Figure 1

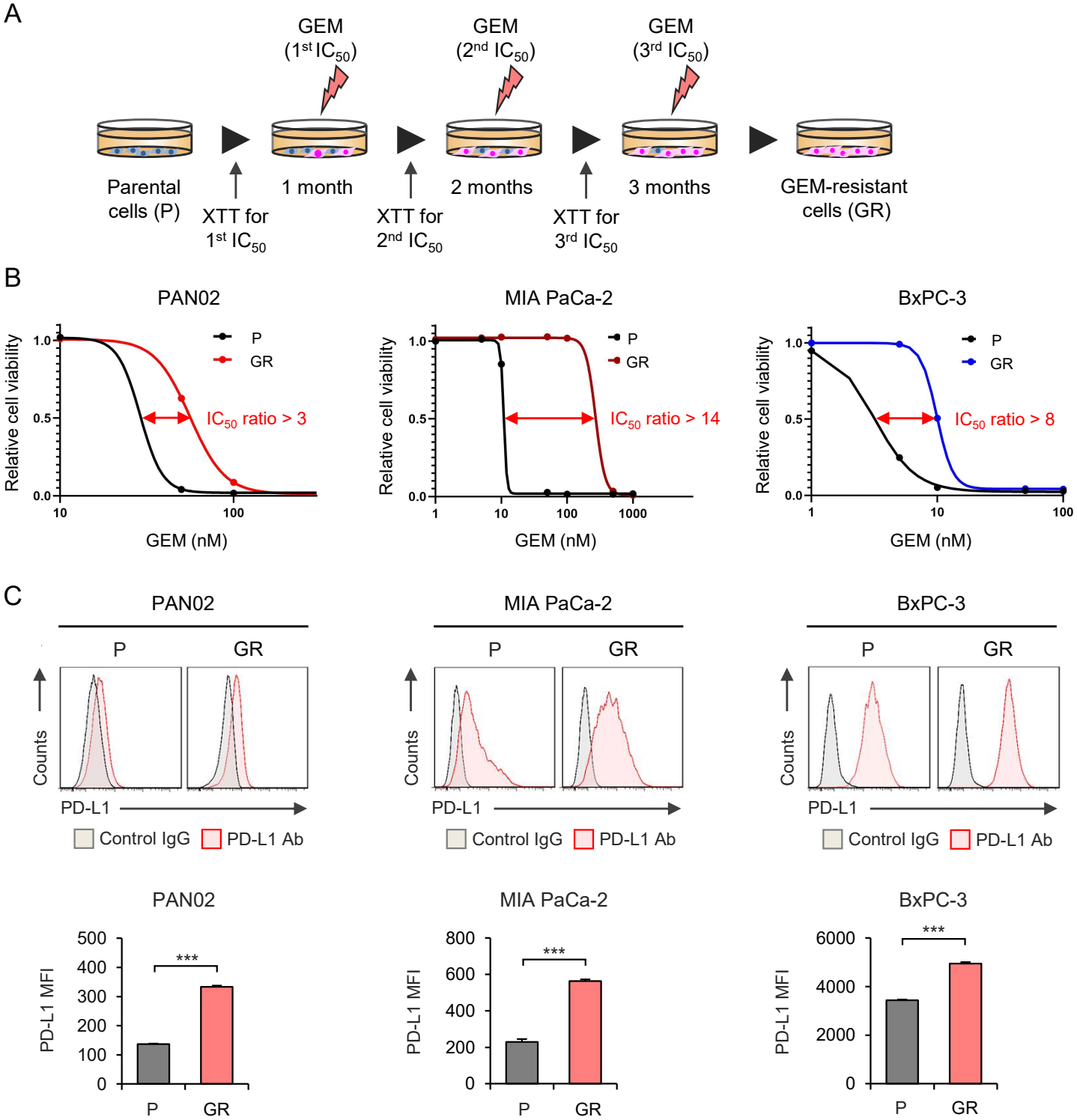

A
GEM (1st IC50)
GEM (2nd IC50)
GEM (3rd IC50)
Parental cells (P)
XTT for 1st IC50
1 month
XTT for 2nd IC50
2 months
XTT for 3rd IC50
3 months
GEM-resistant cells (GR)
B
PAN02
MIA PaCa-2
BxPC-3
Relative cell viability
P
GR
IC50 ratio > 3
IC50 ratio > 14
IC50 ratio > 8
GEM (nM)
C
Counts
PD-L1
Control IgG
PD-L1 Ab
PD-L1 MFI
***

Figure 2

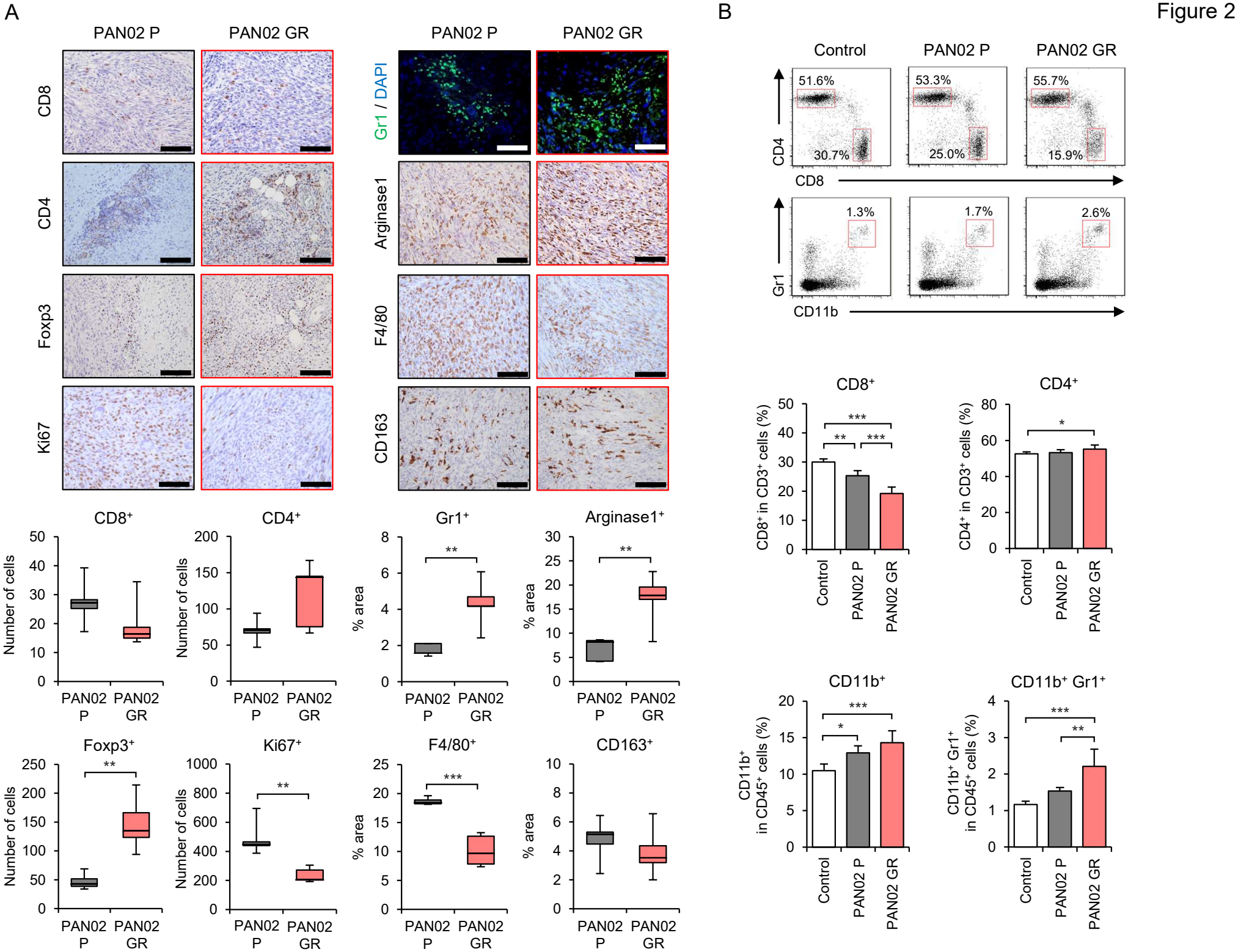

A
PAN02 P
PAN02 GR
CD8
CD4
Foxp3
Ki67
Gr1 / DAPI
Arginase1
F4/80
CD163
CD8+
CD4+
Gr1+
Arginase1+
Foxp3+
Ki67+
F4/80+
CD163+
Number of cells
% area
PAN02 P
PAN02 GR
B
Control
PAN02 P
PAN02 GR
51.6%
30.7%
53.3%
25.0%
55.7%
15.9%
CD4
CD8
1.3%
1.7%
2.6%
Gr1
CD11b
CD8+ in CD3+ cells (%)
CD4+ in CD3+ cells (%)
CD11b+ in CD45+ cells (%)
CD11b+ Gr1+ in CD45+ cells (%)

Figure 3

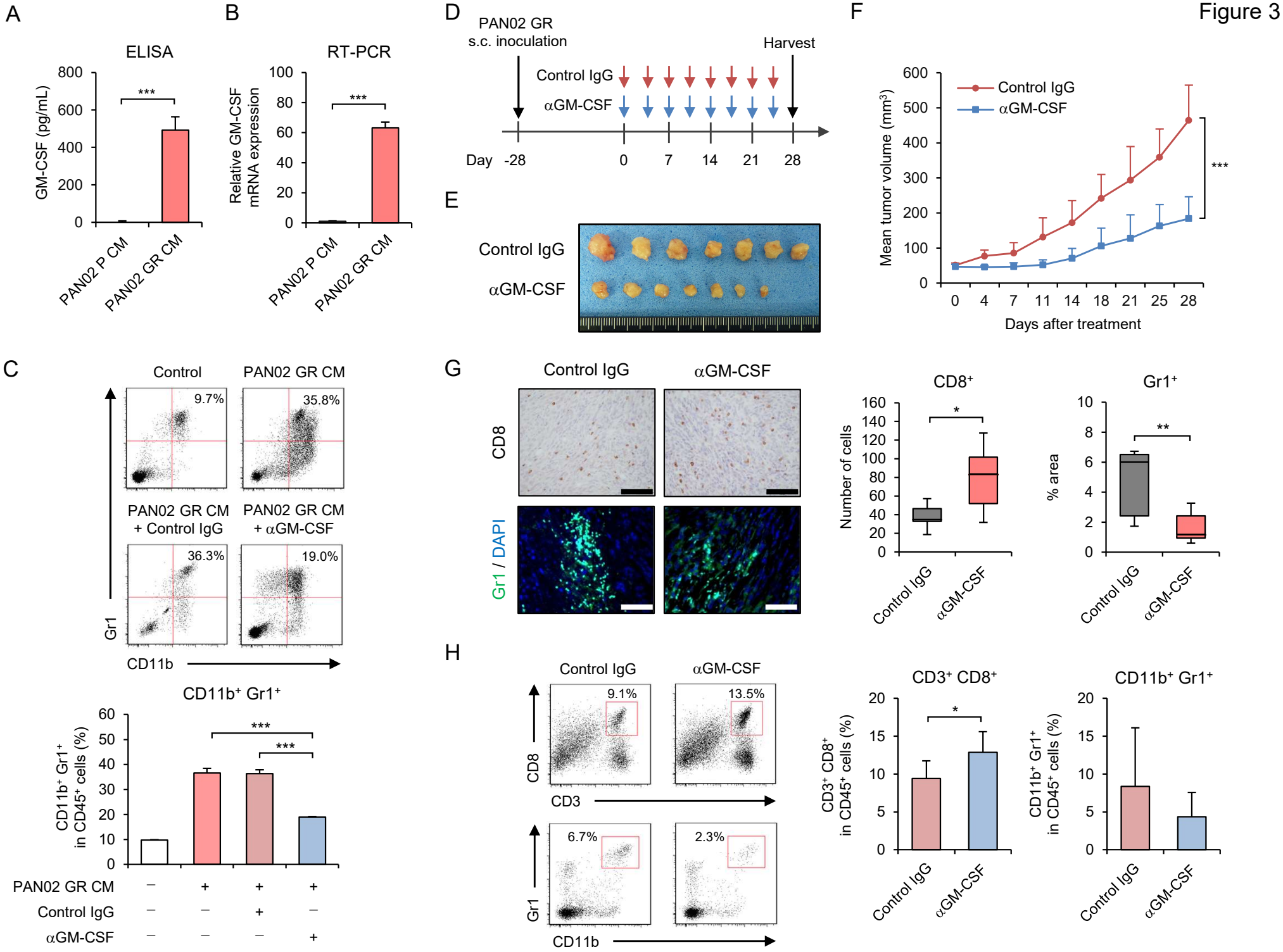

A
ELISA
GM-CSF (pg/mL)
800
600
400
200
0
***
PAN02 P CM
PAN02 GR CM
B
RT-PCR
Relative GM-CSF mRNA expression
100
80
60
40
20
0
***
PAN02 P CM
PAN02 GR CM
C
Control
PAN02 GR CM
9.7%
35.8%
PAN02 GR CM + Control IgG
PAN02 GR CM + αGM-CSF
36.3%
19.0%
Gr1
CD11b
CD11b+ Gr1+
CD11b+ Gr1+ in CD45+ cells (%)
60
50
40
30
20
10
0
***
***
PAN02 GR CM − + + +
Control IgG − − + −
αGM-CSF − − − +
D
PAN02 GR s.c. inoculation
Harvest
Control IgG
αGM-CSF
Day -28 0 7 14 21 28
E
Control IgG
αGM-CSF
F
Mean tumor volume (mm3)
600
500
400
300
200
100
0
Control IgG
αGM-CSF
***
0 4 7 11 14 18 21 25 28
Days after treatment
G
Control IgG
αGM-CSF
CD8
Gr1 / DAPI
CD8+
Number of cells
160
140
120
100
80
60
40
20
0
*
Control IgG
αGM-CSF
Gr1+
% area
10
8
6
4
2
0
**
Control IgG
αGM-CSF
H
Control IgG
αGM-CSF
9.1%
13.5%
CD8
CD3
6.7%
2.3%
Gr1
CD11b
CD3+ CD8+
CD3+ CD8+ in CD45+ cells (%)
20
15
10
5
0
*
Control IgG
αGM-CSF
CD11b+ Gr1+
CD11b+ Gr1+ in CD45+ cells (%)
20
15
10
5
0
Control IgG
αGM-CSF

Figure 4

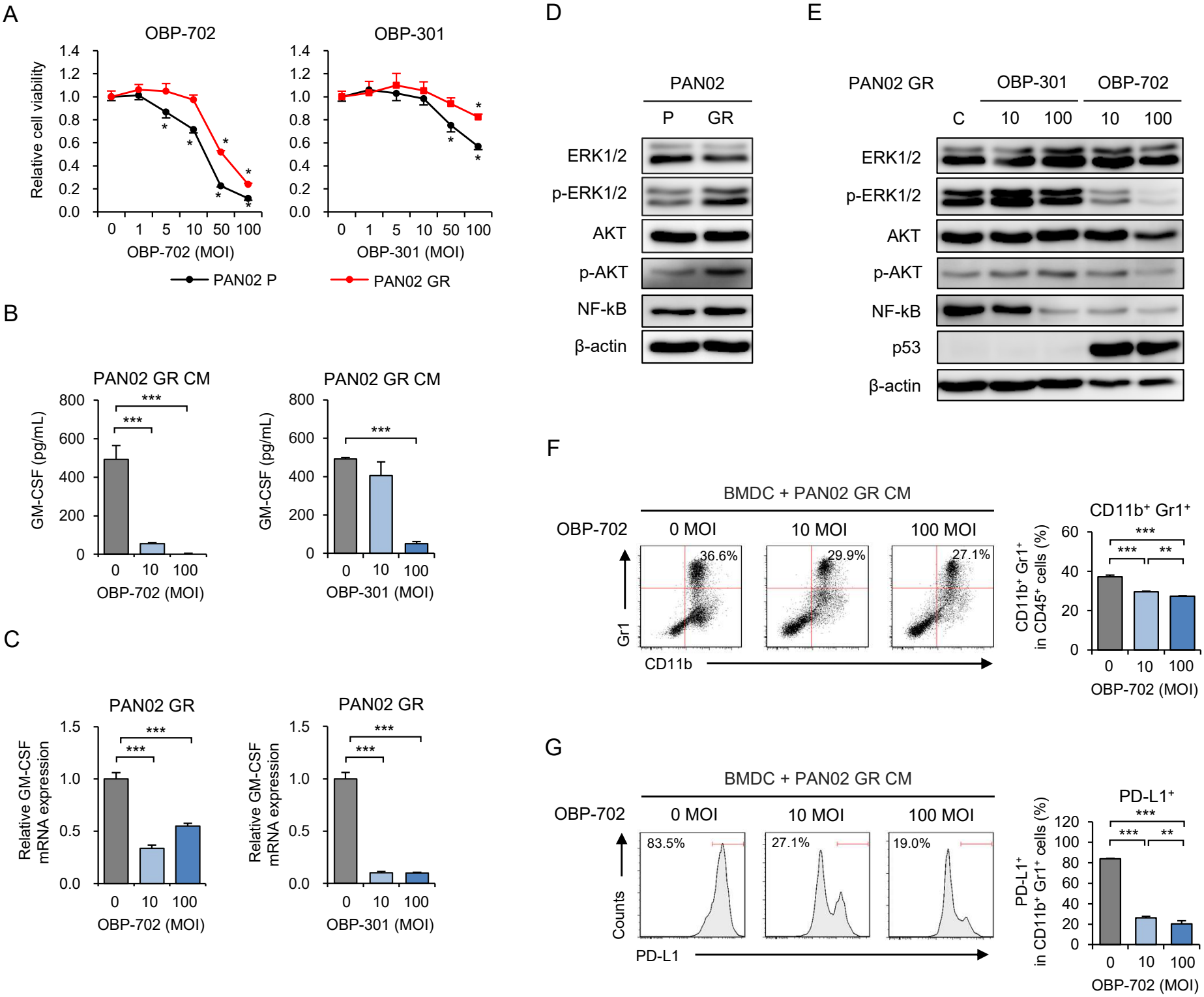

A
OBP-702
OBP-301
Relative cell viability
OBP-702 (MOI)
OBP-301 (MOI)
PAN02 P
PAN02 GR
B
PAN02 GR CM
GM-CSF (pg/mL)
OBP-702 (MOI)
OBP-301 (MOI)
C
PAN02 GR
Relative GM-CSF mRNA expression
OBP-702 (MOI)
OBP-301 (MOI)
D
PAN02
P
GR
ERK1/2
p-ERK1/2
AKT
p-AKT
NF-kB
β-actin
E
PAN02 GR
OBP-301
OBP-702
C
10
100
10
100
ERK1/2
p-ERK1/2
AKT
p-AKT
NF-kB
p53
β-actin
F
BMDC + PAN02 GR CM
OBP-702
0 MOI
10 MOI
100 MOI
36.6%
29.9%
27.1%
Gr1
CD11b
CD11b+ Gr1+
CD11b+ Gr1+ in CD45+ cells (%)
OBP-702 (MOI)
G
BMDC + PAN02 GR CM
OBP-702
0 MOI
10 MOI
100 MOI
83.5%
27.1%
19.0%
Counts
PD-L1
PD-L1+
PD-L1+ in CD11b+ Gr1+ cells (%)
OBP-702 (MOI)

Figure 5

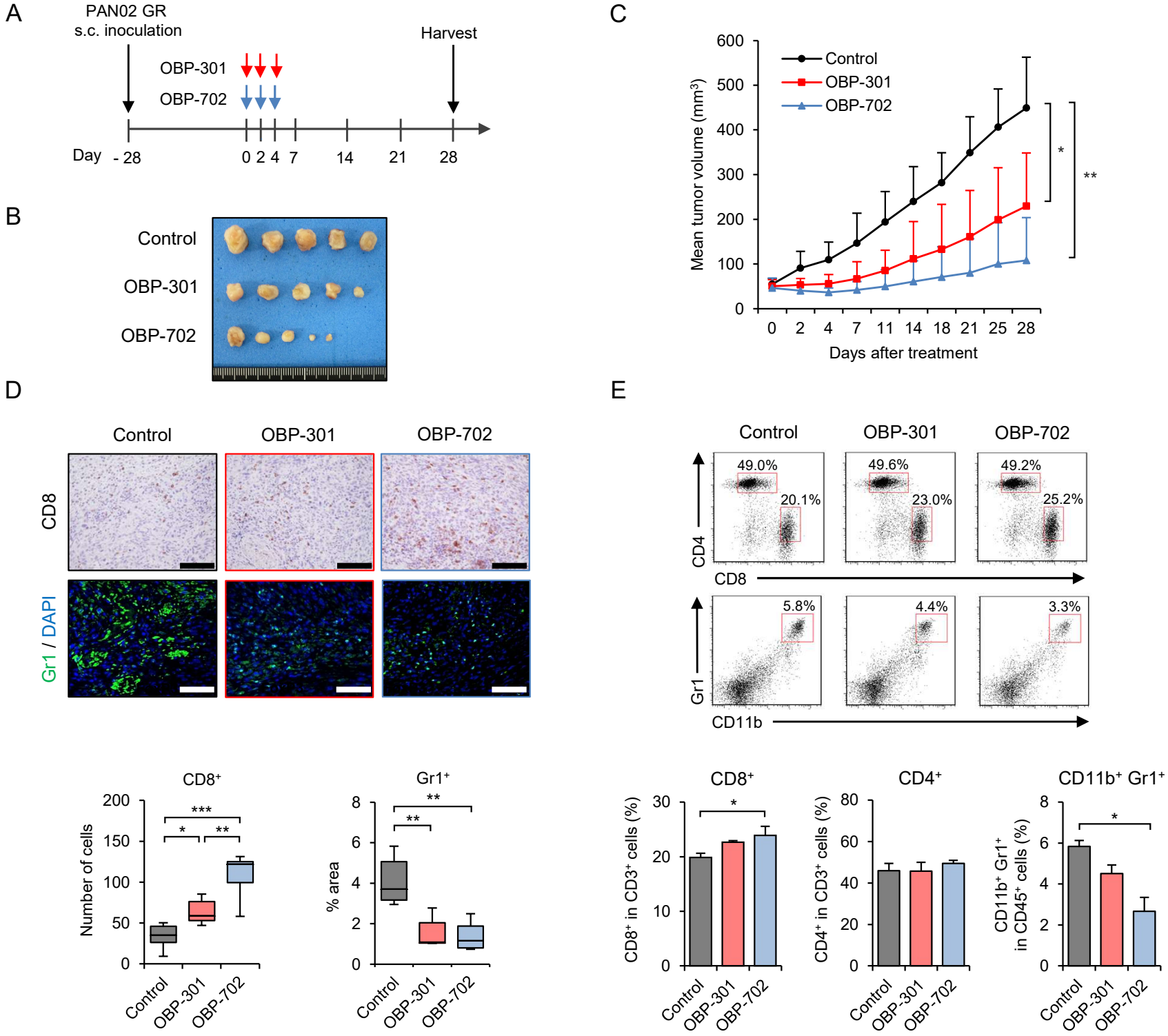
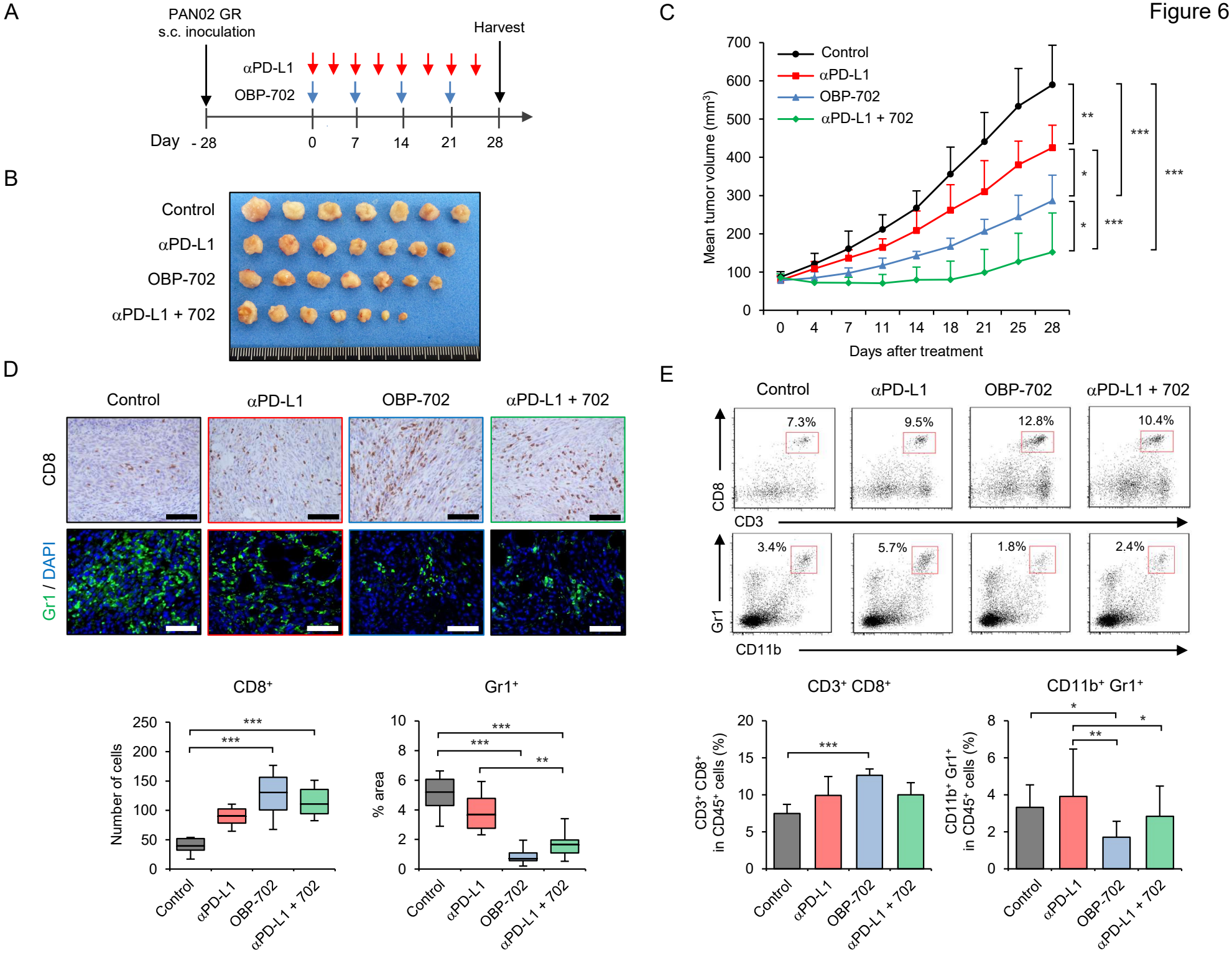

A
PAN02 GR
s.c. inoculation
Harvest
OBP-301
OBP-702
Day - 28
0 2 4 7
14
21
28
B
Control
OBP-301
OBP-702
C
Control
OBP-301
OBP-702
Mean tumor volume (mm³)
Days after treatment
D
Control
OBP-301
OBP-702
CD8
Gr1 / DAPI
CD8⁺
Number of cells
Gr1⁺
% area
E
Control
OBP-301
OBP-702
49.0%
20.1%
49.6%
23.0%
49.2%
25.2%
CD4
CD8
5.8%
4.4%
3.3%
Gr1
CD11b
CD8⁺
CD8⁺ in CD3⁺ cells (%)
CD4⁺
CD4⁺ in CD3⁺ cells (%)
CD11b⁺ Gr1⁺
CD11b⁺ Gr1⁺ in CD45⁺ cells (%)

Figure 6


A
PAN02 GR
s.c. inoculation
Harvest
αPD-L1
OBP-702
Day
- 28
0
7
14
21
28
B
Control
αPD-L1
OBP-702
αPD-L1 + 702
C
Control
αPD-L1
OBP-702
αPD-L1 + 702
Mean tumor volume (mm³)
Days after treatment
D
Control
αPD-L1
OBP-702
αPD-L1 + 702
CD8
Gr1 / DAPI
CD8⁺
Gr1⁺
Number of cells
% area
E
7.3%
9.5%
12.8%
10.4%
3.4%
5.7%
1.8%
2.4%
CD8
CD3
Gr1
CD11b
CD3⁺ CD8⁺
CD11b⁺ Gr1⁺
CD3⁺ CD8⁺ in CD45⁺ cells (%)
CD11b⁺ Gr1⁺ in CD45⁺ cells (%)