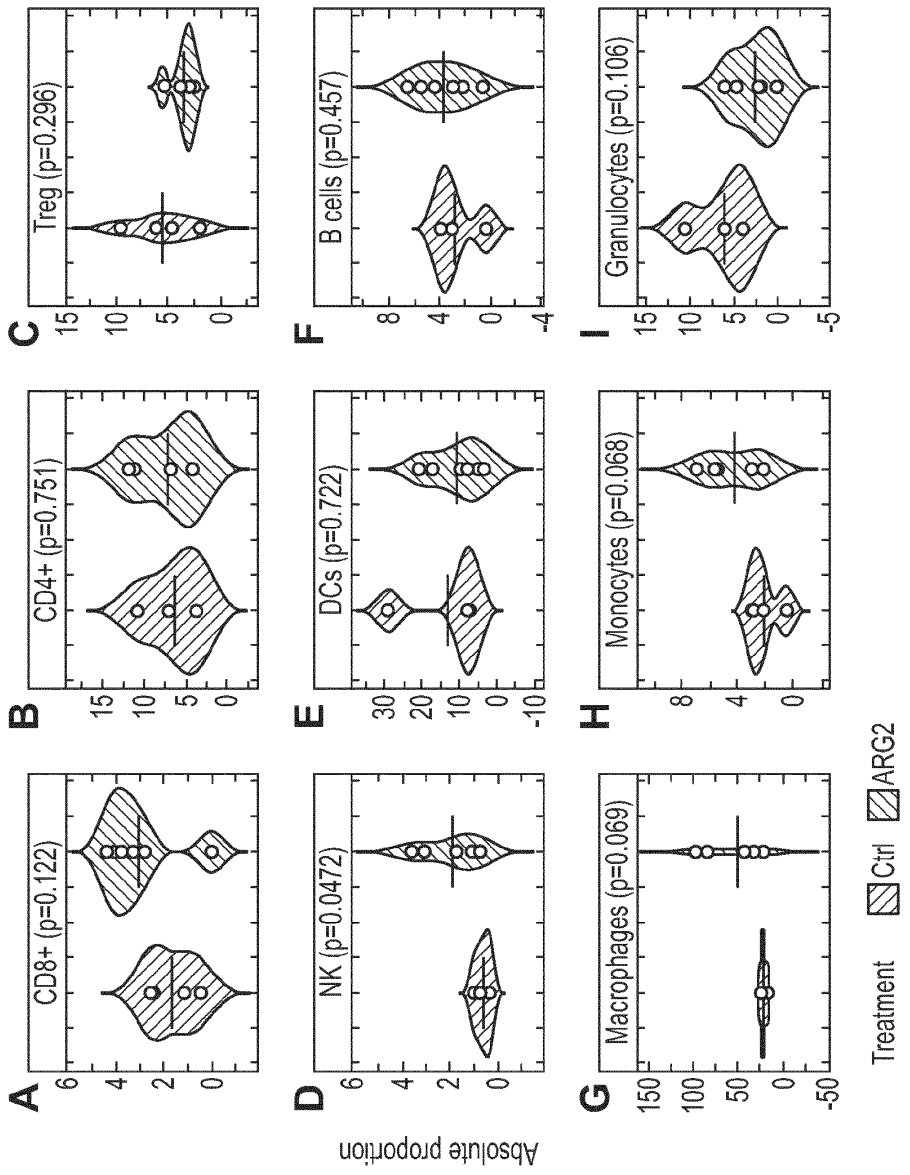

A
CD8+ (p=0.122)
B
CD4+ (p=0.751)
C
Treg (p=0.296)
D
NK (p=0.0472)
E
DCs (p=0.722)
F
B cells (p=0.457)
G
Macrophages (p=0.069)
H
Monocytes (p=0.068)
I
Granulocytes (p=0.106)
Absolute proportion
Treatment
Ctrl
ARG2

FIGURE 17

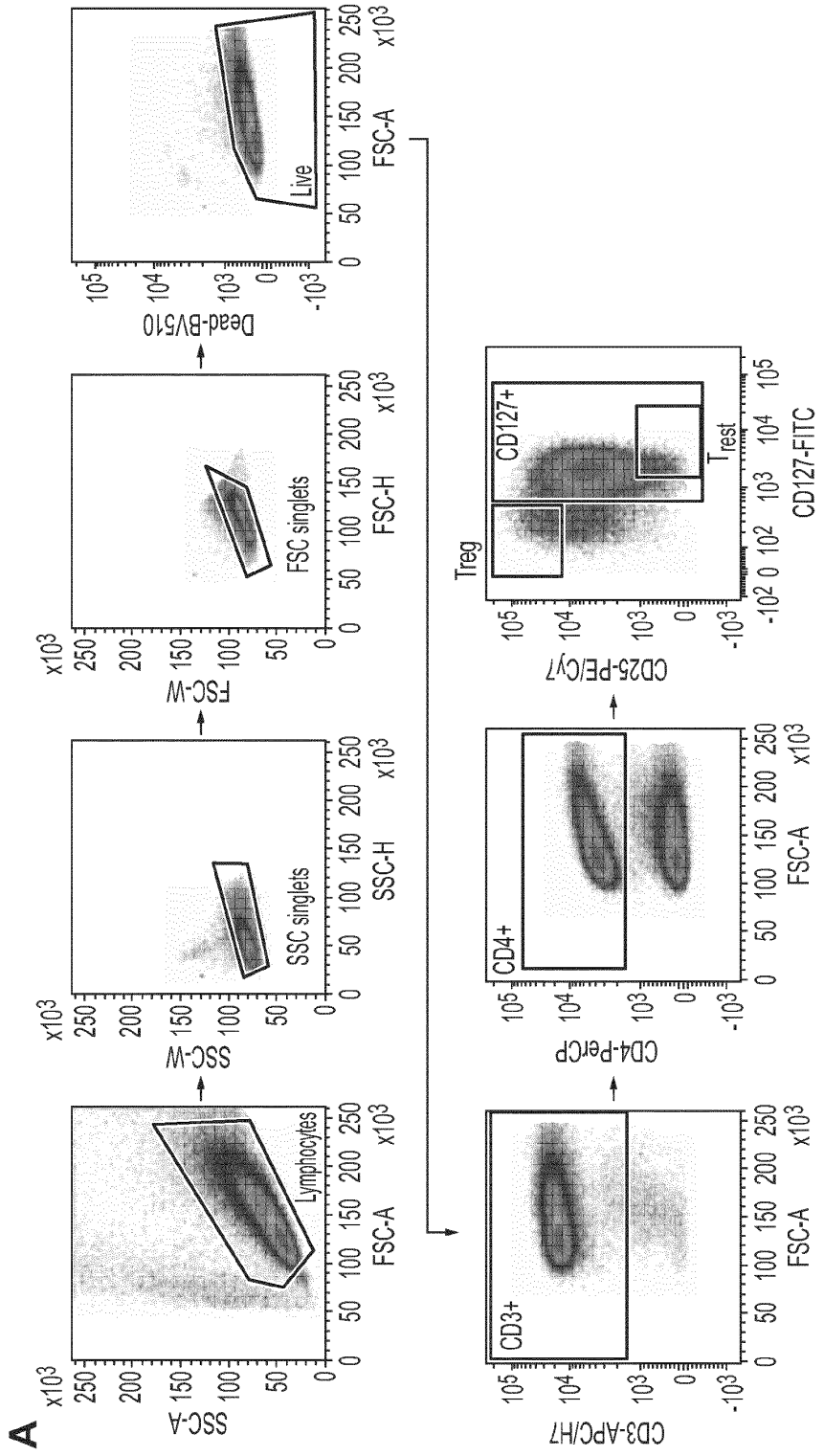

A
SSC-A
FSC-A
Lymphocytes
SSC-W
SSC-H
SSC singlets
FSC-W
FSC-H
FSC singlets
Dead-BV510
Live
CD3-APC/H7
CD3+
CD4-PerCP
CD4+
CD25-PE/Cy7
CD127-FITC
CD127+
Treg
Trest

FIGURE 17 (Cont.)

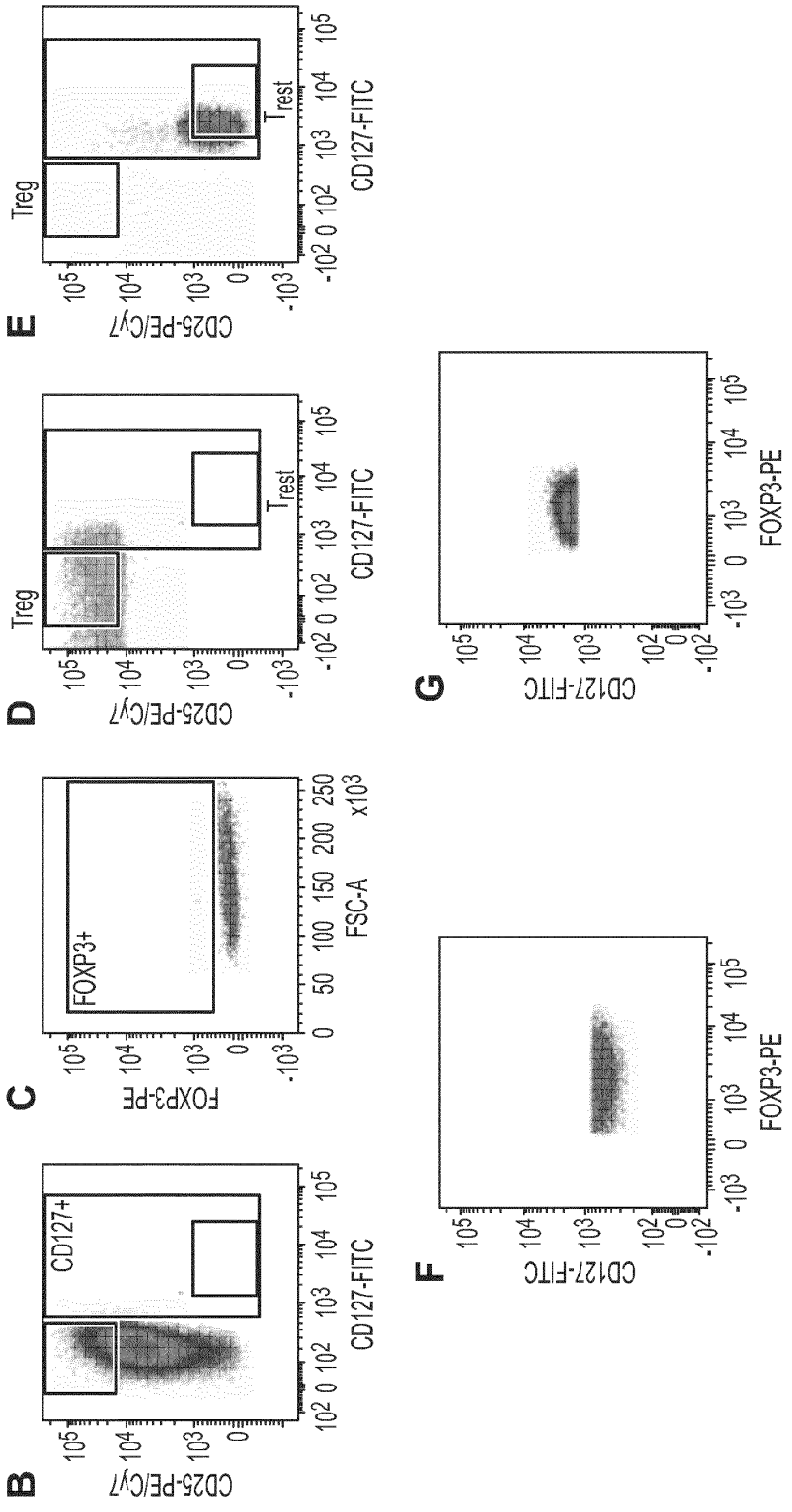


FIGURE 18. Differentially expressed genes (DEG) in Pan02 tumors from mice treated with ARG2 vaccine compared to mice that received a control vaccine (cut off p-adjusted value <0.05 and absolute log2 fold change >0)

DEG - UPREGULATED				DEG - DOWNREGULATED			
Nr.	Gene	Log2 fold change	FDR	Nr.	Gene	Log2 fold change	FDR
1	Foxo4	0.22	5.00E-02	1	Get4	-0.20	3.11E-02
2	Fam193b	0.28	2.19E-02	2	Sf1	-0.21	5.00E-02
3	Tmem126b	0.45	5.00E-02	3	Samm50	-0.22	3.90E-02
4	Deptor	0.50	6.57E-03	4	Snx4	-0.24	3.06E-02
5	Lipe	0.60	7.61E-05	5	Tent4a	-0.28	1.32E-02
6	Rn18s	0.60	3.20E-02	6	Pip5k1a	-0.32	4.55E-02
7	Zfp953	0.62	1.98E-02	7	Pphln1	-0.34	4.55E-02
8	Gpr146	0.65	3.12E-02	8	Rfc5	-0.36	5.00E-02
9	Slc2a4rg-ps	0.66	4.85E-02	9	Glce	-0.36	3.33E-02
10	Snta1	0.67	1.07E-02	10	Pcbp2	-0.38	2.07E-02
11	Txnip	0.68	4.81E-03	11	Rpl37	-0.38	4.81E-03
12	Gsn	0.72	3.73E-02	12	Tamm41	-0.40	2.03E-02
13	Kif9	0.75	5.00E-02	13	Rpl8	-0.41	3.97E-02
14	Gbp7	0.76	3.76E-02	14	Espl1	-0.42	8.41E-03
15	Tmod2	0.80	3.98E-02	15	Scaf11	-0.50	4.12E-02
16	Rcsd1	0.81	4.22E-02	16	Tubgcp2	-0.52	4.63E-02
17	Naaa	0.81	3.96E-02	17	Arv1	-0.52	2.96E-02
18	Nnmt	0.82	3.94E-02	18	Cks2	-0.59	3.78E-02
19	Gm4951	0.83	2.67E-02	19	Cep72	-0.61	2.96E-02
20	Esr1	0.85	3.31E-02	20	Micall2	-0.62	2.22E-02
21	Acad12	0.87	1.35E-02	21	Utp4	-0.63	2.71E-02
22	Clec2d	0.88	2.56E-02	22	Incenp	-0.63	3.98E-02
23	Iqgap2	0.89	3.96E-02	23	Neil3	-0.78	2.77E-02
24	Cep85l	0.90	2.75E-02	24	Inhba	-0.85	2.46E-02
25	Stard8	0.91	3.98E-02	25	Htr1b	-1.20	3.90E-02
26	Glul	0.91	4.39E-02	26	Egr1	-1.27	3.96E-02
27	mt-Tp	0.95	4.51E-02	27	5730471H19Rik	-1.32	2.03E-02
28	Lrg1	0.96	4.66E-02	28	Gemin4	-1.78	2.90E-02
29	Calml4	1.00	1.32E-02	29	Clstn2	-1.85	3.73E-02
30	Tsc22d3	1.00	5.00E-02	30	9130024F11Rik	-2.19	9.07E-03
31	Sord	1.03	3.96E-02	31	Gm46606	-2.81	4.25E-02
32	Rilp	1.03	4.29E-02	32	Gm17322	-3.14	3.31E-02
33	A4galt	1.05	4.87E-03	33	Gzmd	-3.42	1.65E-02
34	Arhgap26	1.06	4.49E-02				
35	Dnhd1	1.07	2.07E-02				
36	Mill2	1.10	3.90E-02				
37	Gm7694	1.14	2.34E-02				
38	Abcd2	1.14	1.79E-07				
39	Gmpr	1.14	5.00E-02				
40	Cysltr1	1.19	2.84E-02				
41	Ppp1r9a	1.19	2.44E-02				
42	Cyp4b1	1.19	7.31E-03				
43	Slc36a2	1.19	4.44E-02				
44	Lifr	1.21	2.30E-02				
45	Slc12a8	1.23	4.63E-02				
46	Ccr2	1.24	4.85E-02				
47	Nqo1	1.24	4.25E-02				
48	Cib2	1.24	8.06E-03				
49	Adm	1.26	2.46E-02				
50	Zfp760	1.26	3.31E-02				
51	Marchf1	1.26	2.71E-02				
52	Tmem38b	1.27	4.87E-03				
53	Fam124a	1.27	2.44E-02				
54	Susd3	1.27	5.00E-02				
55	Pgap6	1.28	4.76E-02				
56	Unc45b	1.29	4.74E-02				
57	Gm26740	1.29	3.83E-02				
58	Nhlrc1	1.29	5.00E-02				
59	Prtg	1.30	2.56E-02				
60	Cd1d1	1.33	2.52E-02				
61	Ak8	1.33	5.00E-02				
62	Kif19a	1.36	3.63E-03				

63	Prtn3	1.36	4.87E-02				
64	Reps2	1.36	6.71E-03				
65	Acyp2	1.36	3.73E-02				
66	Tslp	1.37	4.02E-02				
67	Rragd	1.37	4.14E-02				
68	A530010L16Rik	1.38	5.00E-02				
69	Dhdh	1.39	3.15E-02				
70	Sectm1a	1.40	9.07E-03				
71	Fam13a	1.40	4.81E-03				
72	Slc38a4	1.41	1.05E-02				
73	Slc43a3	1.41	3.42E-02				
74	Rnase6	1.42	2.44E-02				
75	Vegfd	1.42	4.27E-02				
76	Gbp2b	1.45	4.87E-03				
77	Gspt2	1.47	4.86E-02				
78	Wfdc17	1.49	5.00E-02				
79	Tnfsf10	1.49	4.03E-04				
80	Clec10a	1.49	2.67E-02				
81	Ms4a4d	1.50	2.22E-02				
82	Gm47754	1.54	4.53E-02				
83	Celf3	1.55	4.76E-02				
84	Peg10	1.56	2.90E-02				
85	Gm20522	1.56	1.19E-02				
86	Acsl1	1.57	3.71E-02				
87	Tmem255b	1.57	3.73E-02				
88	Gpc3	1.58	2.10E-02				
89	Prxl2b	1.59	4.36E-02				
90	Clip4	1.60	3.66E-02				
91	9330159M07Rik	1.60	2.44E-02				
92	Ggt5	1.60	5.01E-03				
93	Six1	1.67	4.22E-02				
94	Gfra2	1.72	2.13E-02				
95	Gm11131	1.72	4.29E-02				
96	Tppp3	1.73	3.96E-02				
97	2310040G24Rik	1.73	4.81E-03				
98	Chrdl1	1.73	3.66E-02				
99	Ephx2	1.74	8.14E-03				
100	Gm12185	1.74	2.30E-02				
101	Cyp2j9	1.74	4.19E-02				
102	Kcna6	1.75	2.44E-02				
103	Tmeff2	1.76	2.14E-02				
104	Vtn	1.76	2.10E-02				
105	Ackr1	1.77	3.40E-02				
106	Tek	1.78	2.26E-02				
107	Agtr1a	1.79	4.63E-02				
108	1600010M07Rik	1.79	3.80E-02				
109	Plekhb1	1.80	2.56E-02				
110	Adap2os	1.81	3.11E-02				
111	Slfn8	1.82	3.81E-02				
112	Col4a4	1.82	3.73E-02				
113	Ddx60	1.83	3.73E-02				
114	Oas1b	1.84	3.96E-02				
115	Gldc	1.85	2.03E-02				
116	Ifi207	1.86	3.80E-02				
117	A030001D20Rik	1.88	3.32E-02				
118	Slc10a6	1.89	1.49E-02				
119	Cd38	1.90	3.73E-02				
120	Lpar4	1.90	3.73E-02				
121	Cd34	1.91	4.41E-02				
122	Plpp3	1.92	3.80E-02				
123	Myoc	1.93	3.98E-02				
124	Lgi2	1.95	5.01E-04				
125	Hp	1.96	2.01E-04				
126	Ifit1	1.96	4.39E-02				
127	S100b	1.97	5.00E-02				
128	Thrsp	1.98	4.63E-02				
129	Ano3	1.98	2.25E-02				
130	Adamts5	2.00	3.94E-02				
131	Sptbn5	2.00	3.98E-02				

132	Pirb	2.01	4.92E-02				
133	Fgf10	2.01	1.35E-02				
134	BC064078	2.02	3.31E-02				
135	Slfn5	2.03	2.42E-02				
136	Lyz1	2.03	7.45E-03				
137	Clec4b1	2.04	3.06E-02				
138	Serpina3c	2.04	9.94E-04				
139	G0s2	2.05	4.81E-03				
140	Ppp1r3c	2.06	4.61E-03				
141	Enpep	2.07	1.04E-02				
142	Zbtb16	2.10	1.39E-03				
143	C4b	2.11	2.11E-02				
144	A530032D15Rik	2.13	1.65E-02				
145	Scn7a	2.13	5.27E-03				
146	Folr2	2.15	2.44E-02				
147	Arhgap20	2.17	7.94E-03				
148	Lrrc18	2.17	7.45E-03				
149	Tril	2.18	2.44E-02				
150	Hcar1	2.18	2.64E-02				
151	Kcna2	2.19	4.41E-02				
152	BC023105	2.19	4.81E-02				
153	Ms4a8a	2.19	6.57E-03				
154	Ifi205	2.20	1.71E-02				
155	Gm16026	2.22	4.46E-02				
156	Cmah	2.23	8.04E-03				
157	Rbp4	2.25	6.57E-03				
158	Pnp2	2.26	4.27E-02				
159	Entpd2	2.26	9.50E-03				
160	Usp18	2.26	4.53E-02				
161	Ebf2	2.30	3.55E-02				
162	Ccl9	2.30	3.96E-02				
163	Gm5431	2.31	2.13E-02				
164	Mx2	2.33	2.67E-02				
165	Cd55	2.33	5.00E-02				
166	Fgf9	2.34	2.67E-02				
167	Dhx58	2.36	4.25E-02				
168	Lyve1	2.38	1.03E-02				
169	Rnf165	2.39	3.36E-02				
170	H2-T24	2.39	3.98E-02				
171	Myrip	2.40	2.56E-02				
172	Gpr88	2.40	3.31E-02				
173	Vat1l	2.40	3.32E-02				
174	Slc28a2	2.41	3.90E-02				
175	Plagl1	2.41	3.73E-02				
176	Gabre	2.42	3.96E-02				
177	Ifi203-ps	2.44	2.64E-02				
178	Cxcl12	2.44	3.32E-02				
179	Vit	2.45	1.04E-05				
180	Papln	2.45	2.30E-02				
181	Slc4a4	2.46	6.44E-03				
182	Ifit3b	2.47	3.19E-02				
183	Sfrp4	2.47	1.65E-02				
184	Cadm3	2.47	4.87E-03				
185	Fabp4	2.48	8.75E-07				
186	H2bu2	2.48	2.90E-02				
187	Ifi204	2.49	2.97E-02				
188	Oas1a	2.49	2.57E-02				
189	Phf11b	2.52	3.60E-02				
190	Osr1	2.54	9.50E-03				
191	Steap4	2.54	2.48E-03				
192	Gm36161	2.56	4.02E-02				
193	Aldh1a1	2.56	4.03E-04				
194	Cadps2	2.56	2.34E-02				
195	Adgrg2	2.59	2.67E-02				
196	G530011O06Rik	2.61	9.11E-03				
197	Ifi209	2.63	3.60E-02				
198	Oas2	2.64	1.64E-02				
199	C1s2	2.66	4.63E-02				
200	Tnxb	2.67	3.83E-02				

201	Ifitm6	2.68	4.86E-03				
202	Gm14461	2.69	3.76E-02				
203	Efhd1	2.70	3.98E-02				
204	Oxtr	2.70	1.86E-02				
205	Adgre4	2.71	3.05E-02				
206	Arhgef37	2.72	3.96E-02				
207	Ccn3	2.73	4.22E-02				
208	Cldn19	2.74	2.90E-02				
209	Cfb	2.74	3.30E-02				
210	Kcna1	2.75	1.53E-02				
211	Mab21l1	2.77	3.31E-02				
212	Barx2	2.79	4.22E-02				
213	Ccl3	2.81	4.78E-02				
214	Isg15	2.83	4.06E-02				
215	Trim30c	2.83	1.65E-02				
216	Pwwp3b	2.83	3.83E-02				
217	Plac9a	2.84	3.63E-03				
218	Otof	2.88	2.30E-02				
219	BC147527	2.88	7.14E-03				
220	Ifi44	2.89	6.44E-03				
221	Oas1g	2.92	2.50E-02				
222	C7	2.93	7.90E-04				
223	Ptx3	2.94	3.01E-02				
224	Mpz	2.97	6.57E-03				
225	Fgf16	2.98	3.66E-02				
226	Mx1	3.06	2.03E-02				
227	Opcml	3.06	2.07E-02				
228	A530020G20Rik	3.07	3.05E-02				
229	Saa3	3.15	3.73E-02				
230	Spta1	3.17	2.84E-02				
231	Gm47445	3.17	4.92E-02				
232	Aass	3.18	1.05E-02				
233	Gdf10	3.18	5.27E-03				
234	Oas3	3.20	2.56E-02				
235	Gzma	3.20	4.57E-02				
236	Lmx1a	3.20	4.29E-02				
237	Gm15675	3.21	2.81E-02				
238	Gabra3	3.24	1.56E-03				
239	1700019D03Rik	3.26	1.56E-02				
240	Gm49839	3.28	4.69E-02				
241	Chga	3.31	2.33E-02				
242	Ifi27l2a	3.32	4.81E-03				
243	Ptchd1	3.33	4.76E-02				
244	Cmpk2	3.37	1.05E-02				
245	Cd36	3.37	2.56E-02				
246	Ifi208	3.38	8.49E-03				
247	Phf11a	3.43	1.93E-02				
248	Pex5l	3.50	4.87E-03				
249	Irf7	3.53	1.42E-02				
250	Hsd17b14	3.54	7.45E-03				
251	A130071D04Rik	3.55	3.86E-02				
252	Gdf3	3.59	3.96E-02				
253	Agtr2	3.60	3.63E-03				
254	5330406M23Rik	3.63	3.96E-02				
255	Ifi206	3.64	6.57E-03				
256	Ifi213	3.69	8.96E-03				
257	Nrk	3.73	2.10E-02				
258	Gm43775	3.88	3.66E-02				
259	Rsad2	3.89	1.31E-02				
260	Ppp2r2b	3.90	3.96E-02				
261	Ugt8a	3.96	3.96E-02				
262	Clec3b	3.97	1.89E-03				
263	Ighv5-17	4.15	3.78E-02				
264	Cd5l	4.15	1.56E-02				
265	Hspd1-ps4	4.15	3.26E-02				
266	Lpl	4.17	4.87E-03				
267	Ly6i	4.20	4.81E-02				
268	Ms4a4c	4.33	1.07E-02				
269	Ly6c2	4.34	1.32E-02				

270	Rhov	4.40	2.90E-02				
271	Neto1	4.50	2.46E-02				
272	Slfn4	4.58	2.84E-02				
273	Rtl3	4.86	1.50E-03				
274	Igkv6-17	5.00	2.84E-02				
275	Gm6545	5.12	6.71E-03				
276	Gm12796	5.19	1.32E-02				
277	Ankdd1a	5.26	3.36E-02				
278	Igkv4-68	5.41	3.80E-02				
279	Gm17749	5.78	2.28E-02				
280	Igkv19-93	5.87	2.67E-02				
281	Npy	6.31	2.85E-02				
282	Gm15056	6.55	3.31E-02				

FIGURE 19. Gene ontology analysis for biological processes associated with differentially upregulated genes between Pan02 tumors from mice that were treated with ARG2 vaccine compared to mice that received a control vaccine.

GO BIOLOGICAL PROCESSES ASSOCIATED WITH THE DIFFERENTIALLY UPREGULATED GENES (FDR<0.05)
Each process is classified as immune-related (1) or non-immune related (0) in column "Immune related (0/1)"

GO biological process complete	Mus musculus - REFLIST (21997)	upload_1 (50)	upload_1 (expected)	upload_1 (over/under)	upload_1 (fold Enrichment)	upload_1 (raw P-value)	upload_1 (FDR)	Immune related (0/1)
response to interferon-beta (GO:0035456)	64	14	0.72	+	19.47	1.64E-13	3.69E-10	1
cellular response to interferon-beta (GO:0035458)	56	13	0.63	+	20.67	6.37E-13	1.11E-09	1
cellular response to cytokine stimulus (GO:0071345)	690	30	7.75	+	3.87	5.39E-10	5.00E-07	1
response to cytokine (GO:0034097)	792	32	8.9	+	3.6	7.85E-10	6.51E-07	1
positive regulation of cytokine production (GO:0001819)	499	25	5.61	+	4.46	1.08E-09	8.53E-07	1
immune system process (GO:0002376)	2494	62	28.02	+	2.21	2.17E-09	1.56E-06	1
regulation of cytokine production (GO:0001817)	773	30	8.68	+	3.45	6.77E-09	4.45E-06	1
immune response (GO:0006955)	1614	45	18.13	+	2.48	2.42E-08	1.36E-05	1
regulation of immune system process (GO:0002682)	1637	41	18.39	+	2.23	2.24E-06	8.61E-04	1
positive regulation of interferon-beta production (GO:0032728)	48	7	0.54	+	12.98	2.47E-06	9.27E-04	1
response to type I interferon (GO:0034340)	34	6	0.38	+	15.71	4.95E-06	1.77E-03	1
positive regulation of interleukin-1 beta production (GO:0032731)	62	7	0.7	+	10.05	1.15E-05	3.36E-03	1
positive regulation of type I interferon production (GO:0032481)	68	7	0.76	+	9.16	2.00E-05	4.85E-03	1
cytokine-mediated signaling pathway (GO:0019221)	312	14	3.5	+	3.99	1.86E-05	4.88E-03	1
positive regulation of cytosolic calcium ion concentration (GO:0007204)	313	14	3.52	+	3.98	1.92E-05	4.88E-03	1
cellular response to type I interferon (GO:0071357)	25	5	0.28	+	17.8	1.84E-05	4.93E-03	1
type I interferon signaling pathway (GO:0060337)	25	5	0.28	+	17.8	1.84E-05	5.01E-03	1
regulation of interferon-beta production (GO:0032648)	67	7	0.75	+	9.3	1.83E-05	5.06E-03	1
regulation of innate immune response (GO:0045088)	237	12	2.66	+	4.51	2.41E-05	5.75E-03	1
positive regulation of immune system process (GO:0002684)	1094	29	12.29	+	2.36	2.45E-05	5.75E-03	1
innate immune response (GO:0045087)	875	25	9.83	+	2.54	2.57E-05	5.96E-03	1
regulation of immune response (GO:0050776)	1051	28	11.81	+	2.37	3.24E-05	7.30E-03	1
positive regulation of interleukin-1 production (GO:0032732)	74	7	0.83	+	8.42	3.31E-05	7.36E-03	1
response to interferon-alpha (GO:0035455)	31	5	0.35	+	14.36	4.62E-05	9.98E-03	1
positive regulation of tumor necrosis factor production (GO:0032760)	109	8	1.22	+	6.53	4.98E-05	1.06E-02	1
positive regulation of tumor necrosis factor superfamily cytokine production	111	8	1.25	+	6.42	5.62E-05	1.15E-02	1
regulation of tumor necrosis factor production (GO:0032680)	184	10	2.07	+	4.84	6.58E-05	1.31E-02	1
regulation of tumor necrosis factor superfamily cytokine production	187	10	2.1	+	4.76	7.48E-05	1.46E-02	1
regulation of vasoconstriction (GO:0019229)	86	7	0.97	+	7.25	8.06E-05	1.55E-02	1
cellular response to interferon-alpha (GO:0035457)	19	4	0.21	+	18.74	1.11E-04	2.00E-02	1
regulation of interleukin-1 beta production (GO:0032651)	96	7	1.08	+	6.49	1.54E-04	2.63E-02	1
lymphocyte chemotaxis (GO:0048247)	42	5	0.47	+	10.6	1.70E-04	2.86E-02	1
regulation of type I interferon-mediated signaling pathway (GO:0060338)	42	5	0.47	+	10.6	1.70E-04	2.89E-02	1
regulation of angiogenesis (GO:0045765)	299	12	3.36	+	3.57	2.00E-04	3.22E-02	1
regulation of vasculature development (GO:1901342)	303	12	3.4	+	3.53	2.25E-04	3.52E-02	1
regulation of type I interferon production (GO:0032479)	103	7	1.16	+	6.05	2.31E-04	3.53E-02	1
T cell chemotaxis (GO:0010818)	9	3	0.1	+	29.67	2.77E-04	3.96E-02	1
negative regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000342)	10	3	0.11	+	26.71	3.57E-04	4.85E-02	1
negative regulation of IP-10 production (GO:0071659)	10	3	0.11	+	26.71	3.57E-04	4.89E-02	1
negative regulation of innate immune response (GO:0045824)	84	9	0.94	+	9.54	9.51E-07	4.05E-04	1
negative regulation of immune response (GO:0050777)	188	12	2.11	+	5.68	2.62E-06	9.60E-04	1
negative regulation of defense response (GO:0031348)	238	11	2.67	+	4.11	1.14E-04	2.02E-02	1
negative regulation of immune system process (GO:0002683)	448	15	5.03	+	2.98	2.26E-04	3.49E-02	1
negative regulation of type I interferon-mediated signaling pathway (GO:0060339)	24	4	0.27	+	14.84	2.47E-04	3.70E-02	1
defense response to virus (GO:0051607)	226	21	2.54	+	8.27	6.04E-13	1.19E-09	1
response to virus (GO:0009615)	287	22	3.22	+	6.82	5.87E-12	7.71E-09	1
response to bacterium (GO:0009617)	896	36	10.07	+	3.58	7.04E-11	7.93E-08	1
negative regulation of viral process (GO:0048525)	102	13	1.15	+	11.35	5.12E-10	5.05E-07	1
regulation of viral life cycle (GO:1903900)	143	14	1.61	+	8.72	2.57E-09	1.76E-06	1
regulation of viral genome replication (GO:0045069)	87	11	0.98	+	11.26	1.22E-08	7.68E-06	1
regulation of viral process (GO:0050792)	166	14	1.86	+	7.51	1.50E-08	9.12E-06	1
response to external biotic stimulus (GO:0043207)	1490	59	16.74	+	3.52	2.76E-17	1.45E-13	0

response to other organism (GO:0051707)	1488	59	16.72	+	3.53	2.60E-17	2.05E-13	0
biological process involved in interspecies interaction between organisms	1624	61	18.24	+	3.34	7.75E-17	3.06E-13	0
response to biotic stimulus (GO:0009607)	1529	60	17.18	+	3.49	2.08E-17	3.28E-13	0
response to external stimulus (GO:0009605)	2452	76	27.54	+	2.76	1.40E-16	4.40E-13	0
defense response (GO:0006952)	1493	57	16.77	+	3.4	5.19E-16	1.36E-12	0
defense response to symbiont (GO:0140546)	227	21	2.55	+	8.24	6.54E-13	1.03E-09	0
response to stimulus (GO:0050896)	8671	153	97.4	+	1.57	1.78E-12	2.54E-09	0
defense response to other organism (GO:0098542)	1119	42	12.57	+	3.34	1.19E-11	1.44E-08	0
negative regulation of viral genome replication (GO:0045071)	59	11	0.66	+	16.6	3.09E-10	3.25E-07	0
response to stress (GO:0006950)	3303	76	37.1	+	2.05	5.51E-10	4.82E-07	0
regulation of multicellular organismal process (GO:0051239)	2900	69	32.58	+	2.12	1.22E-09	9.16E-07	0
response to organic substance (GO:0010033)	2608	62	29.3	+	2.12	1.63E-08	9.51E-06	0
cellular response to chemical stimulus (GO:0070887)	2473	59	27.78	+	2.12	2.60E-08	1.41E-05	0
positive regulation of gene expression (GO:0010628)	1203	37	13.51	+	2.74	4.07E-08	2.14E-05	0
response to chemical (GO:0042221)	3577	75	40.18	+	1.87	5.13E-08	2.61E-05	0
cellular response to organic substance (GO:0071310)	1866	48	20.96	+	2.29	7.46E-08	3.67E-05	0
positive regulation of multicellular organismal process (GO:0051240)	1639	44	18.41	+	2.39	8.82E-08	4.21E-05	0
positive regulation of biological process (GO:0048518)	6454	110	72.5	+	1.52	5.19E-07	2.34E-04	0
positive regulation of response to stimulus (GO:0048584)	2367	54	26.59	+	2.03	5.08E-07	2.35E-04	0
regulation of response to external stimulus (GO:0032101)	967	30	10.86	+	2.76	7.50E-07	3.28E-04	0
regulation of nuclease activity (GO:0032069)	27	6	0.3	+	19.78	1.52E-06	6.16E-04	0
positive regulation of response to external stimulus (GO:0032103)	452	19	5.08	+	3.74	1.50E-06	6.21E-04	0
regulation of ribonuclease activity (GO:0060700)	15	5	0.17	+	29.67	2.20E-06	8.66E-04	0
positive regulation of cell communication (GO:0010647)	1764	42	19.82	+	2.12	5.21E-06	1.83E-03	0
sensory perception of smell (GO:0007608)	1124	0	12.63	-	< 0,01	5.51E-06	1.85E-03	0
positive regulation of signaling (GO:0023056)	1771	42	19.89	+	2.11	5.49E-06	1.88E-03	0
ion homeostasis (GO:0050801)	809	25	9.09	+	2.75	7.15E-06	2.35E-03	0
chemical homeostasis (GO:0048878)	1201	32	13.49	+	2.37	7.87E-06	2.48E-03	0
inorganic ion homeostasis (GO:0098771)	760	24	8.54	+	2.81	7.77E-06	2.50E-03	0
positive regulation of cellular process (GO:0048522)	5933	99	66.65	+	1.49	9.84E-06	3.04E-03	0
cellular macromolecule metabolic process (GO:0044260)	4105	21	46.11	-	0.46	1.12E-05	3.33E-03	0
metal ion homeostasis (GO:0055065)	672	22	7.55	+	2.91	1.10E-05	3.34E-03	0
negative regulation of response to biotic stimulus (GO:0002832)	117	9	1.31	+	6.85	1.19E-05	3.40E-03	0
regulation of response to stimulus (GO:0048583)	4055	74	45.55	+	1.62	1.56E-05	4.38E-03	0
regulation of cytosolic calcium ion concentration (GO:0051480)	357	15	4.01	+	3.74	1.96E-05	4.82E-03	0
cation homeostasis (GO:0055080)	751	23	8.44	+	2.73	1.94E-05	4.85E-03	0
homeostatic process (GO:0042592)	1680	39	18.87	+	2.07	1.91E-05	4.94E-03	0
sensory perception of chemical stimulus (GO:0007606)	1224	1	13.75	-	0.07	2.85E-05	6.51E-03	0
regulation of defense response (GO:0031347)	627	20	7.04	+	2.84	3.99E-05	8.74E-03	0
regulation of cellular response to growth factor stimulus (GO:0090287)	299	13	3.36	+	3.87	5.04E-05	1.06E-02	0
regulation of biological quality (GO:0065008)	3901	70	43.82	+	1.6	5.22E-05	1.08E-02	0
regulation of cold-induced thermogenesis (GO:0120161)	146	9	1.64	+	5.49	6.12E-05	1.24E-02	0
cell surface receptor signaling pathway (GO:0007166)	1967	42	22.1	+	1.9	7.21E-05	1.42E-02	0
positive regulation of metabolic process (GO:0009893)	3772	67	42.37	+	1.58	9.07E-05	1.72E-02	0

regulation of response to biotic stimulus (GO:0002831)	364	14	4.09	+	3.42	9.22E-05	1.73E-02	0
positive regulation of signal transduction (GO:0009967)	1555	35	17.47	+	2	9.54E-05	1.77E-02	0
defense response to bacterium (GO:0042742)	513	17	5.76	+	2.95	9.80E-05	1.80E-02	0
cellular protein metabolic process (GO:0044267)	2999	14	33.69	-	0.42	1.08E-04	1.95E-02	0
cellular calcium ion homeostasis (GO:0006874)	470	16	5.28	+	3.03	1.17E-04	2.04E-02	0
divalent inorganic cation homeostasis (GO:0072507)	531	17	5.96	+	2.85	1.46E-04	2.53E-02	0
positive regulation of cold-induced thermogenesis (GO:0120162)	98	7	1.1	+	6.36	1.73E-04	2.87E-02	0
cellular metal ion homeostasis (GO:0006875)	596	18	6.7	+	2.69	1.88E-04	3.09E-02	0
regulation of transmembrane receptor protein serine/threonine kinase signaling	254	11	2.85	+	3.86	1.97E-04	3.20E-02	0
cellular divalent inorganic cation homeostasis (GO:0072503)	495	16	5.56	+	2.88	2.06E-04	3.28E-02	0
calcium ion homeostasis (GO:0055074)	498	16	5.59	+	2.86	2.20E-04	3.47E-02	0
triglyceride metabolic process (GO:0006641)	72	6	0.81	+	7.42	2.33E-04	3.53E-02	0
regulation of morphogenesis of an epithelium (GO:1905330)	73	6	0.82	+	7.32	2.50E-04	3.61E-02	0
nucleic acid metabolic process (GO:0090304)	1804	6	20.27	-	0.3	2.49E-04	3.64E-02	0
cellular cation homeostasis (GO:0030003)	665	19	7.47	+	2.54	2.47E-04	3.64E-02	0
regulation of anatomical structure size (GO:0090066)	556	17	6.25	+	2.72	2.47E-04	3.67E-02	0
macromolecule metabolic process (GO:0043170)	5553	38	62.38	-	0.61	2.80E-04	3.97E-02	0
positive regulation of cell population proliferation (GO:0008284)	1005	25	11.29	+	2.21	3.18E-04	4.47E-02	0
cellular ion homeostasis (GO:0006873)	681	19	7.65	+	2.48	3.30E-04	4.60E-02	0
fatty acid metabolic process (GO:0006631)	366	13	4.11	+	3.16	3.44E-04	4.76E-02	0
regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000341)	27	4	0.3	+	13.19	3.69E-04	4.98E-02	0

IMMUNE-RELATED GO BIOLOGICAL PROCESSES ASSOCIATED WITH THE DIFFERENTIALLY UPREGULATED GENES (FDR<0.05)
Immune-related processes are classified into categories.

GO biological process complete	Category	Selected for representation (figure 14)	upload_1 (FDR)
positive regulation of cytosolic calcium ion concentration (GO:0007204)	Ca2+ immune activation	X	4.88E-03
lymphocyte chemotaxis (GO:0048247)	T cells/lymphocytes	X	2.86E-02
T cell chemotaxis (GO:0010818)	T cells/lymphocytes	X	3.96E-02
cellular response to cytokine stimulus (GO:0071345)	Cytokines	X	5.00E-07
response to cytokine (GO:0034097)	Cytokines		6.51E-07
positive regulation of cytokine production (GO:0001819)	Cytokines	X	8.53E-07
regulation of cytokine production (GO:0001817)	Cytokines		4.45E-06
cytokine-mediated signaling pathway (GO:0019221)	Cytokines		4.88E-03
negative regulation of chemokine (C-X-C motif) ligand 2 production (GO:2000342)	Cytokines	X	4.85E-02
negative regulation of CXCL10 (IP-10) production (GO:0071659)	Cytokines	X	4.89E-02
positive regulation of tumor necrosis factor production (GO:0032760)	Cytokines		1.06E-02
positive regulation of tumor necrosis factor superfamily cytokine production (GO:1903557)	Cytokines	X	1.15E-02
regulation of tumor necrosis factor production (GO:0032680)	Cytokines		1.31E-02
regulation of tumor necrosis factor superfamily cytokine production (GO:1903555)	Cytokines		1.46E-02
response to interferon-beta (GO:0035456)	Type I interferons	X	3.69E-10
cellular response to interferon-beta (GO:0035458)	Type I interferons		1.11E-09
positive regulation of interferon-beta production (GO:0032728)	Type I interferons		9.27E-04
response to type I interferon (GO:0034340)	Type I interferons		1.77E-03
positive regulation of type I interferon production (GO:0032481)	Type I interferons	X	4.85E-03
cellular response to type I interferon (GO:0071357)	Type I interferons	X	4.93E-03
type I interferon signaling pathway (GO:0060337)	Type I interferons		5.01E-03
regulation of interferon-beta production (GO:0032648)	Type I interferons		5.06E-03
response to interferon-alpha (GO:0035455)	Type I interferons	X	9.98E-03
cellular response to interferon-alpha (GO:0035457)	Type I interferons		2.00E-02
regulation of type I interferon-mediated signaling pathway (GO:0060338)	Type I interferons		2.89E-02
regulation of type I interferon production (GO:0032479)	Type I interferons		3.53E-02
positive regulation of interleukin-1 beta production (GO:0032731)	IL-1		3.36E-03
positive regulation of interleukin-1 production (GO:0032732)	IL-1	X	7.36E-03
regulation of interleukin-1 beta production (GO:0032651)	IL-1		2.63E-02
immune system process (GO:0002376)	General immune response	X	1.56E-06
immune response (GO:0006955)	General immune response		1.36E-05
regulation of immune system process (GO:0002682)	General immune response		8.61E-04
regulation of innate immune response (GO:0045088)	General immune response		5.75E-03
positive regulation of immune system process (GO:0002684)	General immune response		5.75E-03
innate immune response (GO:0045087)	General immune response		5.96E-03
regulation of immune response (GO:0050776)	General immune response		7.30E-03
regulation of vasoconstriction (GO:0019229)	Angiogenesis		1.55E-02
regulation of angiogenesis (GO:0045765)	Angiogenesis	X	3.22E-02
regulation of vasculature development (GO:1901342)	Angiogenesis	X	3.52E-02