

Figure 1A.

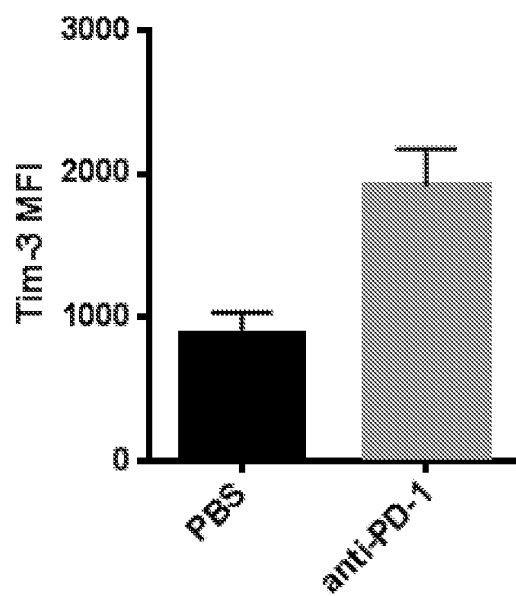


Figure 1B.

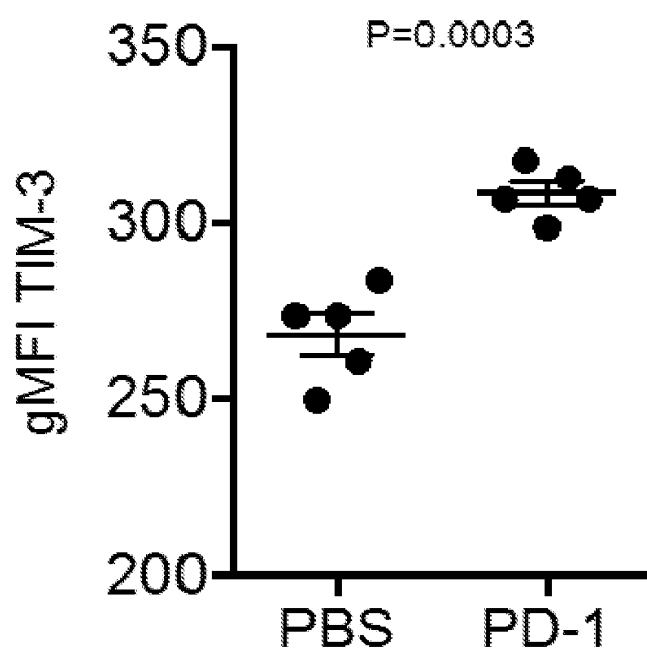


Figure 1C.

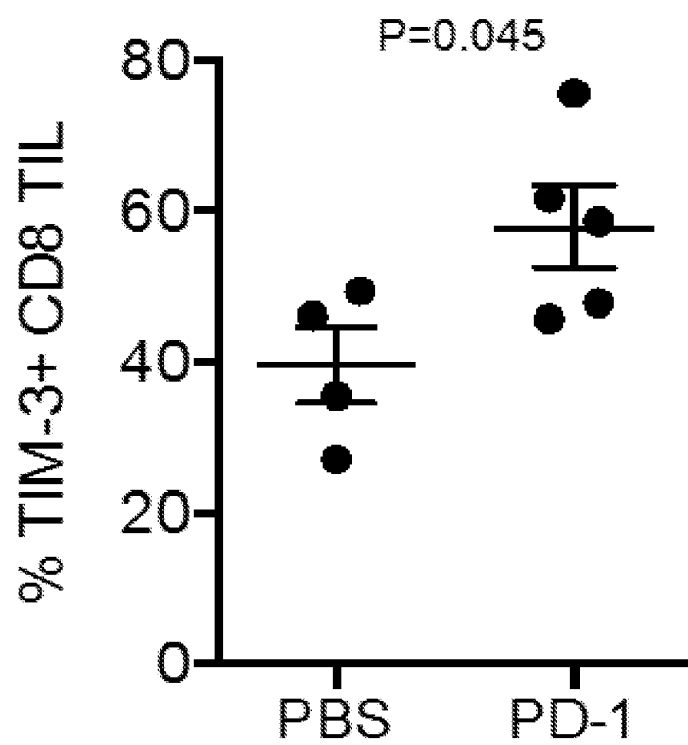


Figure 2A.

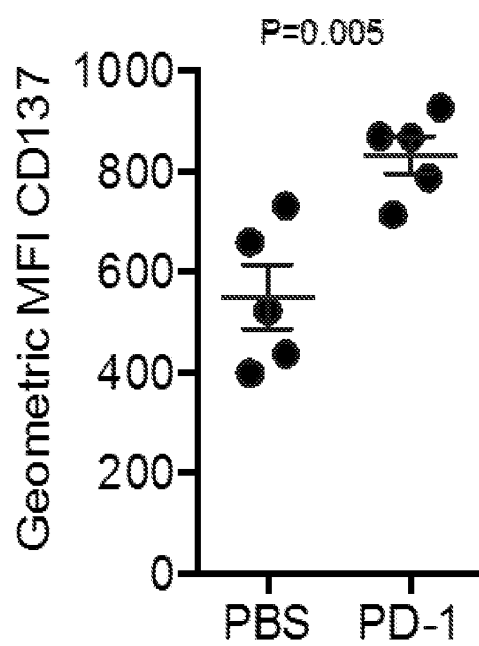


Figure 2B.

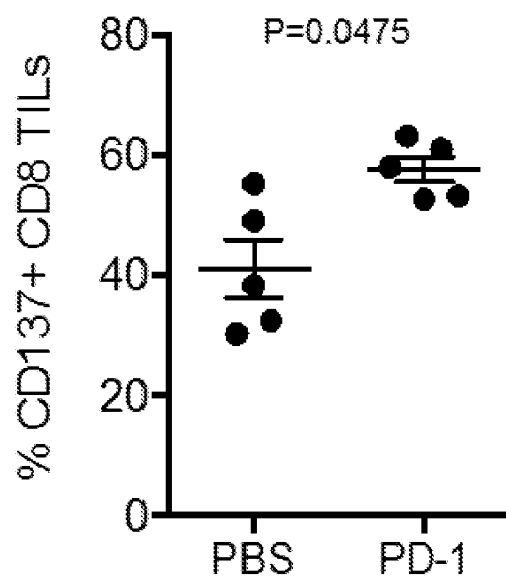


Figure 3A.

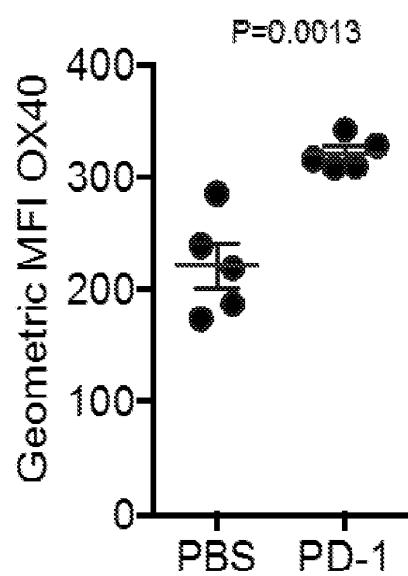


Figure 3B.

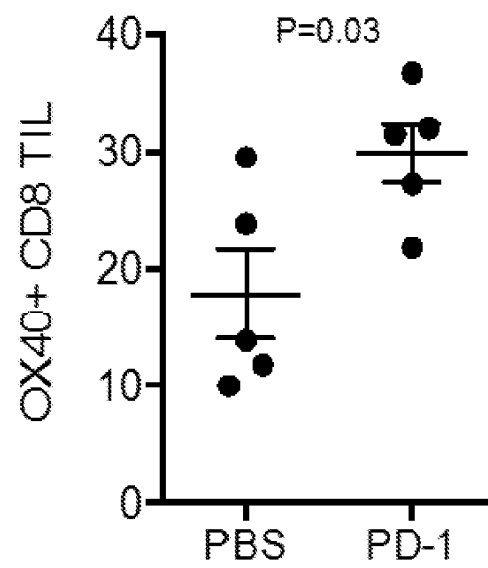


Figure 4A.

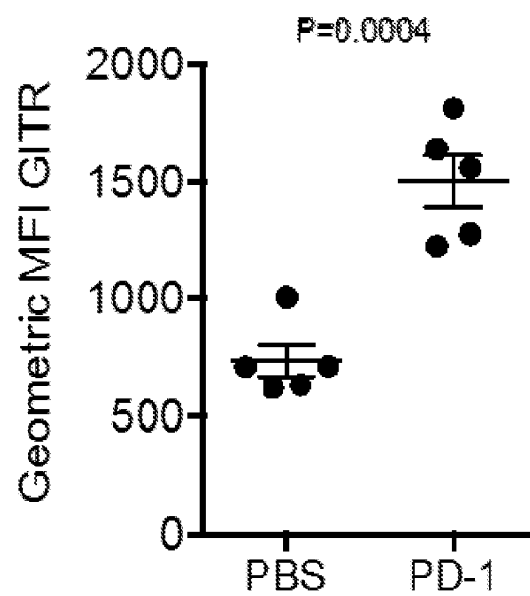


Figure 4B.

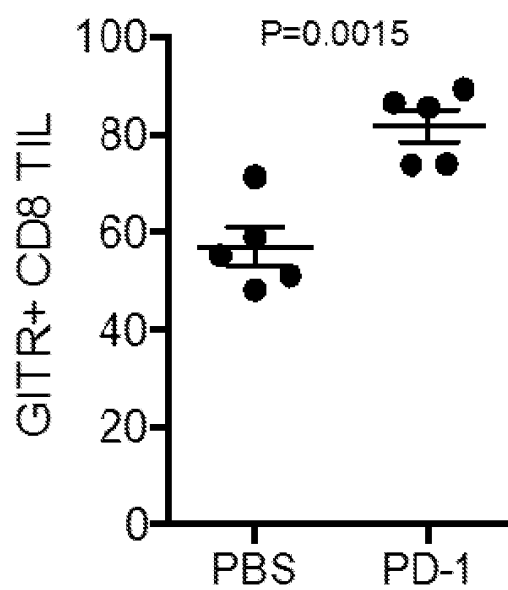


Figure 5.

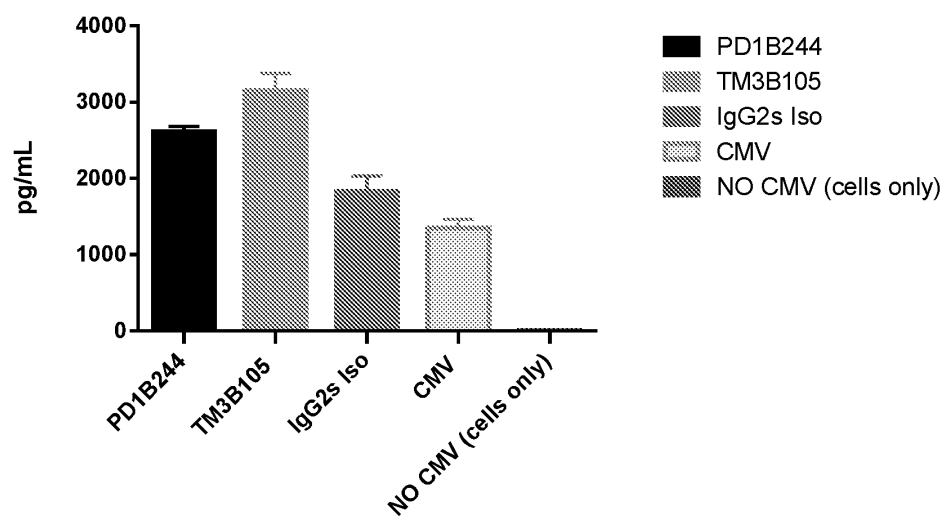


Figure 6.

Antibody	HCDR1					
	Sequence					SEQ ID NO:
PD1B114	S	Y	A	I	S	10
PD1B149	S	Y	A	I	S	10
PD1B160	S	Y	A	I	S	10
PD1B162	S	Y	A	I	S	10
PD1B164	S	Y	A	I	S	10
PD1B11	S	Y	A	I	S	10
PD1B183	S	Y	A	I	S	10
PD1B184	S	Y	A	I	S	10
PD1B185	S	Y	A	I	S	10
PD1B187	S	Y	A	I	S	10
PD1B71	S	Y	A	I	S	10
PD1B177	D	Y	V	I	S	11
PD1B70	S	Y	A	I	S	10
PD1B175	S	Y	V	I	H	12
PD1B194	S	Y	A	I	S	10
PD1B195	S	Y	A	I	S	10
PD1B196	S	Y	A	I	S	10
PD1B197	S	Y	V	I	H	12
PD1B198	S	Y	V	I	H	12
PD1B199	D	Y	V	I	S	11
PD1B200	D	Y	V	I	S	11
PD1B201	D	Y	V	I	S	11
HCDR1 genus	X ₁	Y	X ₂	I	X ₃	82

PD-1 mAb HCDR1 genus sequence:

X₁YX₂IX₃ (SEQ ID NO: 82),

wherein

X₁ is S or D;

X₂ is V or A; and

X₃ is H or S.

Figure 7.

Antibody	HCDR2																	SEQ ID NO.
	Sequence																	
PD1B114	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B149	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B160	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B162	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B164	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B11	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B183	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B184	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B185	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B187	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B71	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B177	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B70	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B175	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B194	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B195	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B196	G	I	I	P	I	F	D	T	A	N	Y	A	Q	K	F	Q	G	14
PD1B197	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B198	G	I	I	P	I	F	G	T	A	N	Y	A	Q	K	F	Q	G	13
PD1B199	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B200	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
PD1B201	G	I	I	P	I	Y	G	T	A	N	Y	A	Q	K	F	Q	G	15
HCDR2 genus	G	I	I	P	I	X ₄	X ₅	T	A	N	Y	A	Q	K	F	Q	G	83

PD-1 mAb HCDR2 genus sequence

GIIPX₄X₅TANYAQKFQG (SEQ ID NO: 83),

wherein

X₄ is Y or F; and

X₅ is G or D.

Figure 8.

Antibody	HCDR3															SEQ ID NO:
	Sequence															
PD1B114	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16	
PD1B149	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16	
PD1B160	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16	
PD1B162	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16	
PD1B164	P	G	L	A	A	A	Y	D	T	G	N	L	D	Y	16	
PD1B11	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B183	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B184	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B185	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B187	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B194	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B195	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
PD1B196	P	G	L	A	A	A	Y	D	T	G	S	L	D	Y	17	
HCDR3 genus 1	P	G	L	A	A	A	Y	D	T	G	X ₆	L	D	Y	84	

PD-1 mAb HCDR3 genus 1

PGLAAAYDTGX₆LDY (SEQ ID NO: 84),

wherein

X₆ is N or S.

Figure 9.

Antibody	HCDR3											SEQ ID NO.
	Sequence											
PD1B71	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B177	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B70	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B175	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B197	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B198	G	Y	V	R	A	T	G	M	L	D	Y	19
PD1B199	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B200	G	T	L	D	R	T	G	H	L	D	Y	18
PD1B201	G	T	L	D	R	T	G	H	L	D	Y	18
HCDR3 genus 2	G	X ₇	X ₈	X ₉	X ₁₀	T	G	X ₁₁	L	D	Y	85

PD-1 mAb HCDR3 genus 2

GX₇X₈X₉X₁₀TGX₁₁LDY (SEQ ID NO: 85),

wherein

X₇ is T or Y;

X₈ is L or V;

X₉ is D or R;

X₁₀ is R or A; and

X₁₁ is H or M.

Figure 10.

Antibody	LCDR1											SEQ ID NO:
	Sequence											
PD1B114	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B149	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B160	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B162	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B164	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B11	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B183	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B184	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B185	R	A	S	Q	S	V	R	N	Y	L	A	21
PD1B187	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B71	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B177	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B70	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B175	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B194	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B195	R	A	S	Q	S	V	D	S	Y	L	A	22
PD1B196	R	A	S	Q	S	V	R	S	Y	L	A	23
PD1B197	R	A	S	Q	S	V	S	N	Y	L	A	24
PD1B198	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B199	R	A	S	Q	S	V	S	S	Y	L	A	20
PD1B200	R	A	S	Q	S	V	D	N	Y	L	A	25
PD1B201	R	A	S	Q	S	V	S	N	Y	L	A	24
LCDR1 genus	R	A	S	Q	S	V	X ₁₂	X ₁₃	Y	L	A	86

PD-1 mAb LCDR1 genus

RASQSVX₁₂X₁₃YLA (SEQ ID NO: 86),

wherein

X₁₂ is S, R or D; and

X₁₃ is S or N.

Figure 11.

Antibody	LCDR2							SEQ ID NO:
	Sequence							
PD1B114	D	A	S	N	R	A	T	26
PD1B149	D	A	S	N	R	A	T	26
PD1B160	D	A	S	D	R	A	T	27
PD1B162	D	A	S	N	R	A	T	26
PD1B164	D	A	S	Y	R	A	T	28
PD1B11	D	A	S	N	R	A	T	26
PD1B183	D	A	S	N	R	A	T	26
PD1B184	D	A	S	N	R	A	T	26
PD1B185	D	A	S	D	R	A	T	27
PD1B187	D	A	S	N	R	A	T	26
PD1B71	D	A	S	N	R	A	T	26
PD1B177	D	A	S	N	R	A	T	26
PD1B70	D	A	S	N	R	A	T	26
PD1B175	D	A	S	N	R	A	T	26
PD1B194	D	A	S	Y	R	A	T	28
PD1B195	D	A	S	N	R	A	T	26
PD1B196	D	A	S	N	R	A	T	26
PD1B197	D	A	S	N	R	A	T	26
PD1B198	D	A	S	S	R	A	T	29
PD1B199	D	A	S	T	R	A	T	30
PD1B200	D	A	S	N	R	A	T	26
PD1B201	D	A	S	N	R	A	T	26
LCDR2 genus	D	A	S	X ₁₄	R	A	T	87

PD-1 mAb LCDR2 genus

DASX₁₄RAT (SEQ ID NO: 87),

wherein

X₁₄ is N, D, Y, S or T.

Figure 12.

Antibody	LCDR3									SEQ ID NO:
	Sequence									
PD1B114	Q	Q	R	S	N	W	P	L	T	31
PD1B149	Q	Q	R	N	Y	W	P	L	T	32
PD1B160	Q	Q	R	G	N	W	P	L	T	33
PD1B162	Q	Q	R	E	Y	W	P	L	T	34
PD1B164	Q	Q	R	D	Y	W	P	L	T	35
PD1B11	Q	Q	R	S	N	W	P	L	T	31
PD1B183	Q	Q	R	G	Y	W	P	L	T	36
PD1B184	Q	Q	R	N	Y	W	P	L	T	32
PD1B185	Q	Q	R	W	N	W	P	L	T	37
PD1B187	Q	Q	R	N	Y	W	P	L	T	32
PD1B71	Q	Q	R	S	N	W	P	L	T	31
PD1B177	Q	Q	R	S	N	W	P	L	T	31
PD1B70	Q	Q	R	S	N	W	P	L	T	31
PD1B175	Q	Q	R	S	N	W	P	L	T	31
PD1B194	Q	Q	R	D	Y	W	P	L	T	35
PD1B195	Q	Q	R	E	Y	W	P	L	T	34
PD1B196	Q	Q	R	N	Y	W	P	L	T	32
PD1B197	Q	Q	R	A	Y	W	P	L	T	38
PD1B198	Q	Q	R	A	E	W	P	L	T	39
PD1B199	Q	Q	R	N	Y	W	P	L	T	32
PD1B200	Q	Q	R	S	A	W	P	L	T	40
PD1B201	Q	Q	R	N	Y	W	P	L	T	32
LCDR3 genus	Q	Q	R	X ₁₅	X ₁₆	W	P	L	T	88

PD-1 mAb LCDR3 genus:

QQRX₁₅X₁₆WPLT (SEQ ID NO: 88),

wherein

X₁₅ is S, N, G, E, D, W, E or A; and

X₁₆ is N, Y, E or A.

Figure 13.

mAb name	HCDR1						SEQ ID NO:
	Sequence						
TM3B103	N	Y	W	M	S		90
TM3B105	S	Y	A	M	S		91
TM3B109	S	Y	A	M	S		91
TM3B108	G	Y	W	M	H		92
TM3B113	D	Y	W	M	S		93
HCDR1 genus	X ₁₇	Y	X ₁₈	M	X ₁₉		164

TIM3 mAb HCDR1 genus:

X₁₇YX₁₈MX₁₉ (SEQ ID NO: 164),

Wherein

X₁₇ is N, S, G or D;

X₁₈ is W or A; and

X₁₉ is S or H.

Figure 14.

mAb	HCDR2																	SEQ ID NO:
	Sequence																	
TM3B103	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B105	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B109	A	I	S	G	S	G	G	S	T	Y	Y	A	D	S	V	K	G	99
TM3B108	A	I	S	Y	S	G	S	S	T	Y	Y	A	D	S	V	K	G	100
TM3B113	V	I	K	Y	S	G	G	S	K	Y	Y	A	D	S	V	K	G	101
HCDR2 genus	X ₂₀	I	X ₂₁	X ₂₂	S	G	G	S	X ₂₃	Y	Y	A	D	S	V	K	G	165

TIM-3 mAb HCDR2 genus

X₂₀IX₂₁X₂₂SGGSX₂₃YYADSVKG (SEQ ID NO: 165),

wherein

X₂₀ is A or V;

X₂₁ is S or K;

X₂₂ is G or Y; and

X₂₃ is T or K.

Figure 15.

mAb	HCDR3										
	Sequence										SEQ ID NO:
TM3B103	D	H	W	D	P	N	F	L	D	Y	107
TM3B105	S	P	-	-	Y	A	P	L	D	Y	108
TM3B109	N	E	E	P	D	D	R	L	D	Y	109
TM3B108	G	T	N				W	L	D	Y	110
TM3B113	E	L	E			G	V	F	D	Y	111
HCDR3 genus	X ₂₄	X ₂₅	X ₂₆	X ₂₇	X ₂₈	X ₂₉	X ₃₀	X ₃₁	D	Y	166

X₂₄X₂₅X₂₆X₂₇X₂₈X₂₉X₃₀X₃₁DY (SEQ ID NO: 166),

wherein

X₂₄ is D, S, N, G or E;

X₂₅ is H, P, E, T or L;

X₂₆ is W, E, N or deleted;

X₂₇ is D, P or deleted;

X₂₈ is P, Y, D or deleted;

X₂₉ is N, A, D, G or deleted;

X₃₀ is F, P, R, W or V; and

X₃₁ is L or F.

Figure 16.

mAb	LCDR1																	
	Sequence																	SEQ ID NO:
TM3B103	R	A	S	Q	S	V	S	S	-					S	Y	L	A	117
TM3B105	R	A	S	Q	S	V	N	-						D	Y	L	A	118
TM3B109	K	S	S	Q	S	V	L	A	S	S	N	N	K	N	Y	L	A	119
TM3B108	R	A	S	Q	S	V	S	S						S	Y	L	A	117
TM3B113	R	A	S	Q	S	V	S	N						S	T	L	A	120
LCDR1 genus	X ₃₂	X ₃₃	S	Q	S	V	X ₃₄	X ₃₅	X ₃₆	X ₃₇	X ₃₈	X ₃₉	X ₄₀	X ₄₁	X ₄₂	L	A	167

X₃₂X₃₃SQSVX₃₄X₃₅X₃₆X₃₇X₃₈X₃₉X₄₀X₄₁X₄₂LA (SEQ ID NO: 167),

wherein

X₃₂ is R or K;

X₃₃ is A or S;

X₃₄ is S, N or L;

X₃₅ is S, A, N or deleted;

X₃₆ is S or deleted;

X₃₇ is S or deleted;

X₃₈ is N or deleted;

X₃₉ is N or deleted;

X₄₀ is K or deleted;

X₄₁ is S, D or N; and

X₄₂ is Y or T.

Figure 17.

mAb	LCDR2							
	Sequence							SEQ ID NO:
TM3B103	G	A	S	S	R	A	T	126
TM3B105	D	A	S	N	R	A	T	127
TM3B109	W	A	S	T	R	E	S	128
TM3B108	G	A	S	S	R	A	T	126
TM3B113	T	A	S	S	R	A	T	129
LCDR2 genus	X ₄₃	A	S	X ₄₄	R	X ₄₅	X ₄₆	168

TIM-3 mAb LCDR2 genus

X₄₃ASX₄₄RX₄₅X₄₆ (SEQ ID NO: 168),

wherein

X₄₃ is G, D, W or T;

X₄₄ is S, N or T;

X₄₅ is A or E; and

X₄₆ is T or S.

Figure 18.

mAb	LCDR3									
	Sequence									SEQ ID NO:
TM3B103	Q	Q	Y	G	S	S	P	L	T	135
TM3B105	Q	Q	G	G	H	A	P	I	T	136
TM3B109	Q	Q	Y	Y	S	T	P	L	T	137
TM3B108	Q	Q	Y	G	S	S	P	L	T	138
TM3B113	Q	Q	S	Y	T	S	P	W	T	139
LCDR3 genus	Q	Q	X ₄₇	X ₄₈	X ₄₉	X ₅₀	P	X ₅₁	T	169

QQX₄₇X₄₈X₄₉X₅₀PX₅₁T (SEQ ID NO: 169),

wherein

X₄₇ is Y, G or S;

X₄₈ is G or Y;

X₄₉ is S, H or T;

X₅₀ is S, A or T; and

X₅₁ is L, I or W.

Figure 19A.

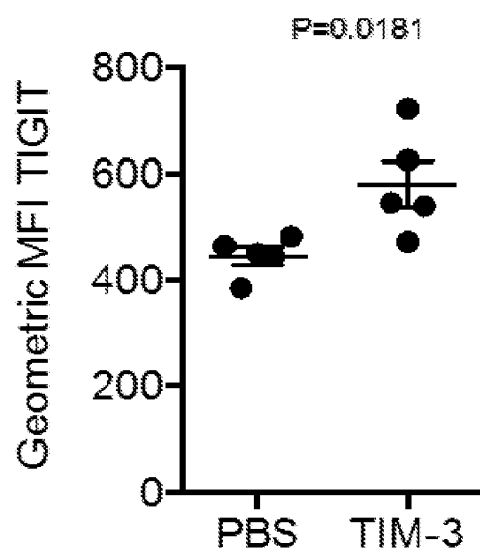


Figure 19B.

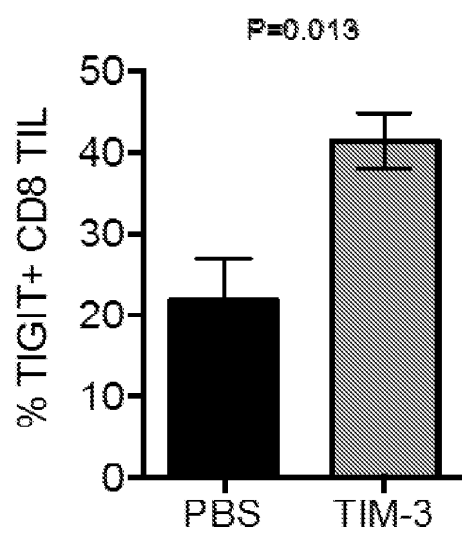


Figure 20A.

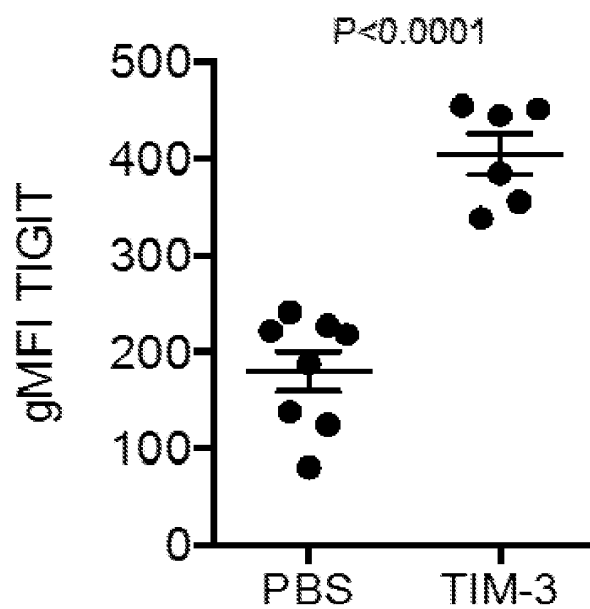


Figure 20B.

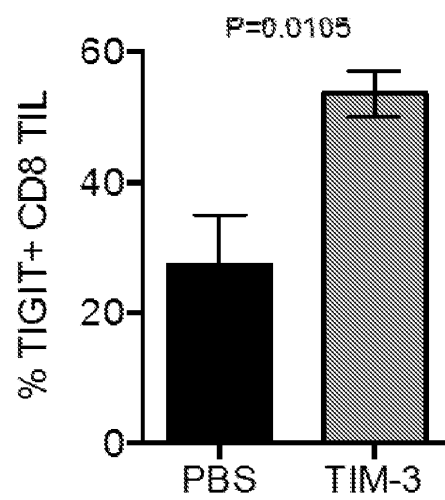


Figure 21.

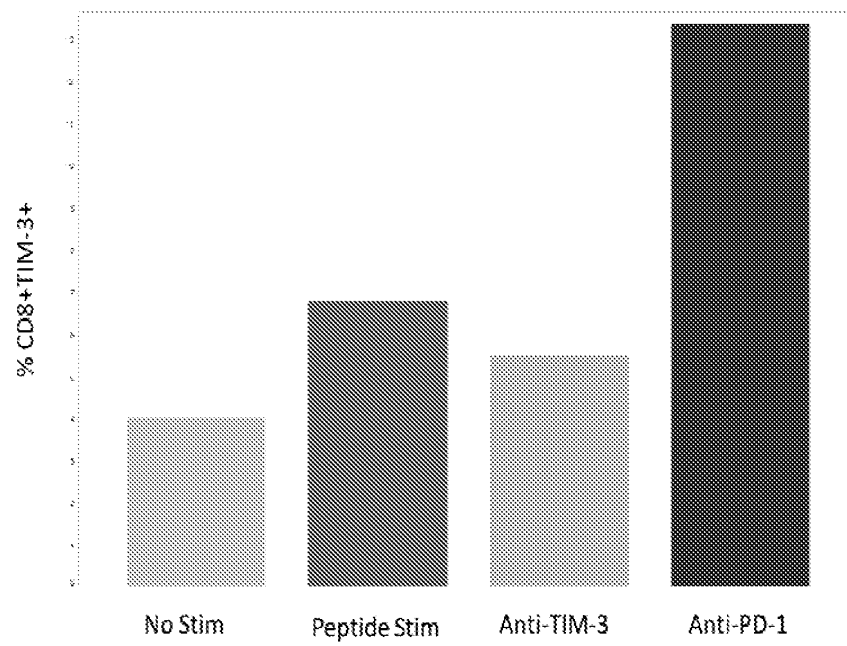


Figure 22A.

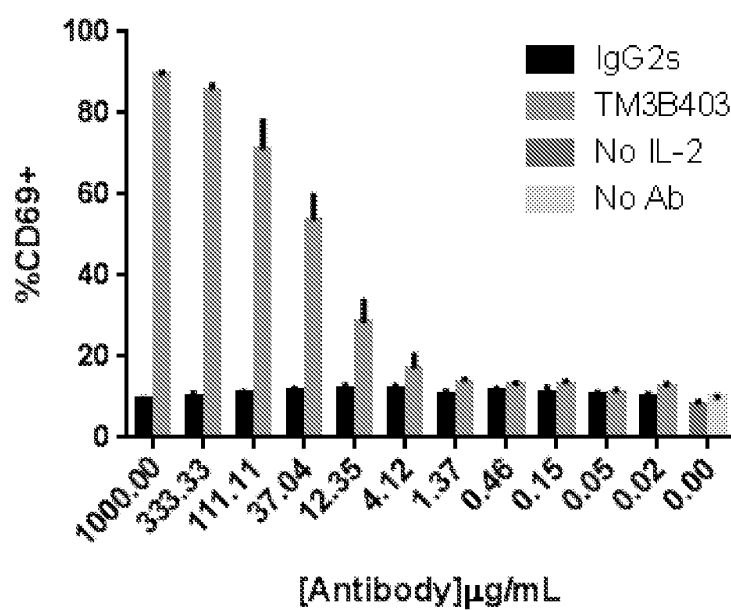


Figure 22B.

