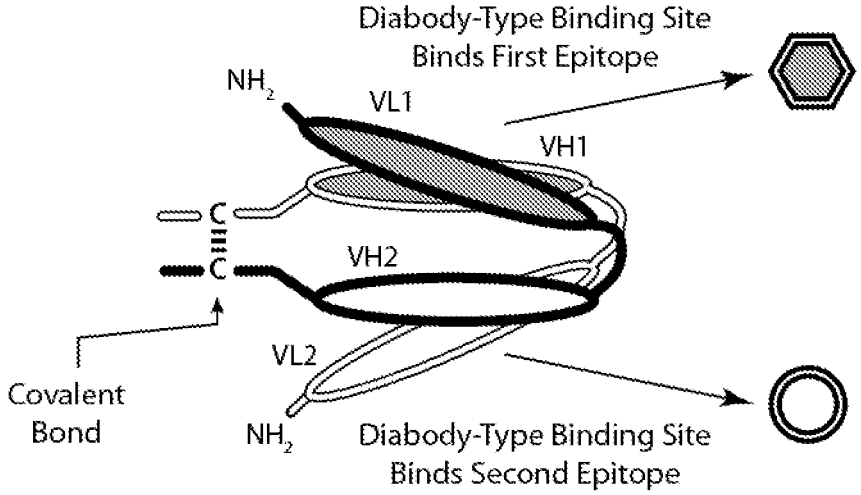


Figure 1

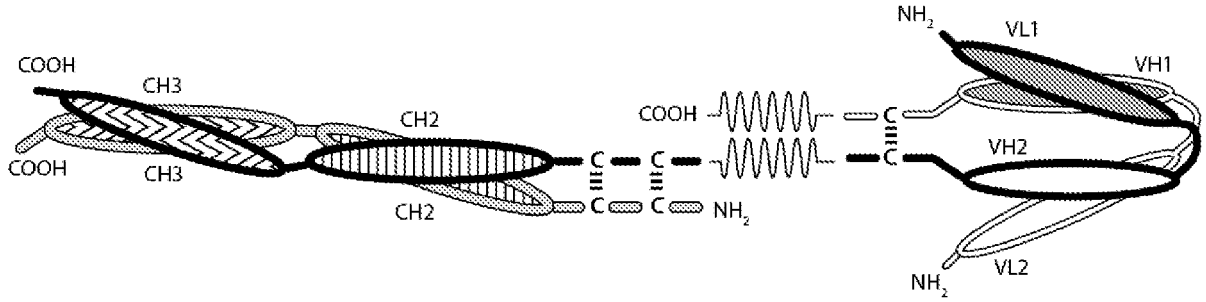


Figure 2

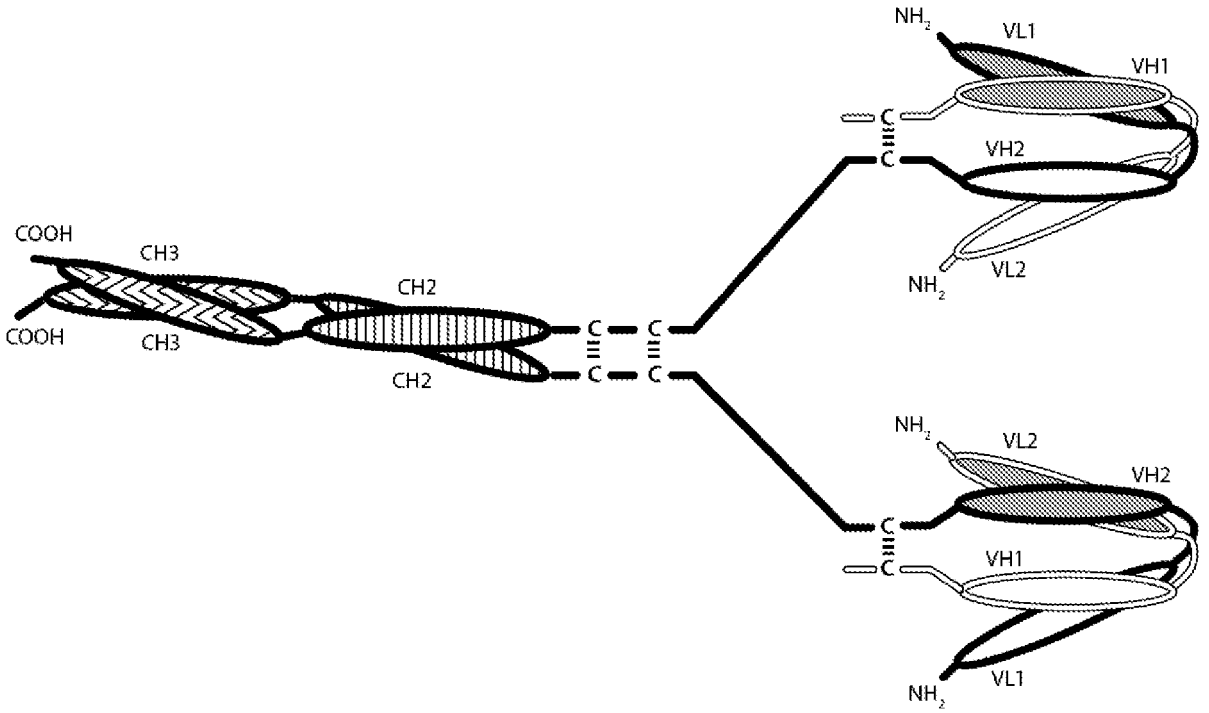


Figure 3

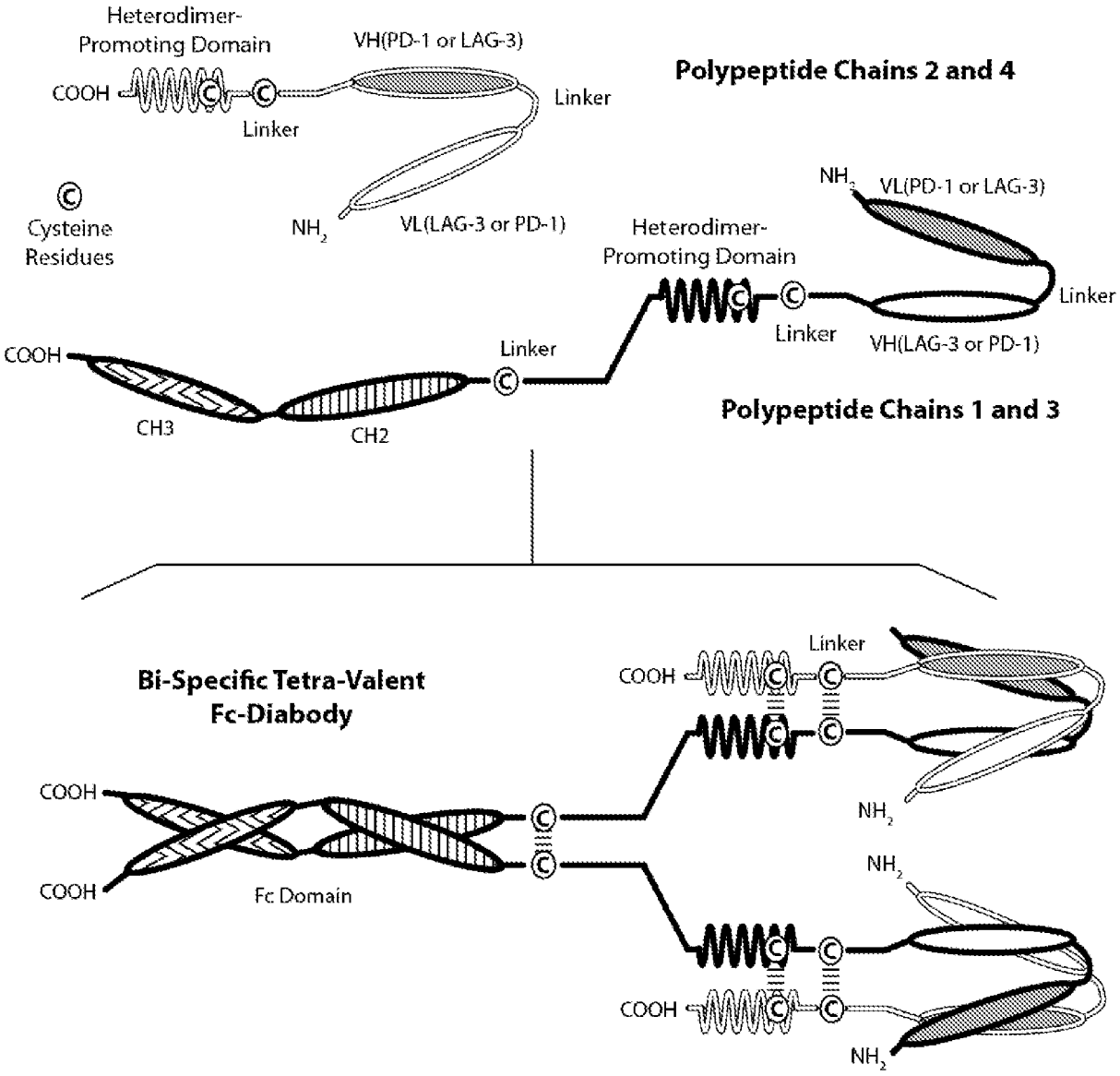

Heterodimer-
Promoting Domain
VH(PD-1 or LAG-3)
COOH
Linker
Linker
Polypeptide Chains 2 and 4
Cysteine
Residues
NH2
VL(LAG-3 or PD-1)
NH2
VL(PD-1 or LAG-3)
Heterodimer-
Promoting Domain
Linker
Linker
VH(LAG-3 or PD-1)
COOH
Linker
CH3
CH2
Polypeptide Chains 1 and 3
Bi-Specific Tetra-Valent
Fc-Diabody
Linker
COOH
COOH
COOH
Fc Domain
NH2
NH2
COOH
NH2

Figure 4

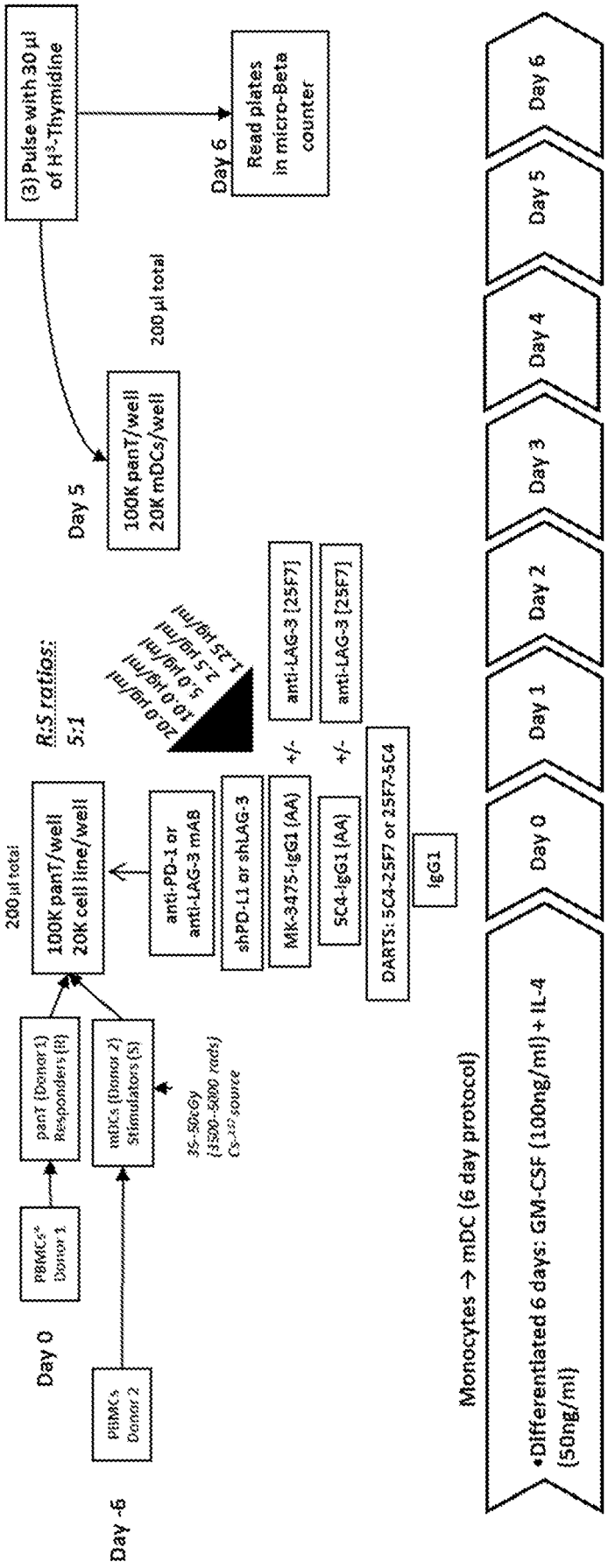

Monocytes → mDC (6 day protocol)
•Differentiated 6 days: GM-CSF (100ng/ml) + IL-4 (50ng/ml)
Day 0
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day -6
PBMCs Donor 2
PBMCs Donor 1
35-50cGy (3500-5000 rads) Cs-137 source
mDCs (Donor 2) Stimulators (S)
panT (Donor 1) Responders (R)
100K panT/well 20K cell line/well
200 µl total
R:S ratios: 5:1
20.0 µg/ml
10.0 µg/ml
5.0 µg/ml
2.5 µg/ml
1.25 µg/ml
anti-PD-1 or anti-LAG-3 mAB
shPD-L1 or shLAG-3
MK-3475-IgG1 (AA)
5C4-IgG1 (AA)
DARTS: 5C4-25F7 or 25F7-5C4
IgG1
+/-
+/-
anti-LAG-3 [25F7]
anti-LAG-3 [25F7]
Day 5
100K panT/well 20K mDCs/well
200 µl total
(3) Pulse with 30 µl of H3-Thymidine
Day 6
Read plates in micro-Beta counter

Figure 5

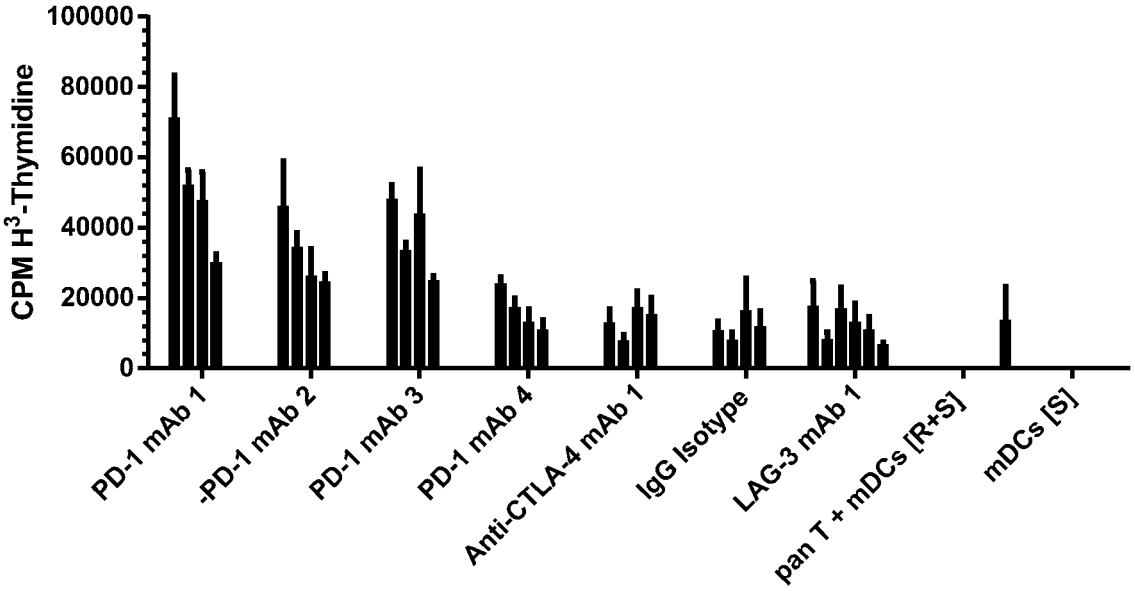

CPM H3-Thymidine
100000
80000
60000
40000
20000
0
PD-1 mAb 1
-PD-1 mAb 2
PD-1 mAb 3
PD-1 mAb 4
Anti-CTLA-4 mAb 1
IgG Isotype
LAG-3 mAb 1
pan T + mDCs [R+S]
mDCs [S]

Figure 6

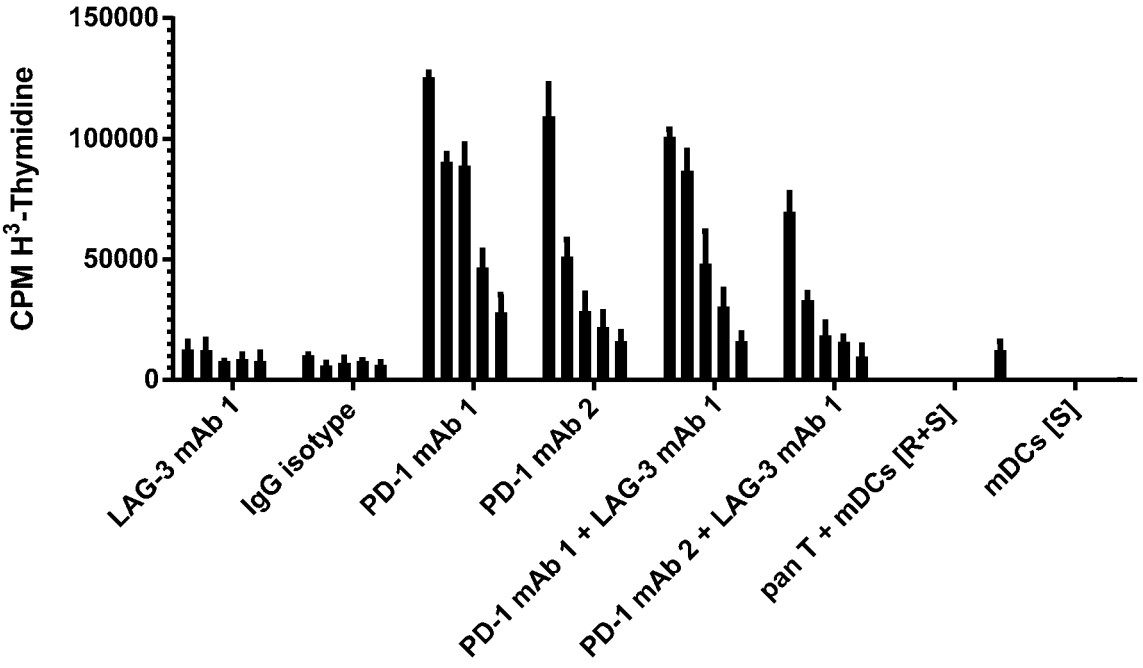

150000
100000
50000
0
CPM H3-Thymidine
LAG-3 mAb 1
IgG isotype
PD-1 mAb 1
PD-1 mAb 2
PD-1 mAb 1 + LAG-3 mAb 1
PD-1 mAb 2 + LAG-3 mAb 1
pan T + mDCs [R+S]
mDCs [S]

Figure 7

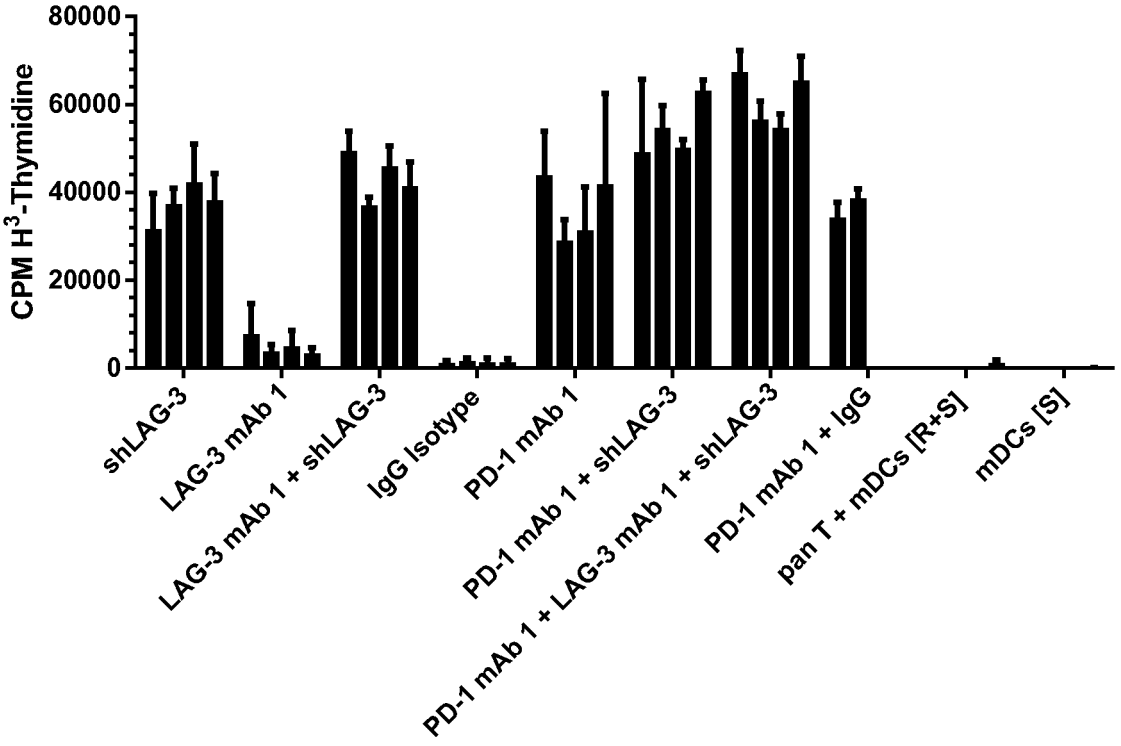

80000
60000
40000
20000
0
CPM H3-Thymidine
shLAG-3
LAG-3 mAb 1
LAG-3 mAb 1 + shLAG-3
IgG Isotype
PD-1 mAb 1
PD-1 mAb 1 + shLAG-3
PD-1 mAb 1 + LAG-3 mAb 1 + shLAG-3
PD-1 mAb 1 + IgG
pan T + mDCs [R+S]
mDCs [S]

Figure 8

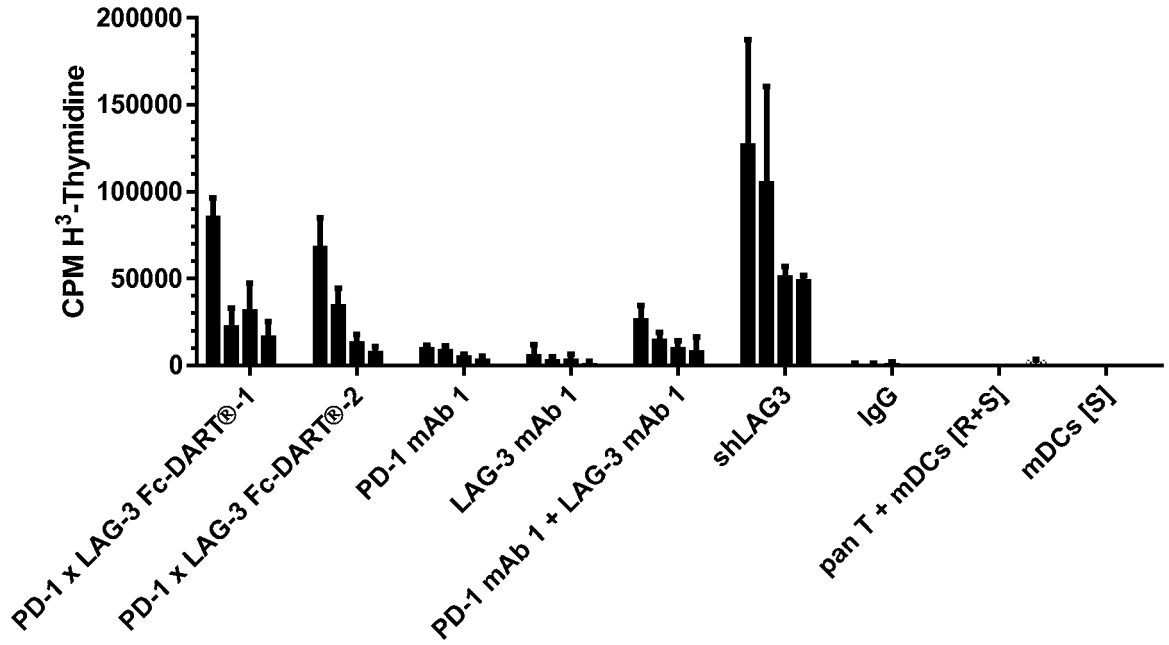

200000
150000
100000
50000
0
CPM H3-Thymidine
PD-1 x LAG-3 Fc-DART®-1
PD-1 x LAG-3 Fc-DART®-2
PD-1 mAb 1
LAG-3 mAb 1
PD-1 mAb 1 + LAG-3 mAb 1
shLAG3
IgG
pan T + mDCs [R+S]
mDCs [S]

Figure 9A

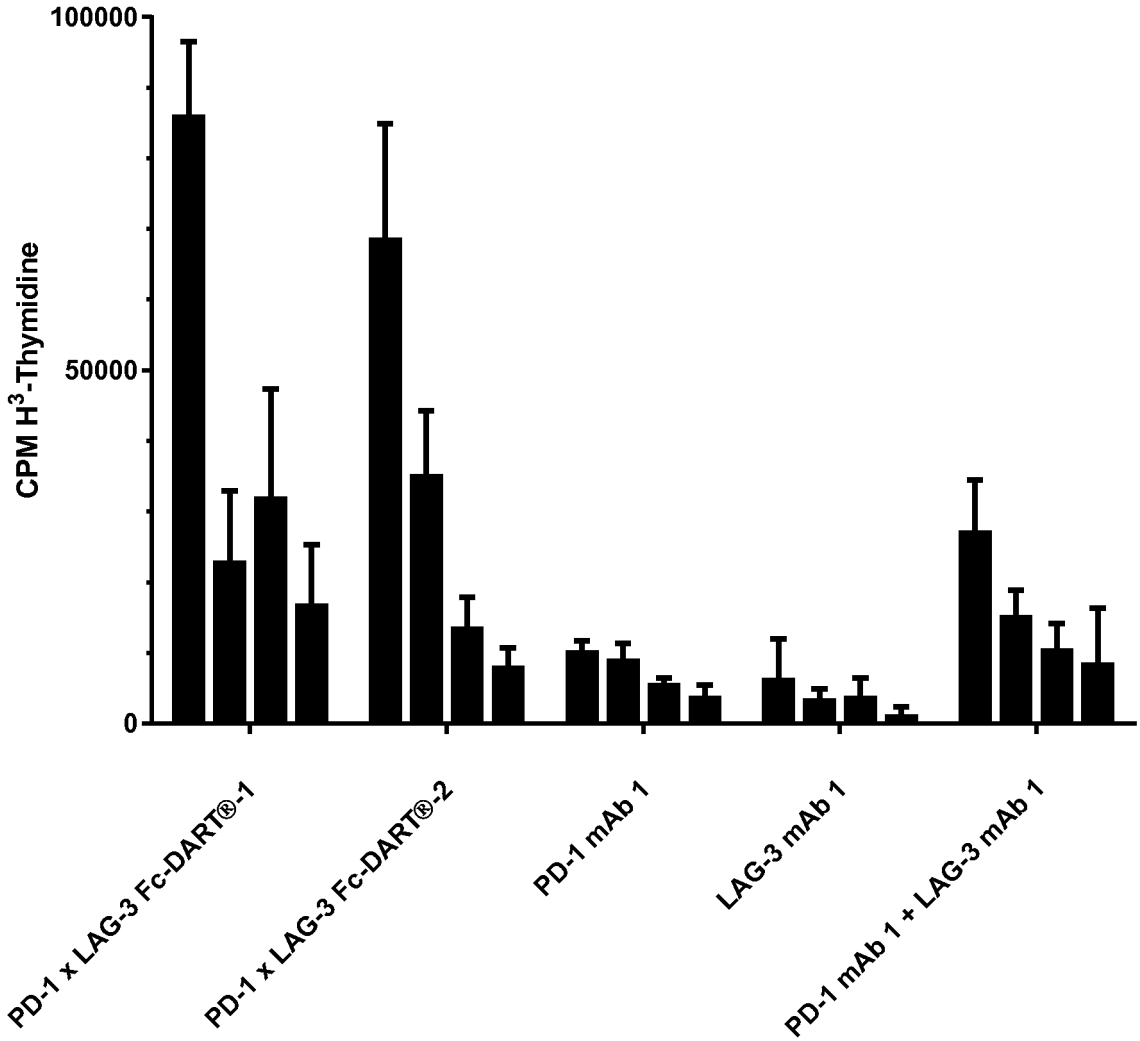

100000
50000
0
CPM H3-Thymidine
PD-1 x LAG-3 Fc-DART®-1
PD-1 x LAG-3 Fc-DART®-2
PD-1 mAb 1
LAG-3 mAb 1
PD-1 mAb 1 + LAG-3 mAb 1

Figure 9B