

[図1]

共通軽鎖 Common Light Chain	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
可変領域 Variable Region	25	DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPKGAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPT FGQGTKVEIK
定常領域 Constant Region	29	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSITYLSSTLTLSKADYEKHKVYACEVTHQ GLSSPVTKSFNRGEC

[図2]

共通軽鎖 Common Light Chain	配列番号 SEQ ID No.	CDR1	配列番号 SEQ ID No.	CDR2	配列番号 SEQ ID No.	CDR3
CDRs	26	RASQSISSYLN	27	AASSLQS	28	QQSYSTPPT

[図3]

生殖系列 V 遺伝子	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
IGHV7-4-1	21	QVQLVQSGSELKKPGASVKVSCKASGYTFTSYAMNWVRQ APGQGLEWMGWINTNTGNPTYAQGFTGRFVFSLDTSVST AYLQICSLKAEDTAVYYCAR
IGHV5-51	22	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQM PGKGLEWMGHIYPGDS DTRYSPSFQGV TISADKSISTAYLQ WSSLKASDTAMYYCAR

[図4]

PD1-1 ~ PD1-5 各 VH および IGHV7-4-1/JH6c とのアラインメント

	FR1	CDR1	FR2	CDR2
IGHV7-4-1 (SEQ ID No. 21)	QVQLVQSGSELKKPGASVKVSCKASGYTFT	SYAMN	WVRQAPCQGLEWMC	WINTNTGNPTYAQGFTG
PD1-1 VH (SEQ ID No. 1)	Q	H-GLH		L-E-F
PD1-2 VH (SEQ ID No. 2)	Q V	H-GLH		
PD1-3 VH (SEQ ID No. 3)	M	H-LH		L-E
PD1-4 VH (SEQ ID No. 4)	Q	H-LH	L	L-E-F
PD1-5 VH (SEQ ID No. 5)	Q	H-LH	L	L-E-F

	FR3	CDR3	FR4
IGHV7-4-1 (SEQ ID No. 21)	RFVPSLDTSVSTAYLQICSLKAEDTAVYYCAR		
D gene (unknown)			
JH6c		HYYYYYYMDV	WGKGTIVTVSS
PD1-1 VH (SEQ ID No. 1)	T S	GDMVVPPTIWN-HF	N-L
PD1-2 VH (SEQ ID No. 2)	S	GDLVVPPTIWN-H-E	L
PD1-3 VH (SEQ ID No. 3)	T N	GDMVVPPTIWN	
PD1-4 VH (SEQ ID No. 4)	T S	GDMVVPPTIWN-HF	N
PD1-5 VH (SEQ ID No. 5)	T S	GDMVVPPTIWN-HF	Q

[図5]

CD19-1～CD19-6 各 VH および IGHV5-51 とのアラインメント

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          -----FR1-----      CDR1-      -----FR2-----      -----CDR2-----
IGHV5-51 (SEQ ID No. 22) |EVQLVQSGAEVKKPGESLKISCKSGYSFT| |SYWIG| |WVRQMPGKGLWWMG| |IIYPGDSDFRYSPSPQG|
CD19-5 VH (SEQ ID No. 30) |Q-----| |---| |-----| |-----|
CD19-1 VH (SEQ ID No. 31) |-----| |---| |-----| |-----|
CD19-4 VH (SEQ ID No. 32) |Q-----S-----F---| |---A| |-----| |-----|
CD19-2 VH (SEQ ID No. 33) |Q-----I---| |---| |-----| |---W-----|
CD19-3 VH (SEQ ID No. 34) |-----| |---| |-----| |-----|
CD19-6 VH (SEQ ID No. 62) |Q-----| |---| |-----| |-----|

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          -----FR3-----      -----CDR3-----      -----FR4-----
IGHV5-51 (SEQ ID No. 22) |QVTISADKSISTAYLQWSSLKASDTAMYYCAR
CD19-5 VH (SEQ ID No. 30) |-----I---| |KTIQGVMTAFDI| |WGQGTMTVYSS
CD19-1 VH (SEQ ID No. 31) |-----V---| |QTIIVTMNAFDI| |WGQGTITVYSS
CD19-4 VH (SEQ ID No. 32) |-----FT---N-----I---| |HTIYATIYNADF| |WGQGTMTVYSS
CD19-2 VH (SEQ ID No. 33) |-----NV-----L---V---| |QTIYATTGLAFDI| |WGQGTITVYSS
CD19-3 VH (SEQ ID No. 34) |-----N-----| |RTIYATIHWASDY| |WGQGTMTVYSS
CD19-6 VH (SEQ ID No. 62) |-----I---| |KTIQGVMTAFDI| |WGRGTMTVYSS

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[図6]

クローン番号 Clone No.	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
PD1-1	1	QVQLVQSGSELKQPGASVKVSKASGYTFTHYGLHWVRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWGNGLTVTVSS
PD1-2	2	QVQLVQSGSELKQPGVSVKVSCKASGYTFTHYGLHWVRQAPGQGLEWMGWINT NTGNPTYAQGFTGRFVFLDTSVSTAYLQISSLKAEDTAVYYCARGDLVVPPTIWN YYHYMEVWGKGLTVTVSS
PD1-3	3	QVQLVQSGSELKQPGASVMVSKASGYTFTHYALHWVRQAPGQGLEWMGWLNT NTENPTYAQGFTGRFVFLDTSVTTAYLQINSLKAEDTAVYYCARGDMVVPPTIW NYYYYMDVWGKGTITVTVSS
PD1-4	4	QVQLVQSGSELKQPGASVKVSKASGYTFTHYALHWLRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWGNGITVTVSS
PD1-5	5	QVQLVQSGSELKQPGASVKVSKASGYTFTHYALHWLRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWQGTTVTVSS

[図7]

クローン番号 Clone No.	配列番号 SEQ ID No.	CDR1	配列番号 SEQ ID No.	CDR2	配列番号 SEQ ID No.	CDR3
PD1-1	6	HYGLH	7	WLNTNTENPTFAQGFTG	8	GDMVVPPTIWNYYHFMDV
PD1-2	9	HYGLH	10	WINTNTGNPTYAQGFTG	11	GDLVVPPTIWNYYHYMEV
PD1-3	12	HYALH	13	WLNTNTENPTYAQGFTG	14	GDMVVPPTIWNYYYYMDV
PD1-4	15	HYALH	16	WLNTNTENPTFAQGFTG	17	GDMVVPPTIWNYYHFMDV
PD1-5	18	HYALH	19	WLNTNTENPTFAQGFTG	20	GDMVVPPTIWNYYHFMDV

[図8]

クローン番号 Clone No.	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
CD19-5	30	QVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMG IYPGDS DTRYSPSFQGGQVTISADKSISTAYLQWSSLKASDTAIYYCARKTI VGVVMTAFDIWGGQTMVTSS
CD19-1	31	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMG IYPGDS DTRYSPSFQGGQVTISADKSISTAYLQWSSLKASDTAMYYCVRQT IVATVMNAFDIWGGQTTVTSS
CD19-4	32	QVQLVQSGAEVKKSGESLKISCKGSGFSFTSYWIAWVRQMPGKGLEWMG IYPGDS DTRYSPSFQGGQVTISADKSFTTAYLQWNSLKASDTAIYYCARHT IVATIYNADFWDGQGTMTVSS
CD19-2	33	QVQLVQSGAEVKKPGESLKISCKGSGYSFISYWIGWVRQMPGKGLEWMGI IWPGDS DTRYSPSFQGGQVTISADKSINVAYLQWSSLKASDTALYYCVRQTI VATTGLAFDIWGGQTLVTSS
CD19-3	34	EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMG IYPGDS DTRYSPSFQGGQVTISADKSINTAYLQWSSLKASDTAMYYCARRT IVATIHWASDYWGQGTMTVSS
CD19-6	62	QVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQMPGKGLEWMG IYPGDS DTRYSPSFQGGQVTISADKSISTAYLQWSSLKASDTAIYYCARKTI VGVVMTAFDIWGRGTMVTSS

[図9]

クローン番号 Clone No.	配列番号 SEQ ID No.	CDR1	配列番号 SEQ ID No.	CDR2	配列番号 SEQ ID No.	CDR3
CD19-5	35	SYWIG	36	IYPGDS DTRYSPSFQG	37	KTIVGVVMTAFDI
CD19-1	38	SYWIG	39	IYPGDS DTRYSPSFQG	40	QTIVATVMNAFDI
CD19-4	41	SYWIA	42	IYPGDS DTRYSPSFQG	43	HTIVATIYNADF
CD19-2	44	SYWIG	45	IWPGDS DTRYSPSFQG	46	QTIVATTGLAFDI
CD19-3	47	SYWIG	48	IYPGDS DTRYSPSFQG	49	RTIVATIHWASDY

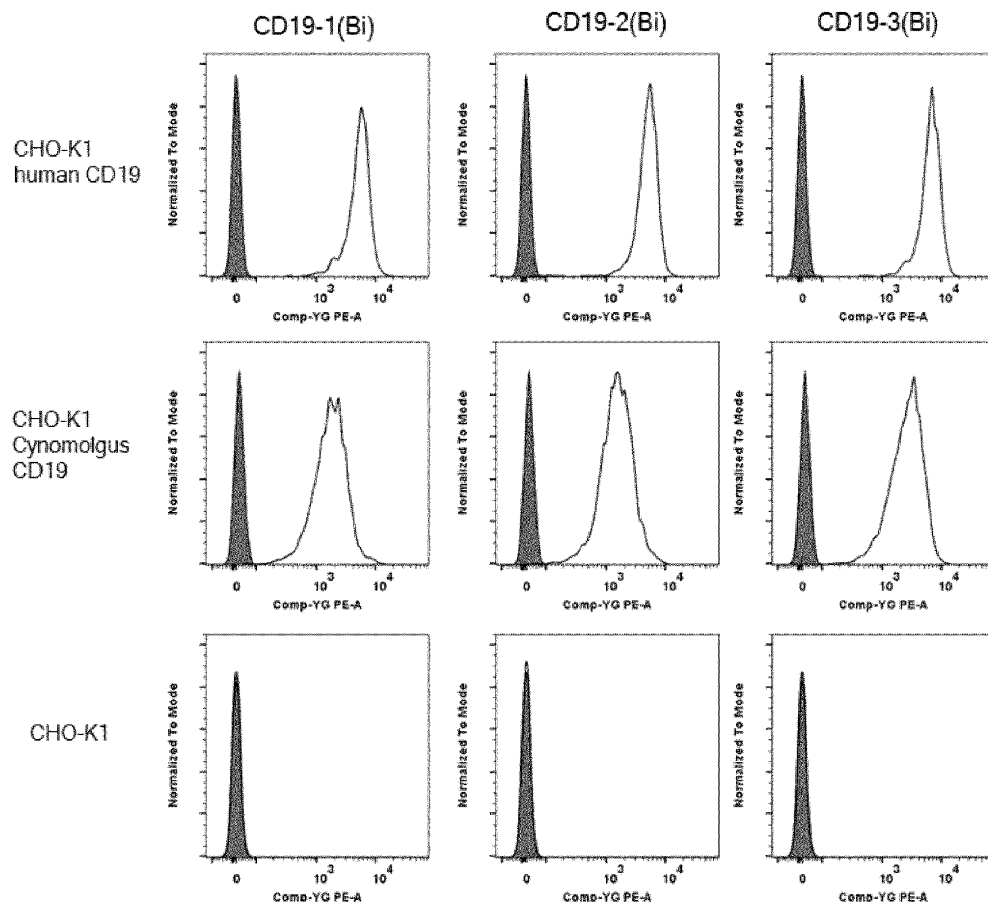
[図10]

	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
PD-1を特異的に認識する第二アームの重鎖可変領域を有する重鎖の定常領域	23	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHITCPP CPAPELGRGSPVFLPPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISK AKGQPREPQVYITDPPSRREEMTKNQVSLTCEVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFELYSKLTVDKSRWQQGNVSCFVSMHEALHNHYTQKSLSLSPG
CD19を特異的に認識する第二アームの重鎖可変領域を有する重鎖の定常領域	24	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHITCPP CPAPELGRGSPVFLPPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISK AKGQPREPQVYITDPPSRREEMTKNQVSLKCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFELYSKLTVDKSRWQQGNVSCFVSMHEALHNHYTQKSLSLSPG
CD19を特異的に認識する第二アームの重鎖可変領域を有する重鎖の定常領域	71	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSCDKTHITCPP CPAPELGRGSPVFLPPKPKDITLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVE VHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKVSNKALPAPIEKTIISK AKGQPREPQVYITDPPSRREEMTKNQVSLKCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFELYSKLTVDKSRWQQGNVSCFVSMHEALHNHYTQKSLSLSPGK GKKA

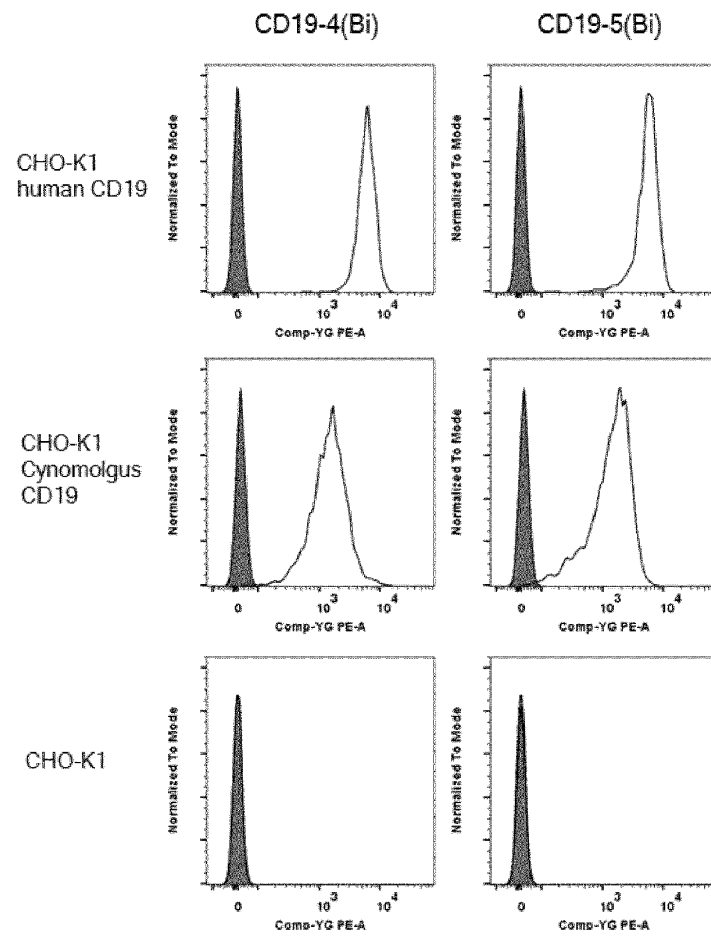
[図11]

クローン番号 Clone No.	Human CD19 Kd (nmol/L)	Human PD-1 Kd (nmol/L)
CD19-1(Bi)	11.3	7.6
CD19-2(Bi)	13.6	6.7
CD19-3(Bi)	5.7	6.8
CD19-4(Bi)	12.5	6.7
CD19-5(Bi)	6.6	7.6
CD19-6(Bi)	3.1	1.4

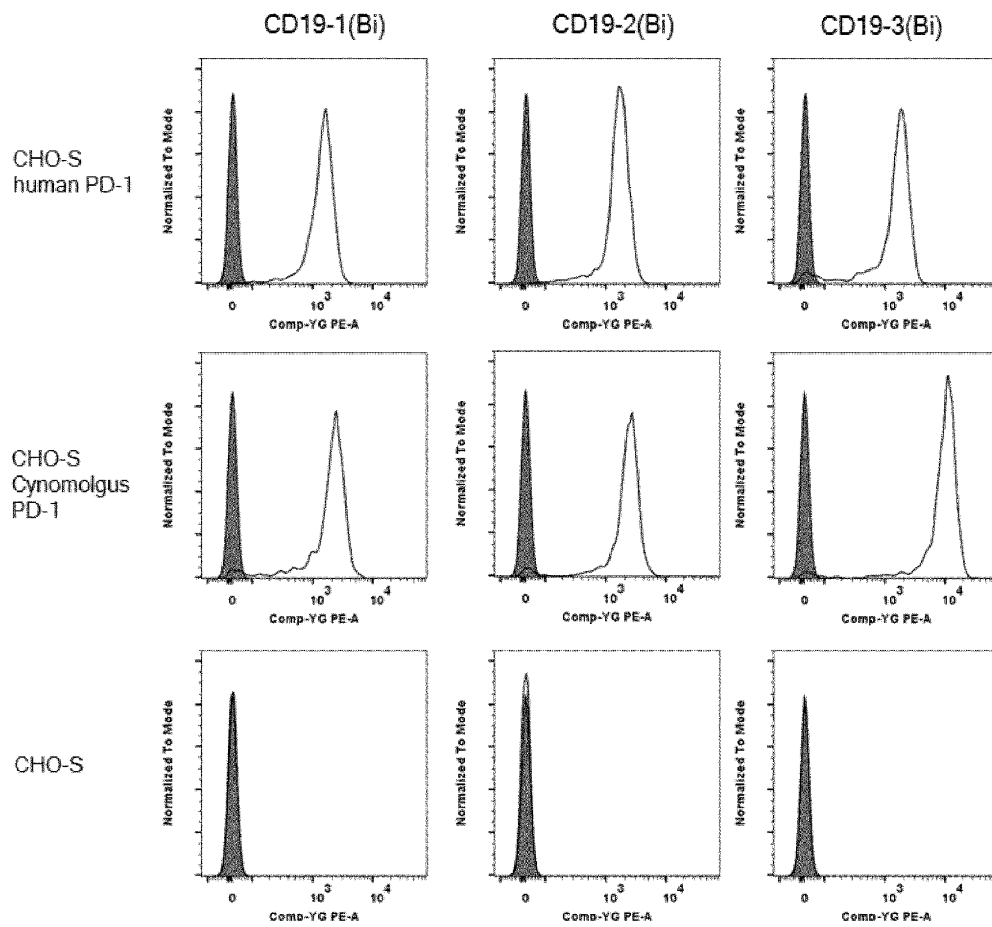
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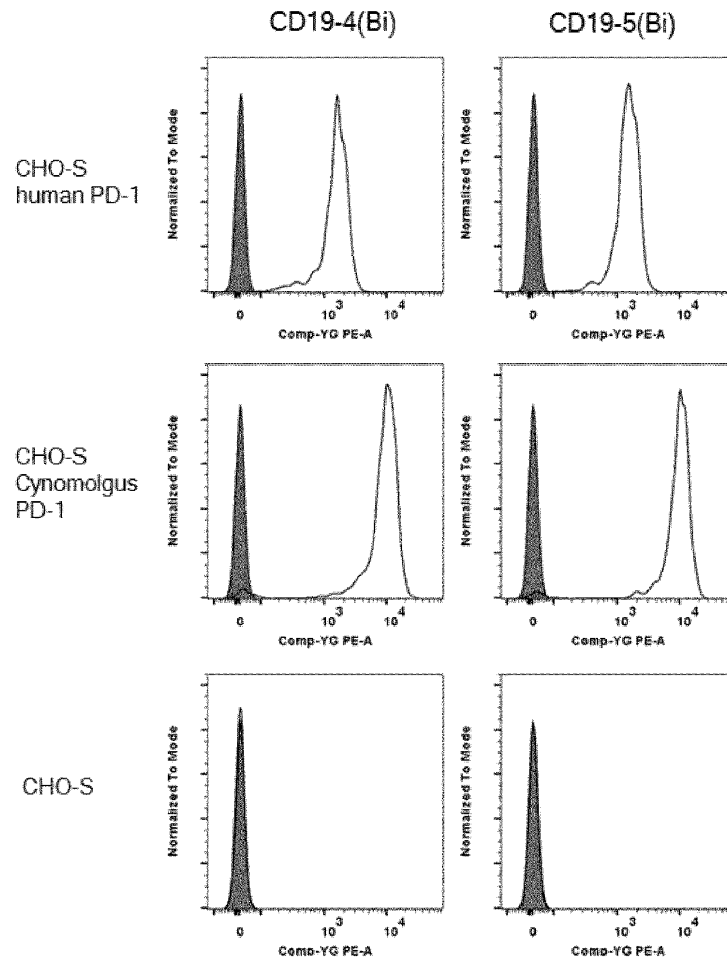
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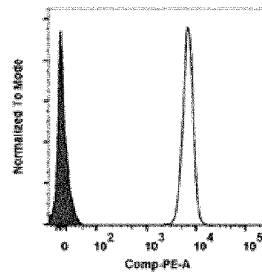
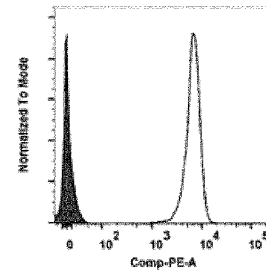
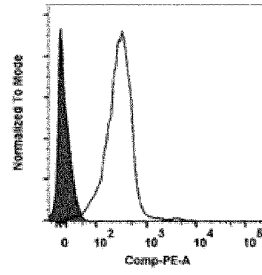
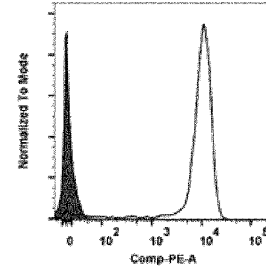
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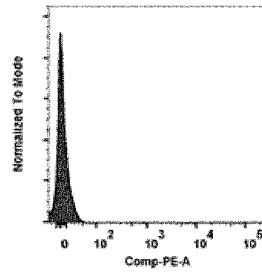
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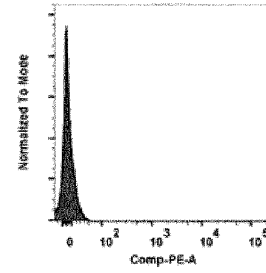
[図16]

CHO-K1
human CD19CHO-S
human PD-1CHO-K1
cynomolgus CD19CHO-S
cynomolgus PD-1

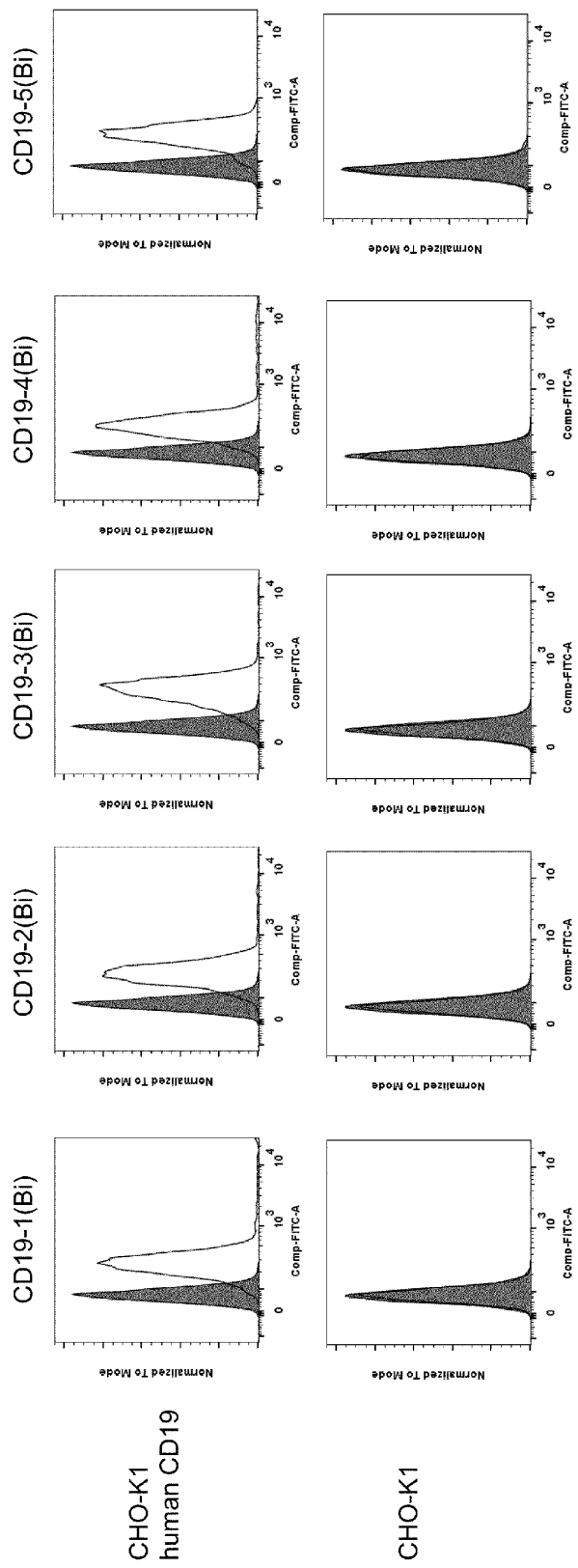
CHO-K1



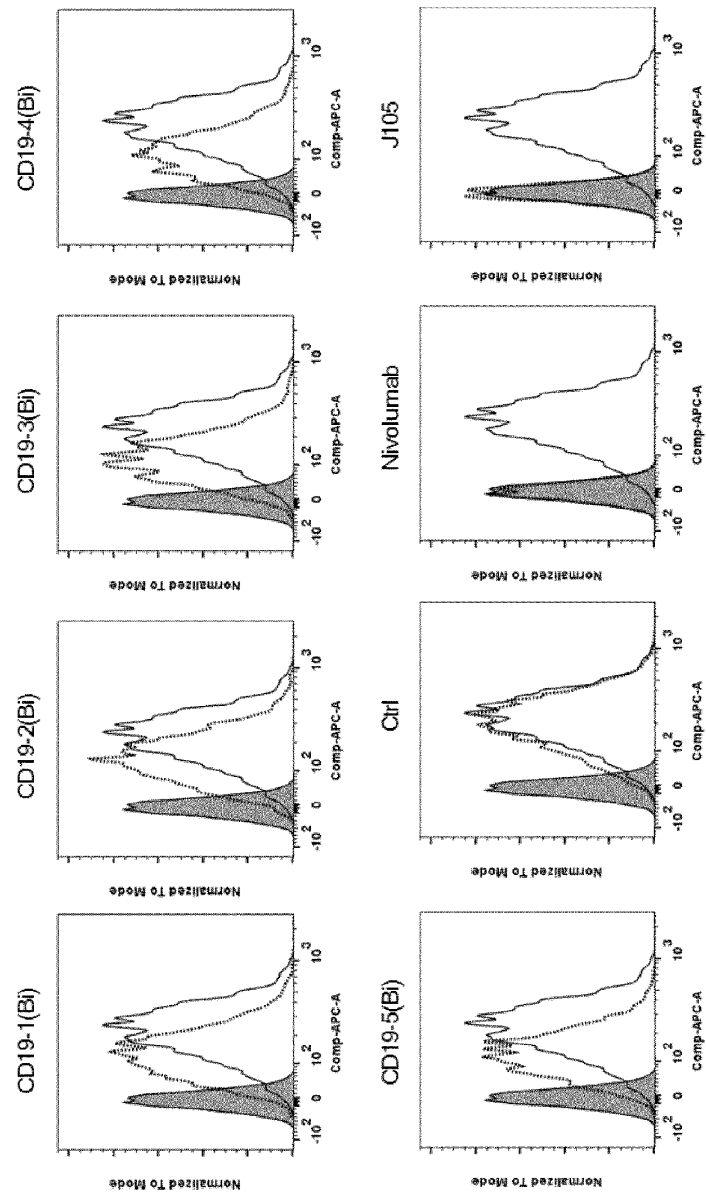
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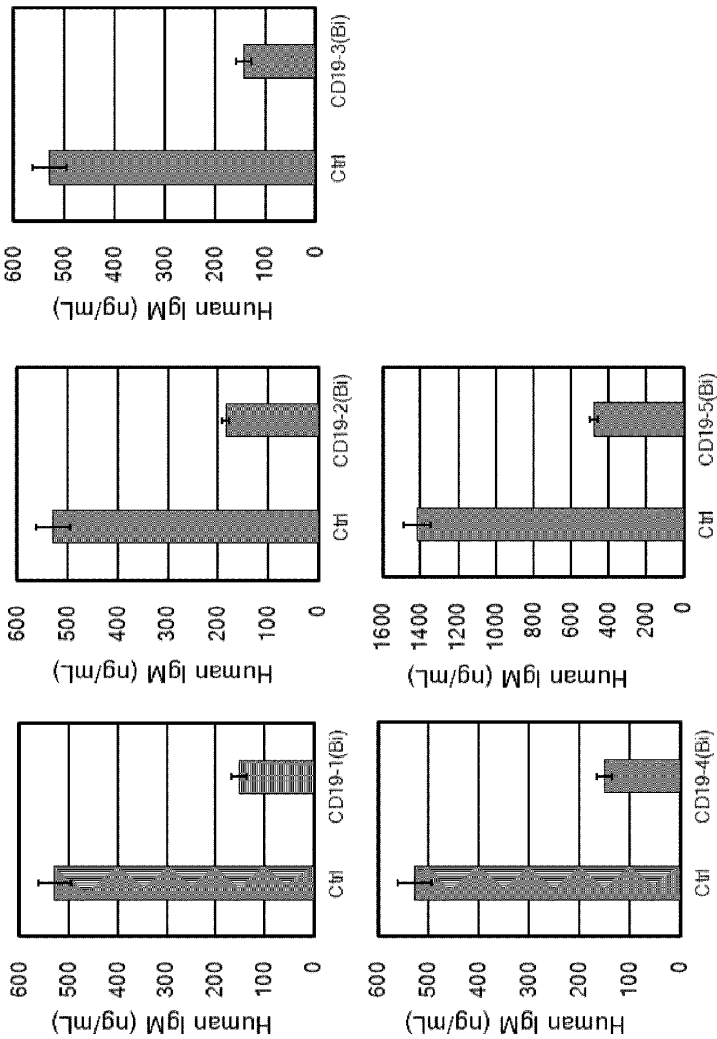
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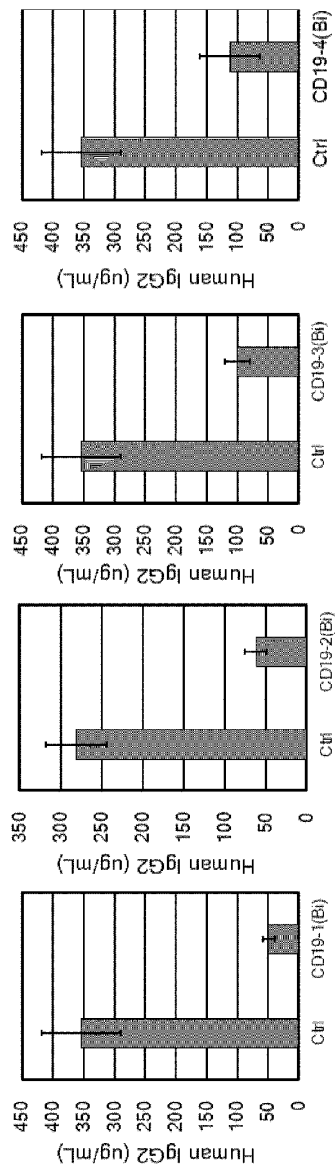
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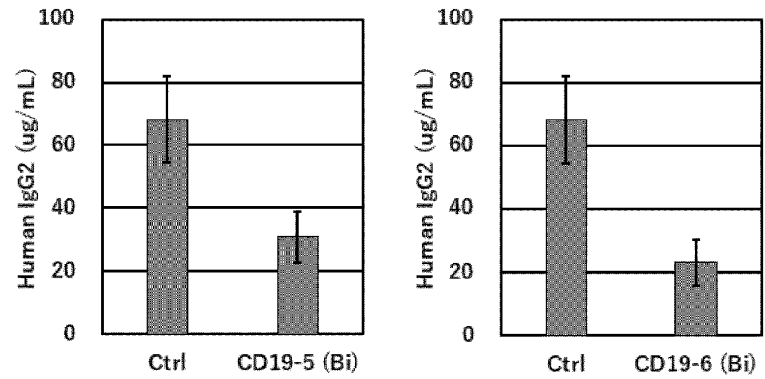
[図19]



[図20]



[図21]



[図22]

