Therapeutic targeting of CD47 for small cell lung cancer

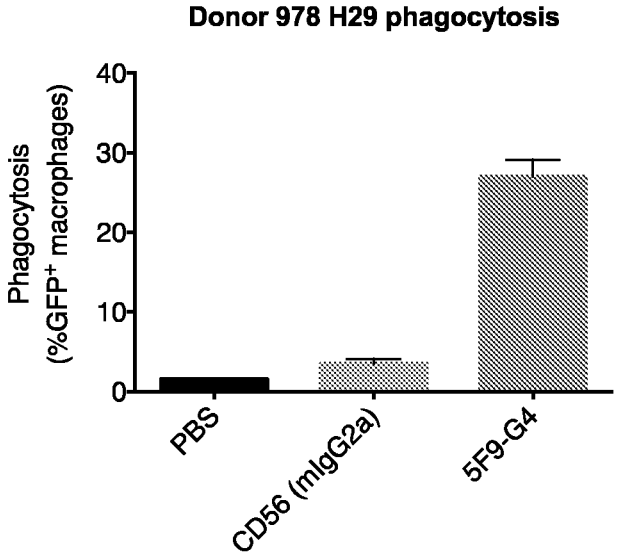


FIGURE 1

CD47-blocking therapies are effective against small cell lung cancer

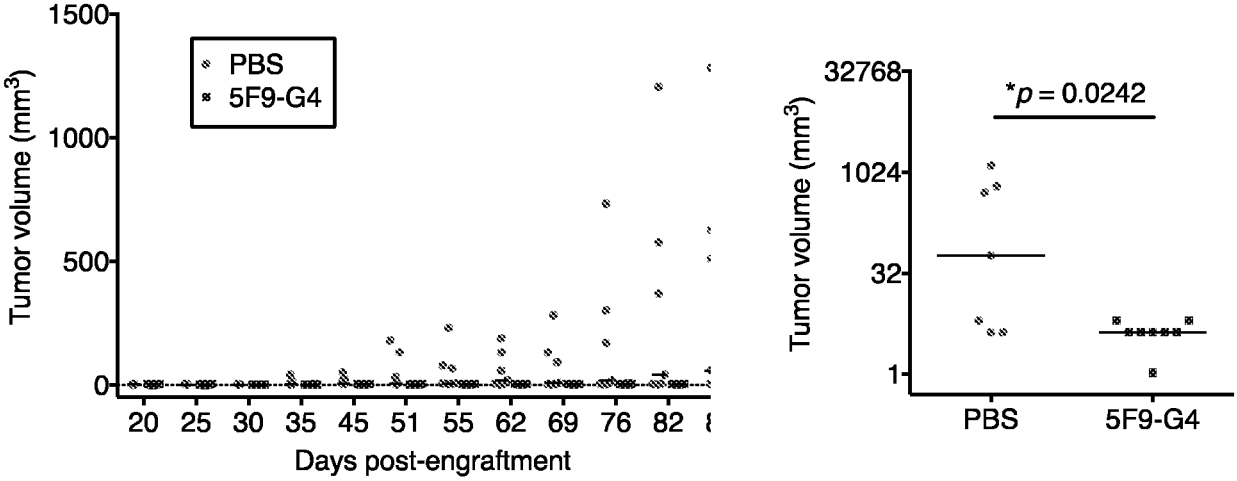


FIGURE 2

Novel therapeutic targets highly expressed on the surface of primary human small cell lung cancer cells

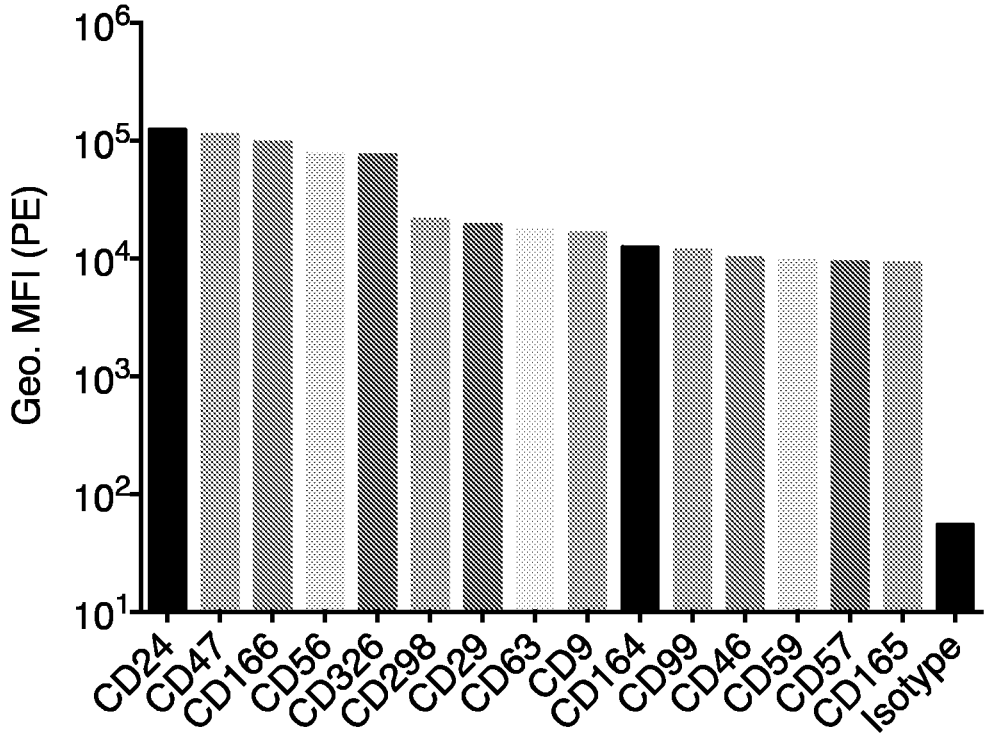


FIGURE 3

Phagocytosis of small cell lung cancer cell lines (H82, H69) with tumor-specific antibodies alone and in combination them with high-affinity SIRPα monomers

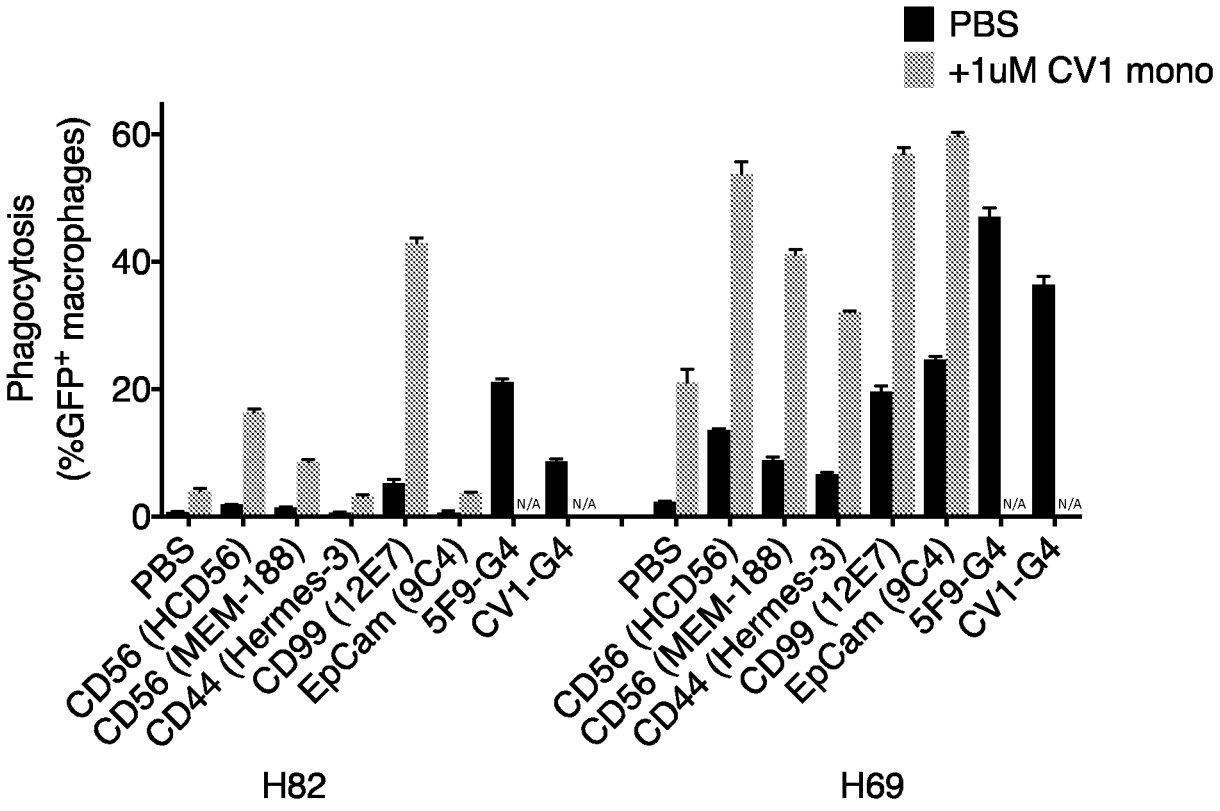


FIGURE 4

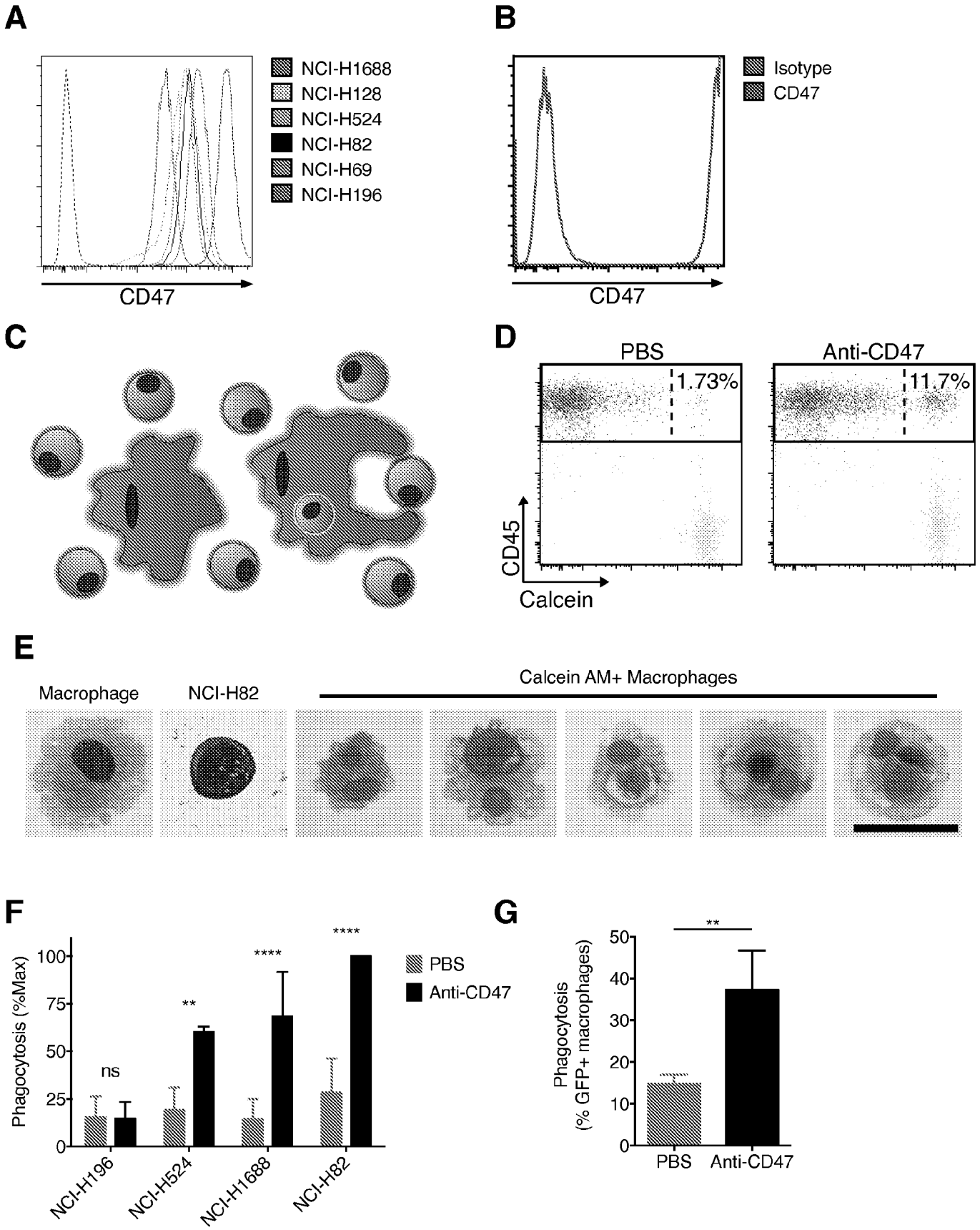

A
NCI-H1688
NCI-H128
NCI-H524
NCI-H82
NCI-H69
NCI-H196
CD47
B
Isotype
CD47
CD47
C
D
PBS
Anti-CD47
1.73%
11.7%
CD45
Calcein
E
Macrophage
NCI-H82
Calcein AM+ Macrophages
F
Phagocytosis (%Max)
100
75
50
25
0
ns
**
****
****
PBS
Anti-CD47
NCI-H196
NCI-H524
NCI-H1688
NCI-H82
G
**
Phagocytosis
(% GFP+ macrophages)
50
40
30
20
10
0
PBS
Anti-CD47

FIGURE 5

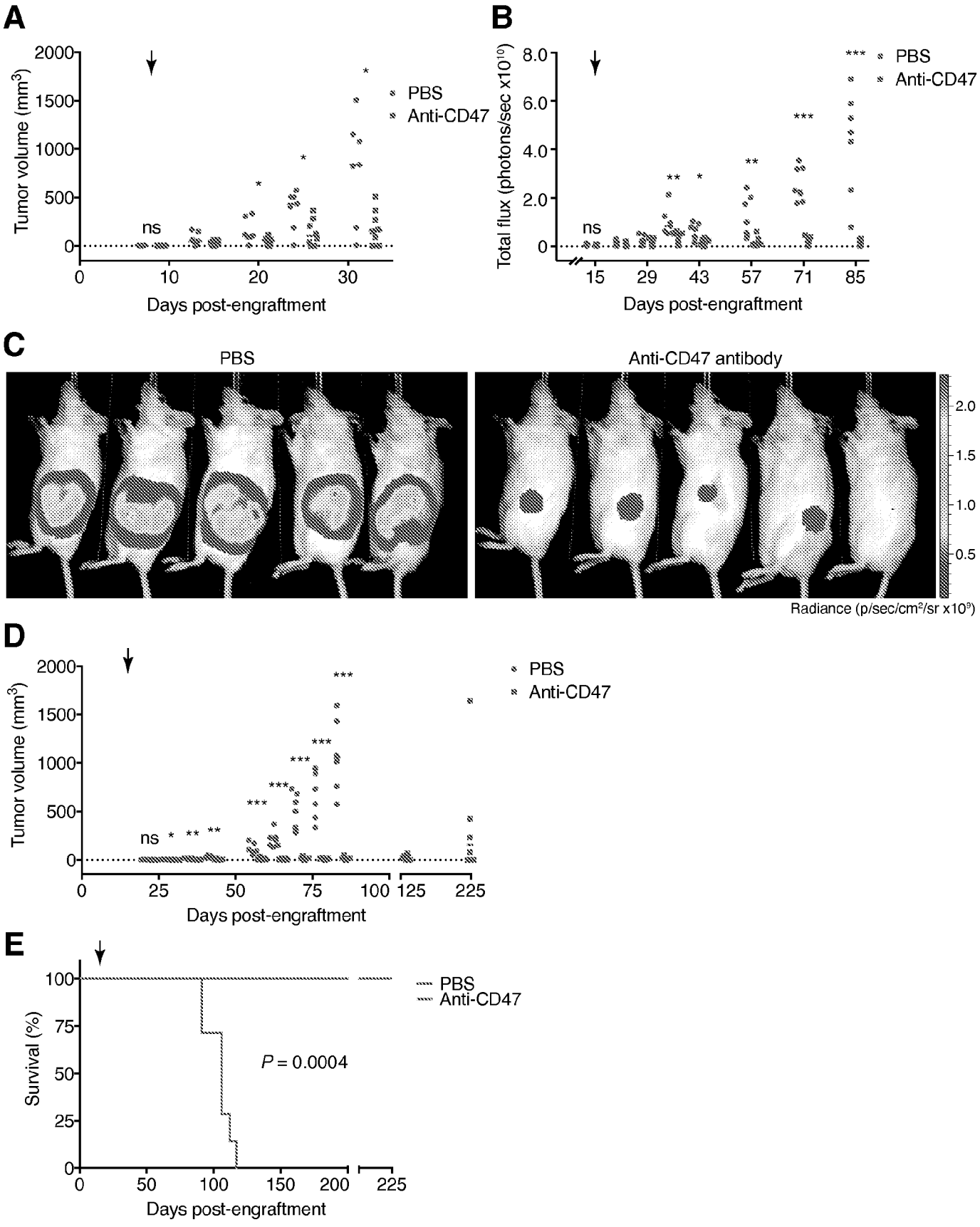

A
Tumor volume (mm3)
2000
1500
1000
500
0
ns
0
10
20
30
Days post-engraftment
PBS
Anti-CD47
B
Total flux (photons/sec x10^10)
8.0
6.0
4.0
2.0
0
ns
15
29
43
57
71
85
Days post-engraftment
PBS
Anti-CD47
C
PBS
Anti-CD47 antibody
2.0
1.5
1.0
0.5
Radiance (p/sec/cm2/sr x10^9)
D
Tumor volume (mm3)
2000
1500
1000
500
0
ns
0
25
50
75
100
125
225
Days post-engraftment
PBS
Anti-CD47
E
Survival (%)
100
75
50
25
0
P = 0.0004
0
50
100
150
200
225
Days post-engraftment
PBS
Anti-CD47

FIGURE 6

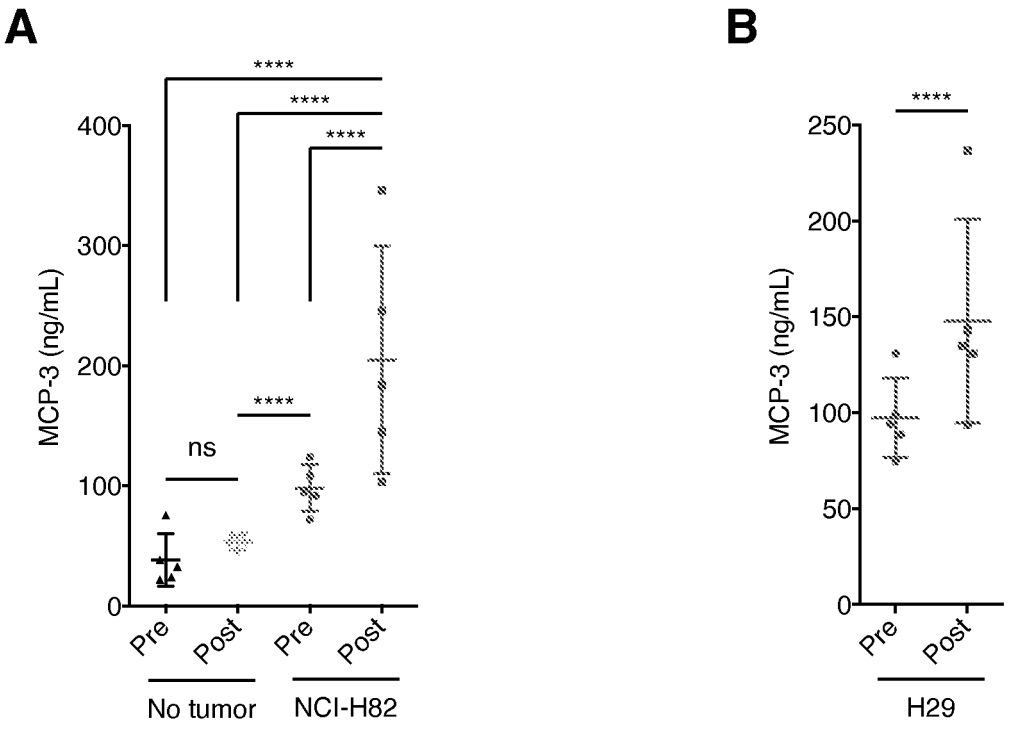

A
****
****
****
****
ns
400
300
200
100
0
MCP-3 (ng/mL)
Pre
Post
Pre
Post
No tumor
NCI-H82
B
****
250
200
150
100
50
0
MCP-3 (ng/mL)
Pre
Post
H29

FIGURE 7

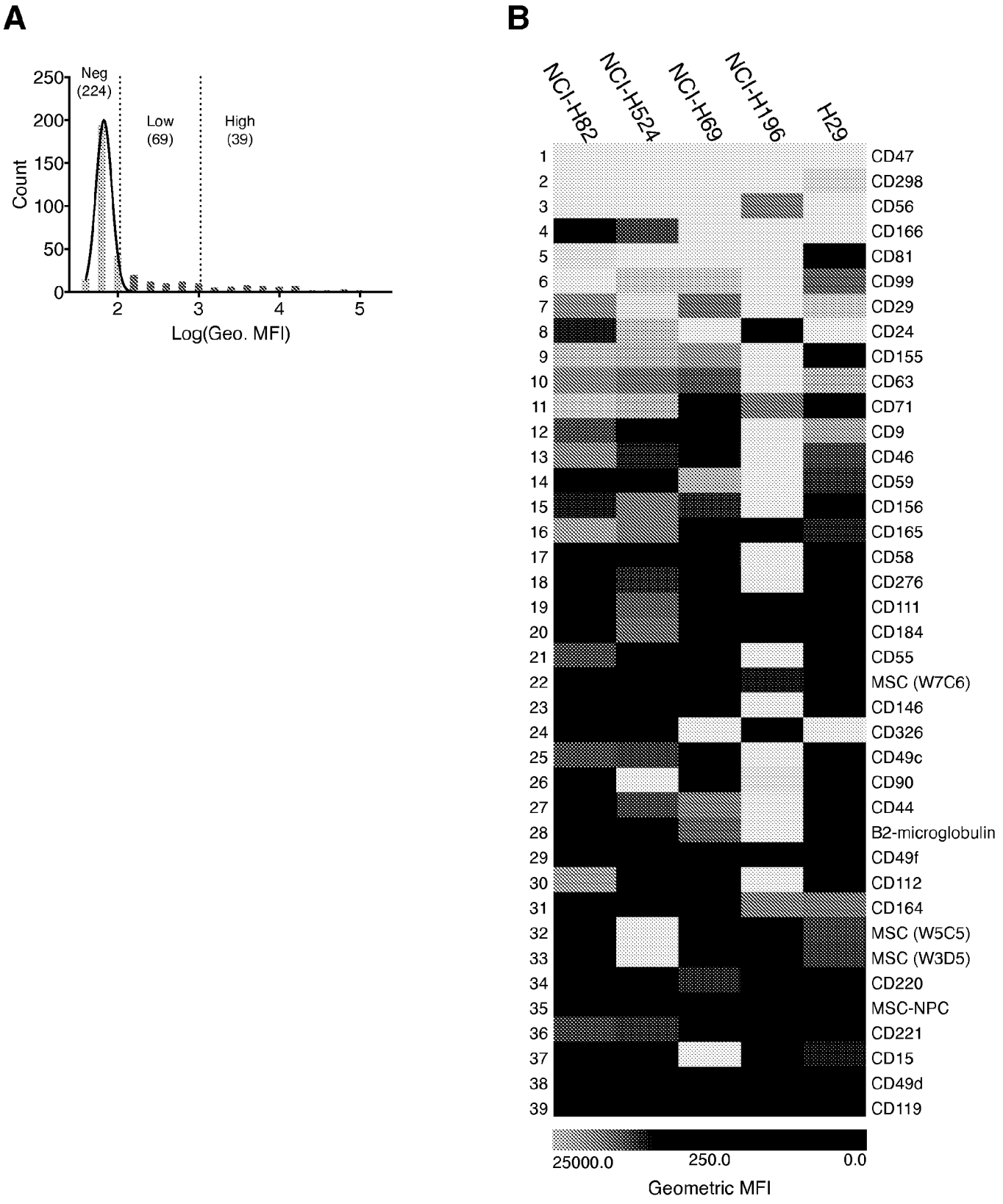
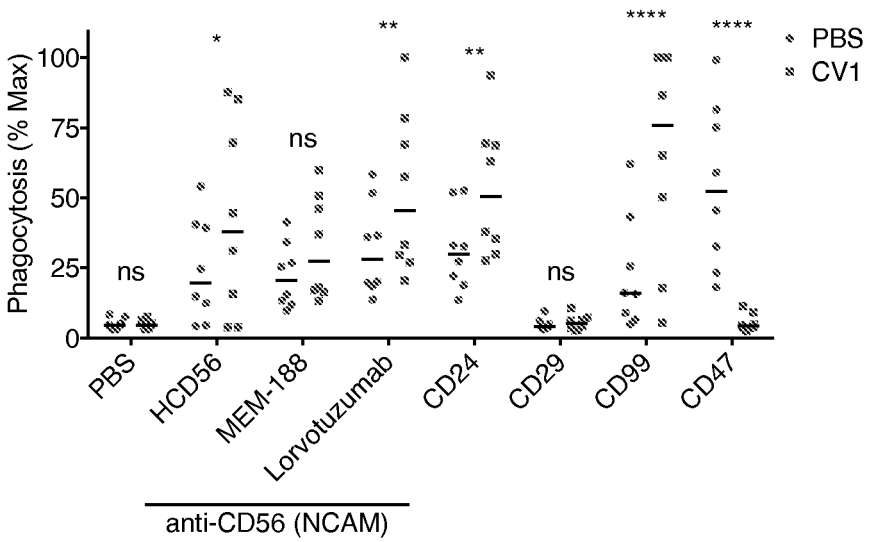
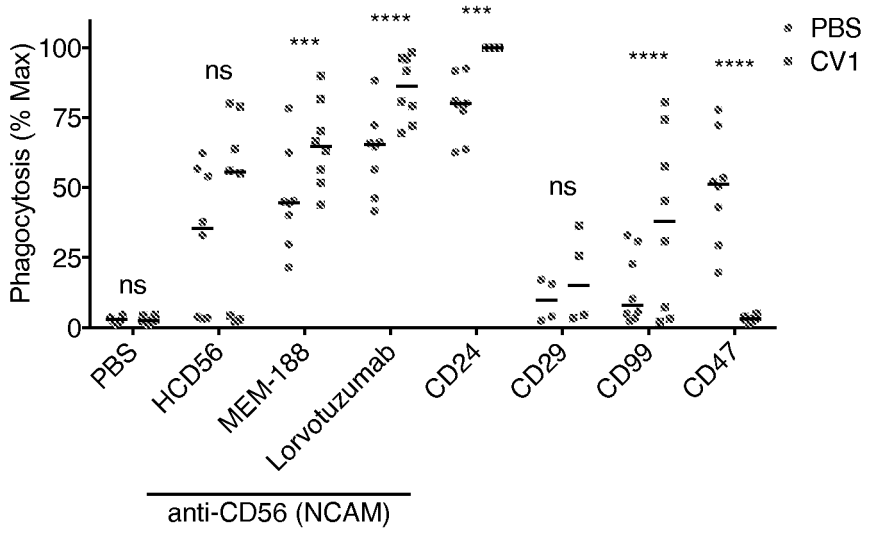

A
Neg
(224)
Low
(69)
High
(39)
Count
250
200
150
100
50
0
2
3
4
5
Log(Geo. MFI)
B
NCI-H82
NCI-H524
NCI-H69
NCI-H196
H29
1 CD47
2 CD298
3 CD56
4 CD166
5 CD81
6 CD99
7 CD29
8 CD24
9 CD155
10 CD63
11 CD71
12 CD9
13 CD46
14 CD59
15 CD156
16 CD165
17 CD58
18 CD276
19 CD111
20 CD184
21 CD55
22 MSC (W7C6)
23 CD146
24 CD326
25 CD49c
26 CD90
27 CD44
28 B2-microglobulin
29 CD49f
30 CD112
31 CD164
32 MSC (W5C5)
33 MSC (W3D5)
34 CD220
35 MSC-NPC
36 CD221
37 CD15
38 CD49d
39 CD119
25000.0
250.0
0.0
Geometric MFI

FIGURE 8

A


Phagocytosis (% Max)
100
75
50
25
0
PBS
CV1
ns
ns
ns
*
**
**
****
****
PBS
HCD56
MEM-188
Lorvotuzumab
CD24
CD29
CD99
CD47
anti-CD56 (NCAM)

B


Phagocytosis (% Max)
100
75
50
25
0
PBS
CV1
ns
ns
ns
***
****
***
****
****
PBS
HCD56
MEM-188
Lorvotuzumab
CD24
CD29
CD99
CD47
anti-CD56 (NCAM)

C

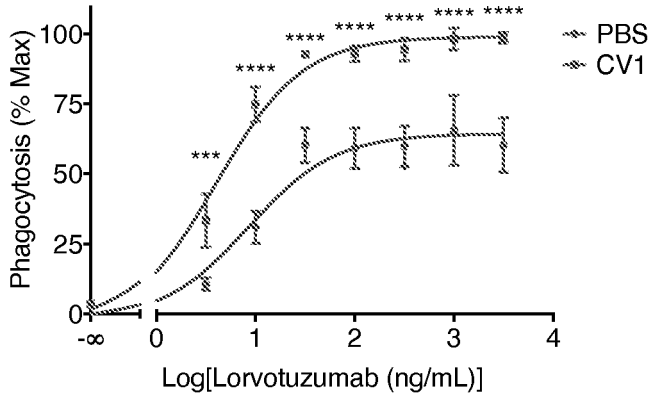

Phagocytosis (% Max)
100
75
50
25
0
PBS
CV1
***
****
****
****
****
****
-∞
0
1
2
3
4
Log[Lorvotuzumab (ng/mL)]

FIGURE 9