

[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	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLI YAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPT FGQGTKVEIK
定常領域 Constant Region	29	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDSYSLSTLTLSKADYEKHKVYACEVTHQ 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	QVQLVQSGSELKKPGASVKVSKASGYTFTSYAMNWWVRQAP GQGLEWMGWINTNTGNPTYAQGFTGRFVSLDTSVSTAYLQI CSLKAEDTAVYYCAR
IGHV3-33	22	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPG KGLEWVAVIWYDGSNKYYADSVKGRFTISRDN SKNTLYLQM NSLRAEDTAVYYCAR

[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)	QVQLVQSGSELKKPGASVKVSKASGYTFTSYAMN	WVRQAPGQGLEWMG	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-E-F	
PD1-5 VH (SEQ ID No. 5)	Q	H-LH	L-E-F	

	FR3	CDR3	FR4
IGHV7-4-1 (SEQ ID No. 21)	RPVPSLDTSVSTAYLQICSLKAEDTAVYYCAR		
D gene (unknown)			
JH6c		HYYYYYMDV	WGKGTTTVSS
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]

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	QVQLVQSGSELKQPGASVKVSCASGYTFTHYGLHWVRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFSLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWNGTLVTVSS
PD1-2	2	QVQLVQSGSELKQPGVSVKVSCKASGYTFTHYGLHWVRQAPGQGLEWMGWINT NTGNPTYAQGFTGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARGDLVVPPTIWN YYHYMEVWVGKGLVTVSS
PD1-3	3	QVQLVQSGSELKQPGASVMVSCASGYTFTHYALHWVRQAPGQGLEWMGWLNT NTENPTYAQGFTGRFVFSLDTSVTTAYLQINSLKAEDTAVYYCARGDMVVPPTIWN NYYYYMDVWVGKGLTVTVSS
PD1-4	4	QVQLVQSGSELKQPGASVKVSCASGYTFTHYALHWLRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFSLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWNGGLTVTVSS
PD1-5	5	QVQLVQSGSELKQPGASVKVSCASGYTFTHYALHWLRQAPGQGLEWMGWLNT NTENPTFAQGFTGRFVFSLDTSVTTAYLQISSLKAEDTAVYYCARGDMVVPPTIWN YYHFMDVWVGQGLTVTVSS

[図6]

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	GDMVVPTTIWNYYHFMDV
PD1-2	9	HYGLH	10	WINTNTGNPTYAQGFTG	11	GDLVVPPTIWNYYHYMEV
PD1-3	12	HYALH	13	WLNTNTENPTYAQGFTG	14	GDMVVPTTIWNYYYYMDV
PD1-4	15	HYALH	16	WLNTNTENPTFAQGFTG	17	GDMVVPTTIWNYYHFMDV
PD1-5	18	HYALH	19	WLNTNTENPTFAQGFTG	20	GDMVVPTTIWNYYHFMDV

[図7]

クローン番号 Clone No.	配列番号 SEQ ID No.	アミノ酸配列 Amino Acid Sequence
CD3-2	36	QVQLVQSGGGVVPGRSLRLSCVASGFTFSSYGMHWVRQAPGKGLEWVAQI WYNARKQEYSDSVKGRFTISRDNLSKNTLYLQMNSLRAEDTAVYYCTRGTGY NWFDPWVGQGLTVTVSS

[図8]

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
CD3-2	37	SYGMH	38	QIWNARKQEYSDSVKG	39	GTGYNWFDP

[図9]

	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一アームの重鎖可変領域を有する重鎖の定常領域	23	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT YICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGRG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKISKAKGQPREPQVYTDPPSREE MTKNQVSLTCEVKGFPYSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH YTQKSLSLSPG
CD3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	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT YICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGRG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKISKAKGQPREPQVYTKPPSREE MTKNQVSLKCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH YTQKSLSLSPG
PD-1を特異的に認識する第一アームの重鎖可変領域を有する重鎖の改変定常領域	45	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT YICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGRG PSVFLFPPKPKDTLDIRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKISKAKGQPREPQVYTDPPSREE MTKNQVSLTCEVKGFPYSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH YTQKSLSLSPG
CD3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改変定常領域	51	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT YICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELGRG PSVFLFPPKPKDTLDIRTPEVTCVVVDVSHEDPEVKFNWY VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKISKAKGQPREPQVYTKPPSREE MTKNQVSLKCLVKGFYPSDIAVEWESNGQPENNYKTTTP VLDSGDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNH YTQKSLSLSPG

[図10]

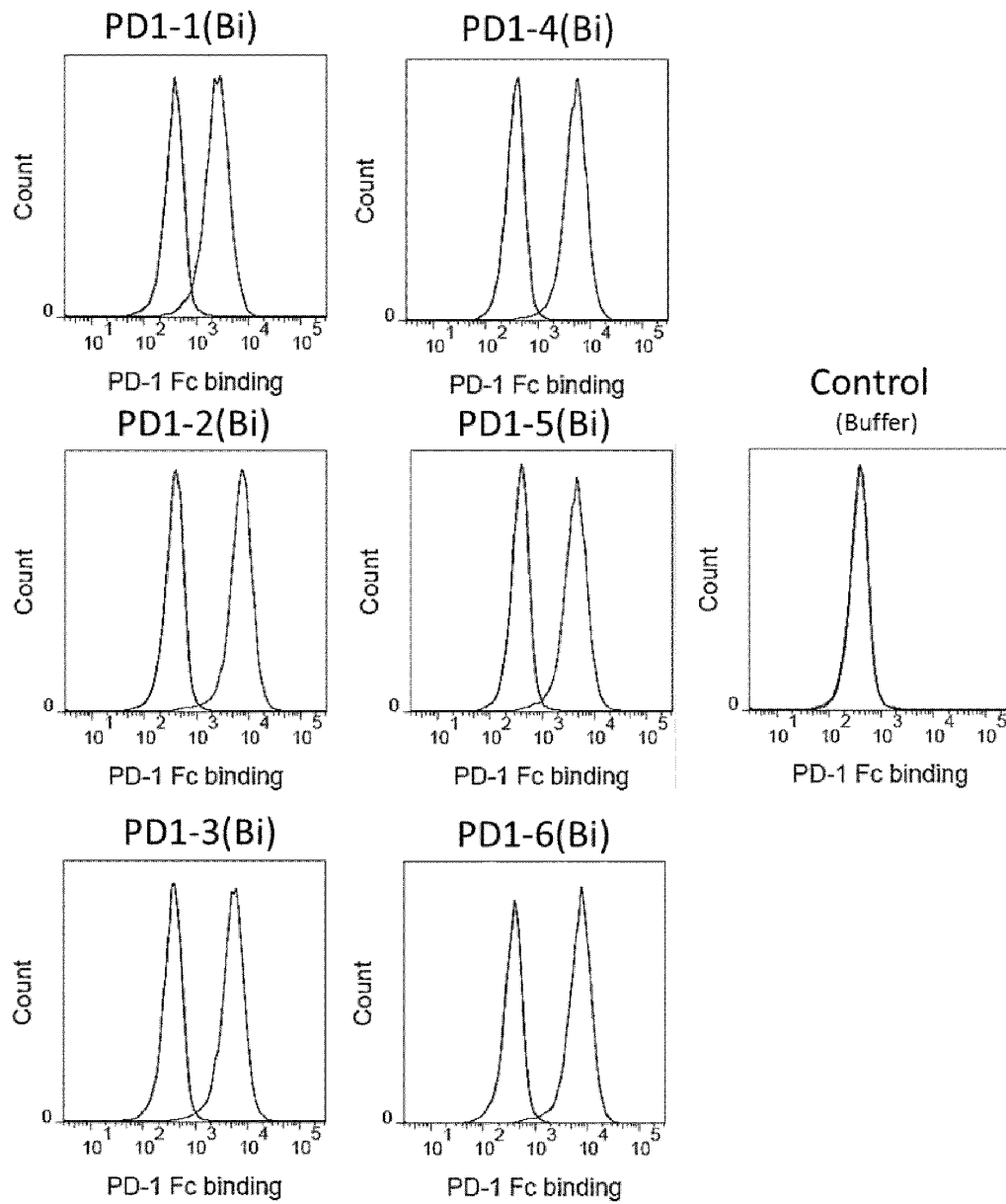
クローン15C3のVHのアミノ酸配列：

QVQLVQSGGIVVPGRSLRLSCVASGFTFSSYGMHWVRQAPGKGLEWVAIIWYNGRKQDYADSVKGRFTISRDN SKN
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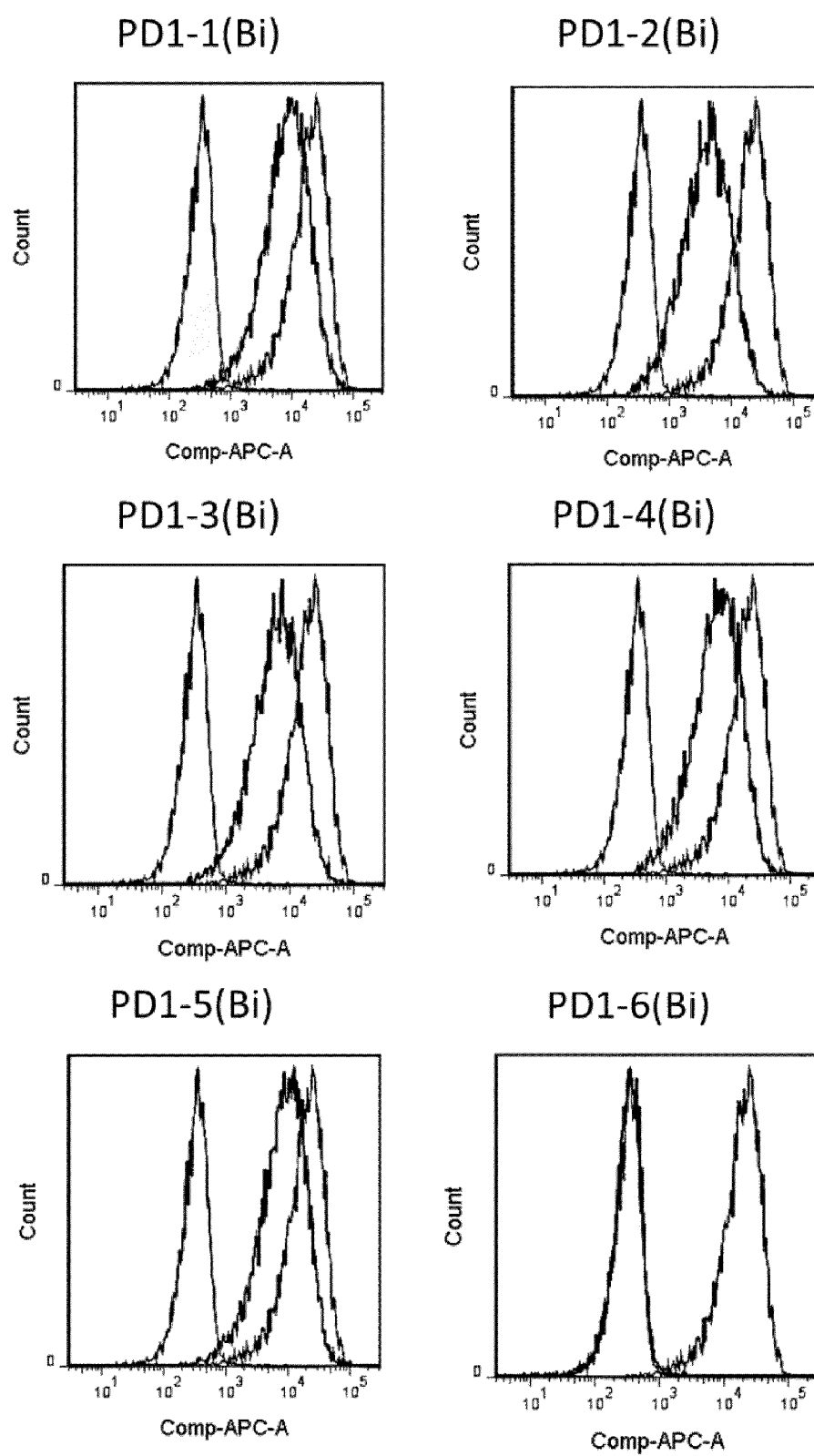
[図11]

第一アームのPD-1結合活性		
クローンNo.	ヒトPD-1	カニクイザルPD-1
	Kd (nmol/L)	Kd (nmol/L)
PD1-1(Bi)	0.6	0.3
PD1-2(Bi)	0.7	0.4
PD1-3(Bi)	3.8	2.0
PD1-4(Bi)	0.9	0.7
PD1-5(Bi)	0.7	0.4
PD1-6(Bi)	0.8	21.8
第二アームのCD3結合活性		
クローンNo.	ヒトCD3δ/CD3ε	
	Kd (nmol/L)	
CD3-2	19.2	

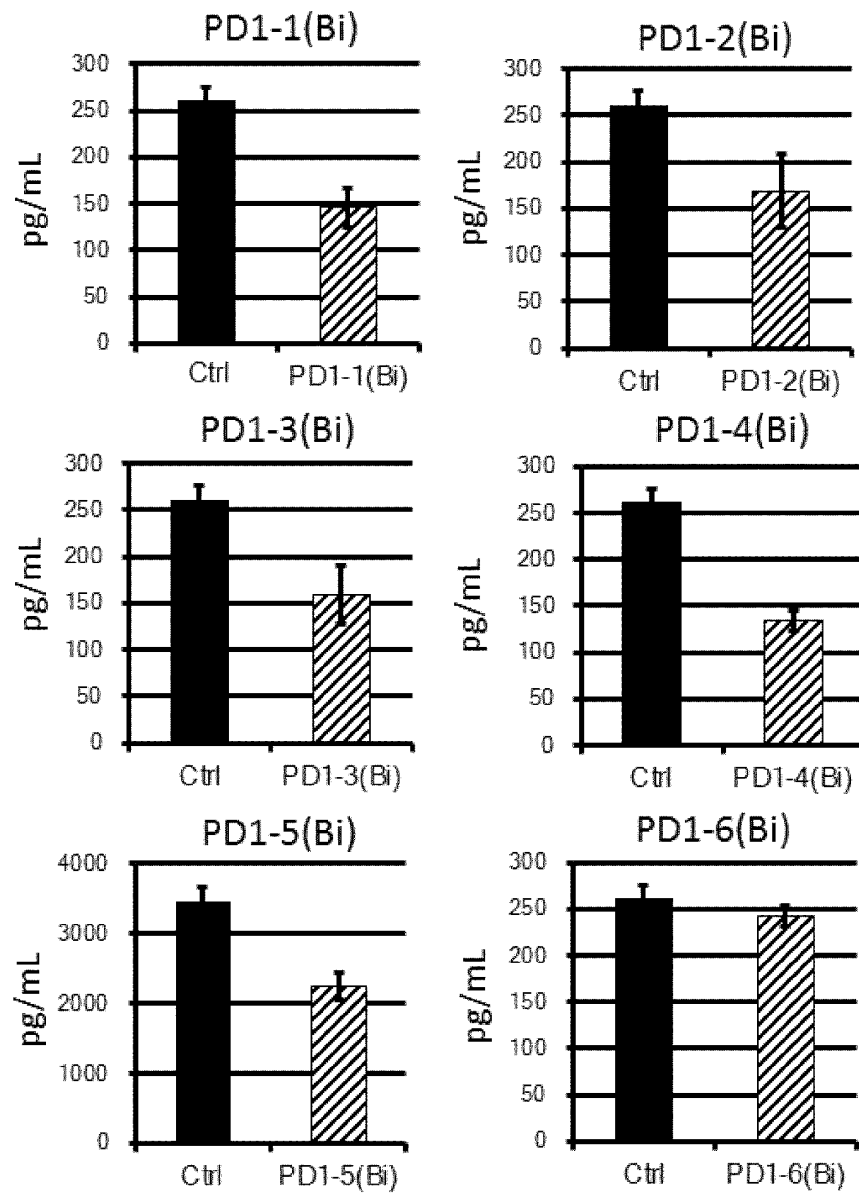
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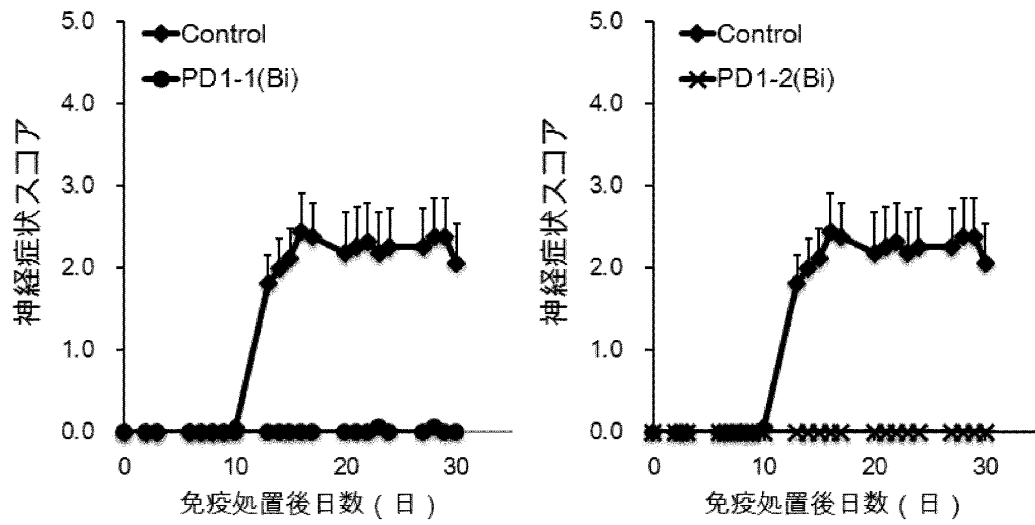
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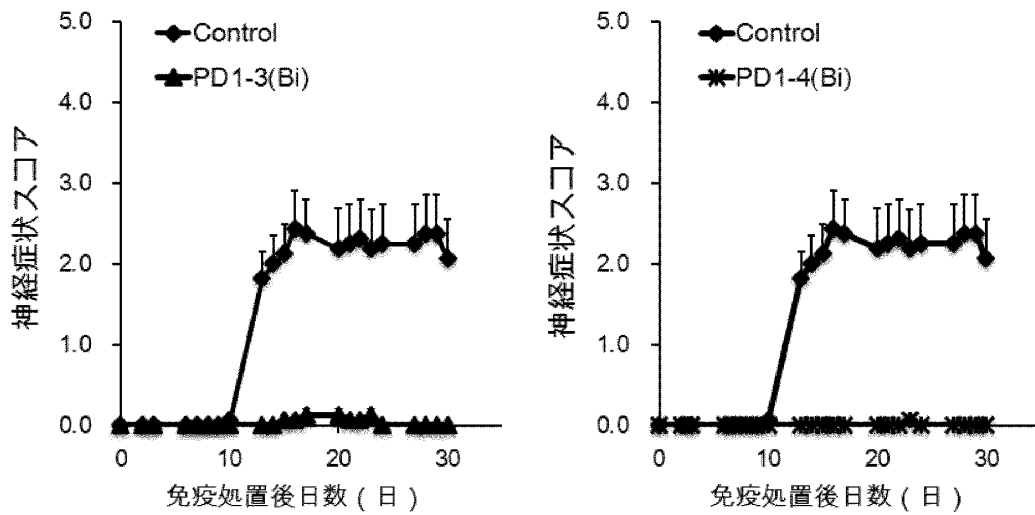
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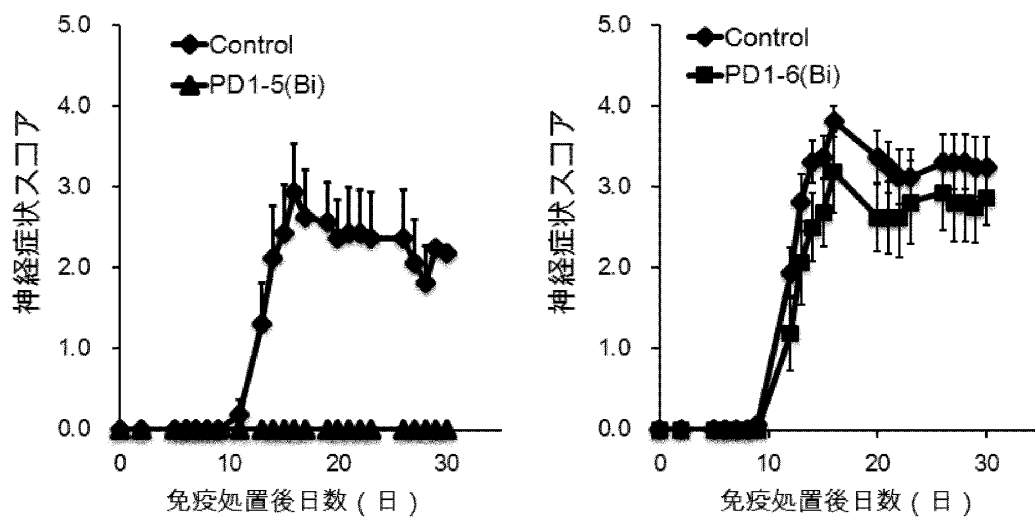
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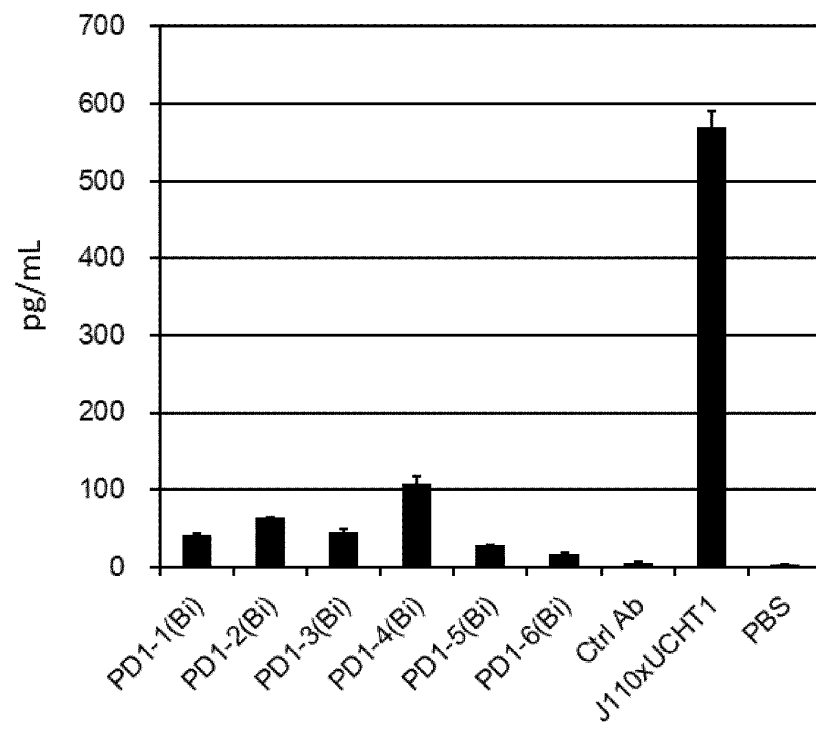
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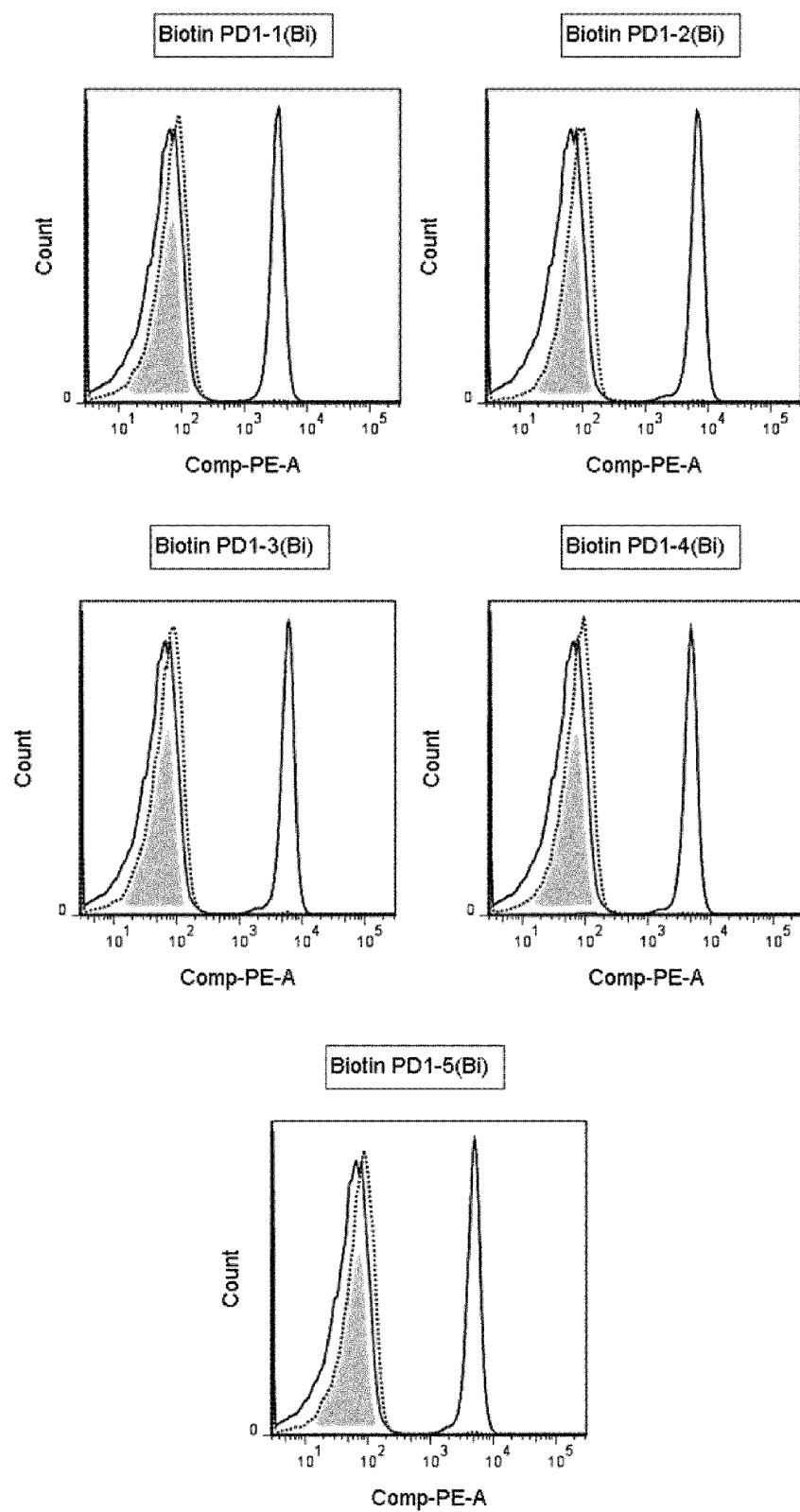
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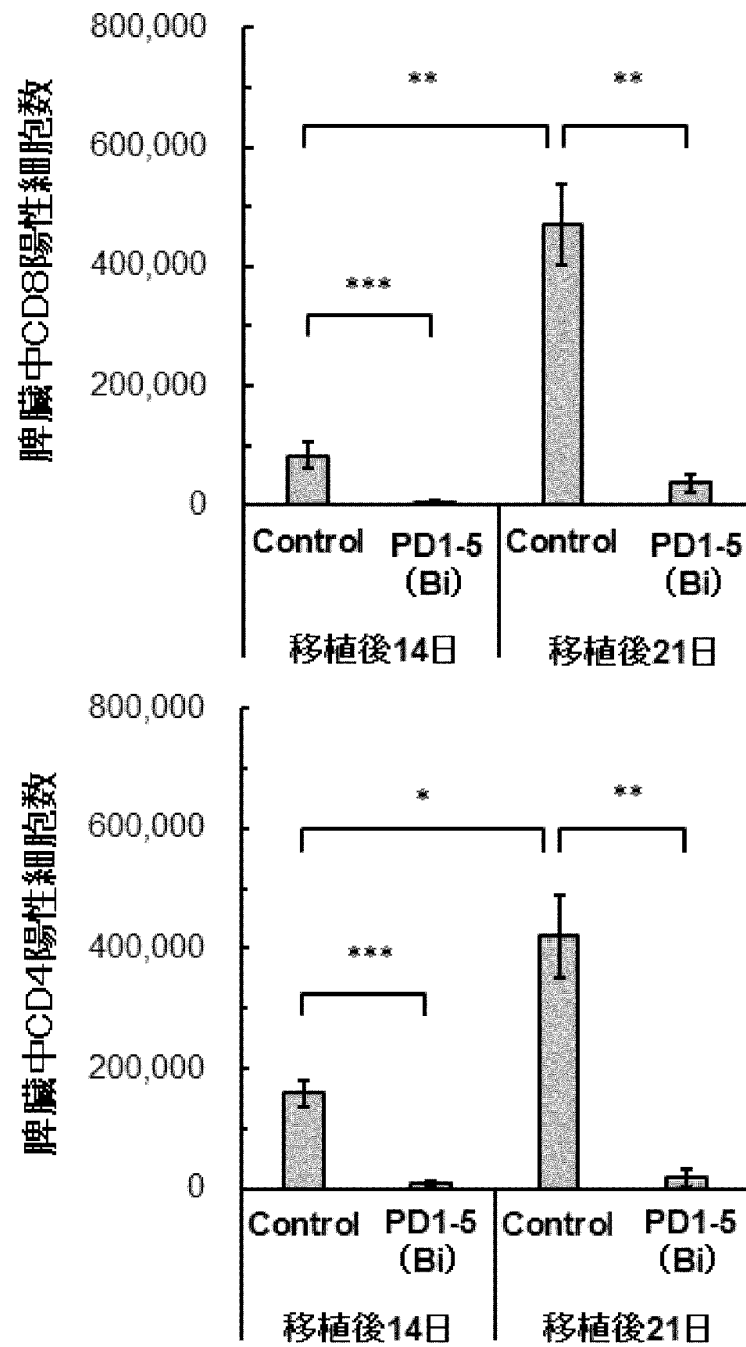
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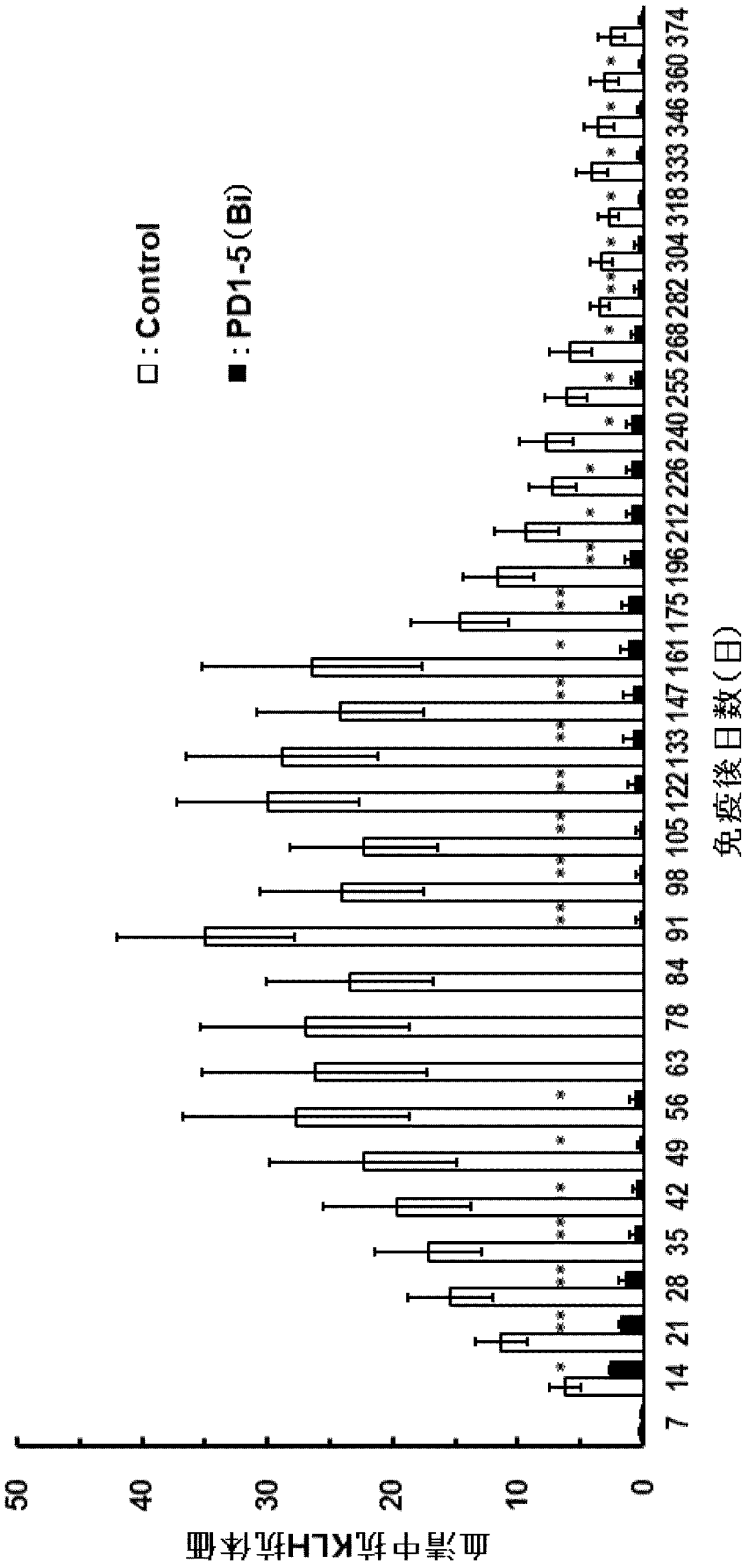
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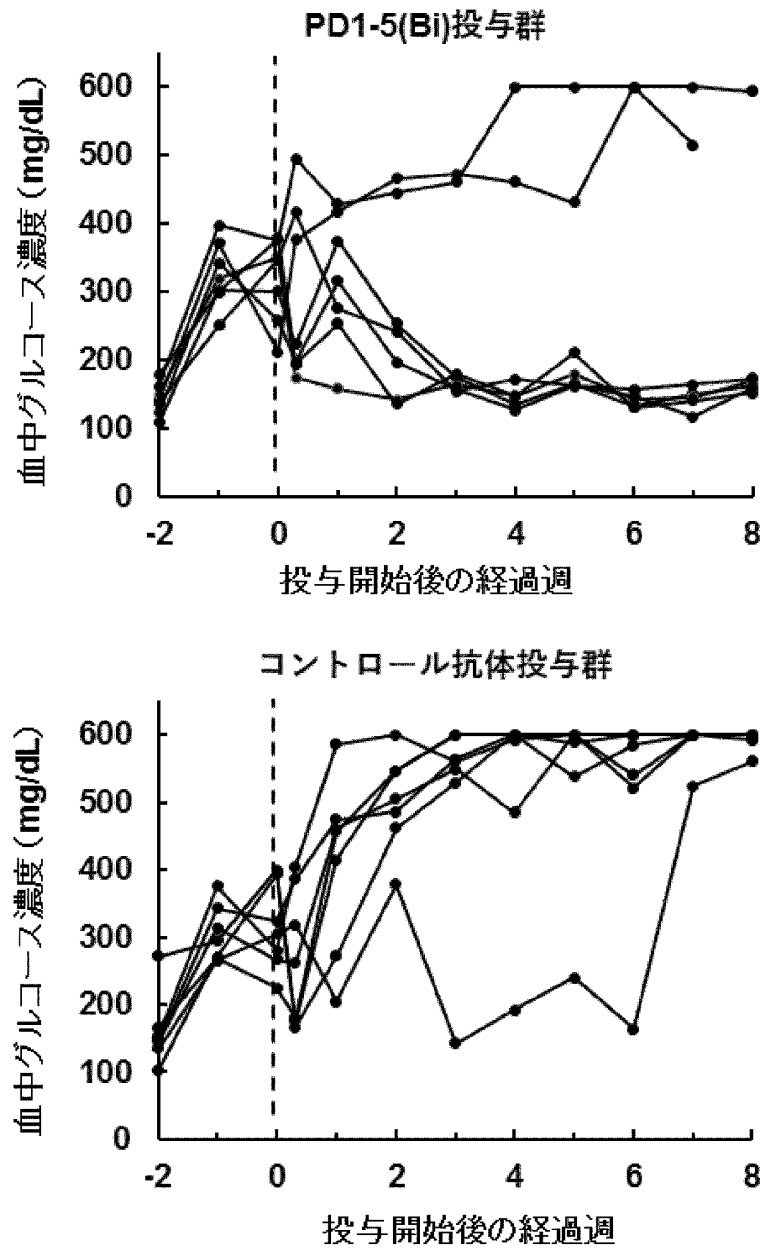
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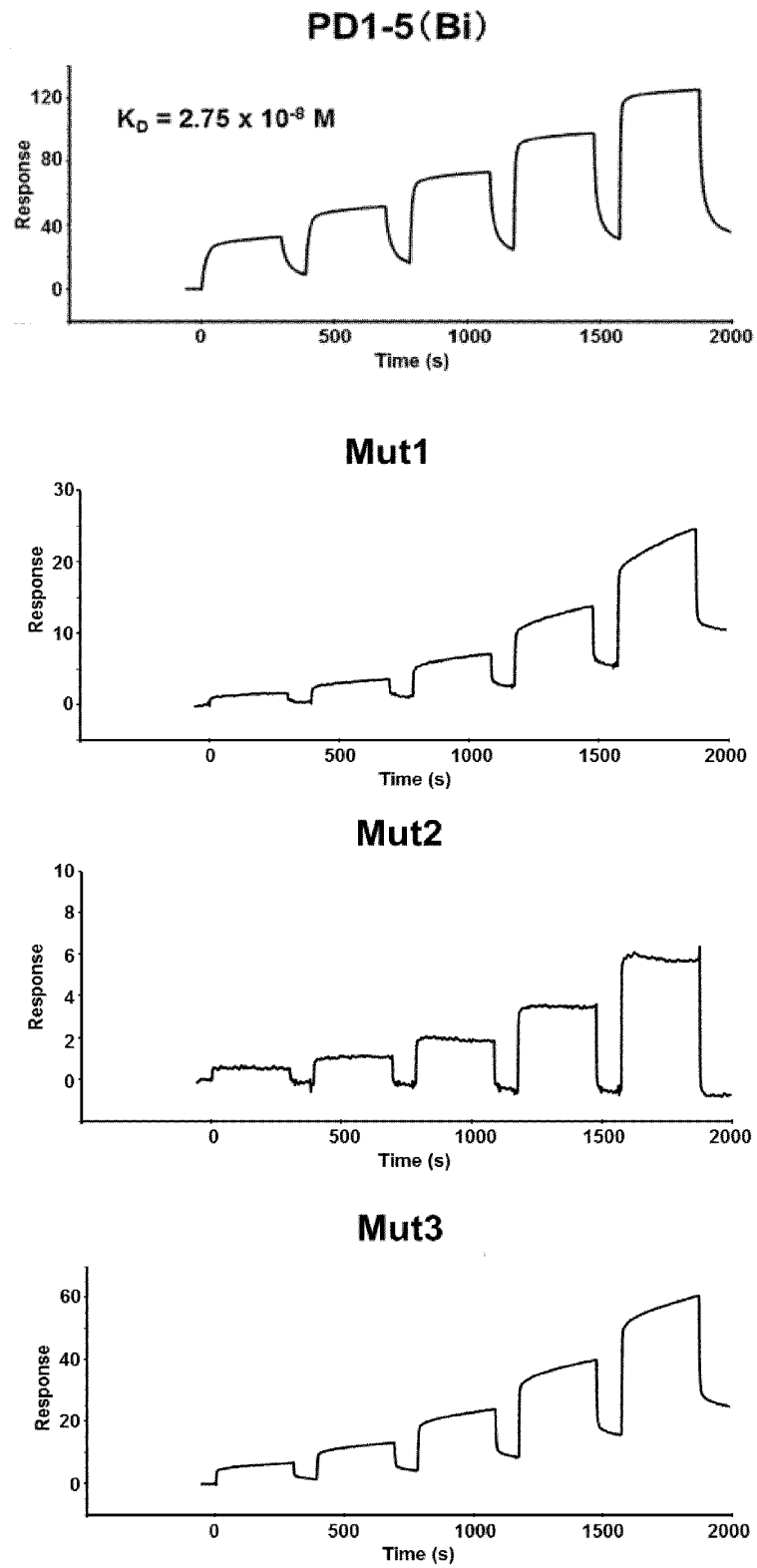
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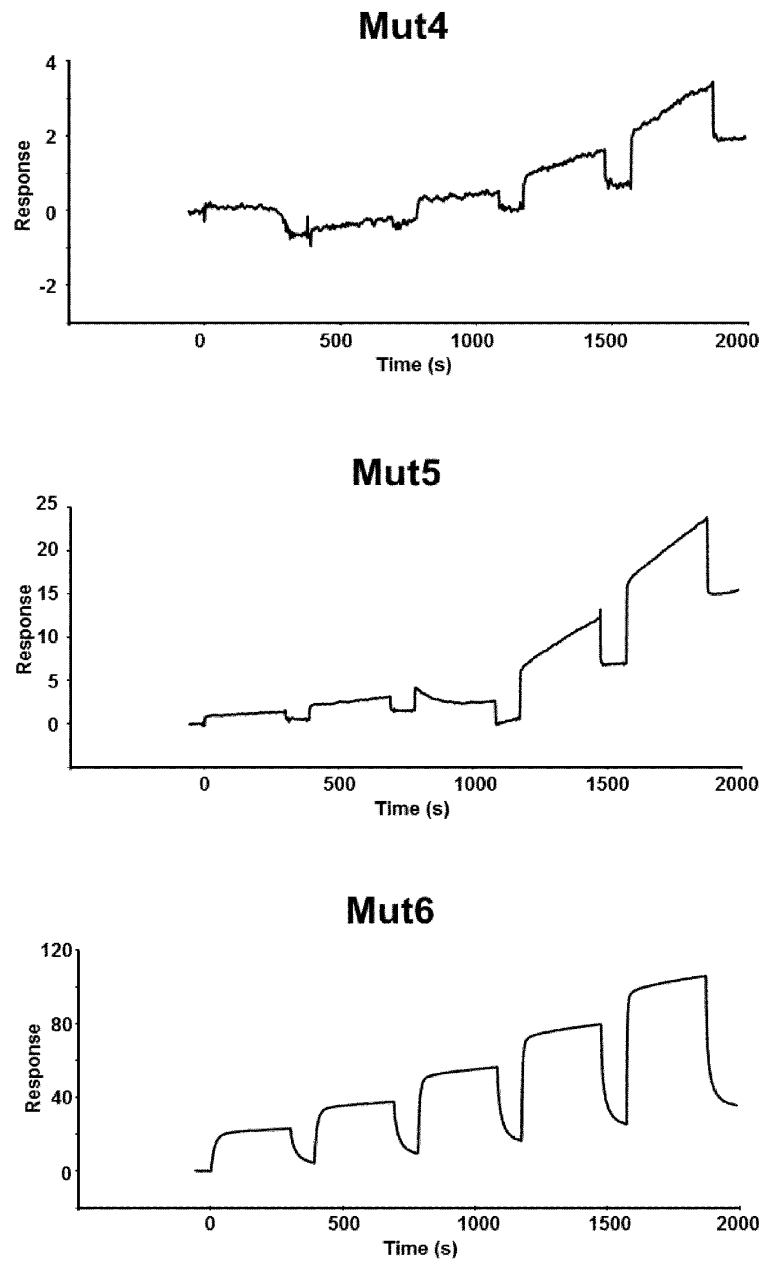
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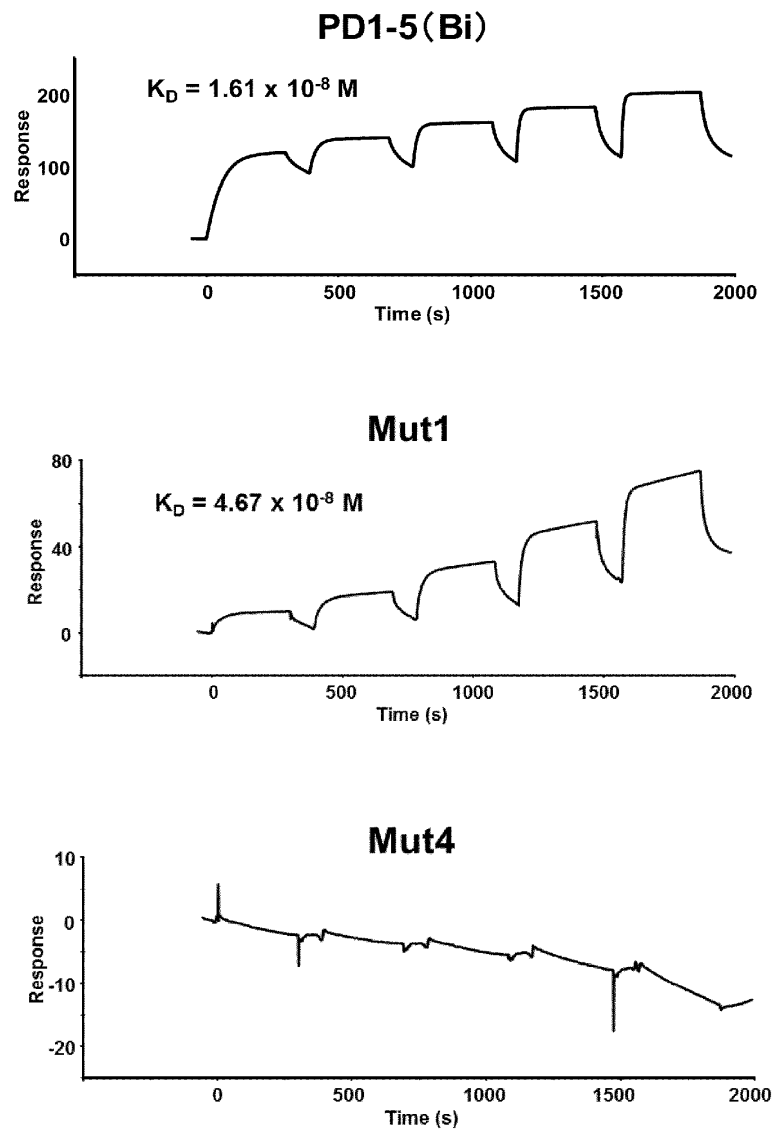
[図23]



[図24]



[図25]



[図26]

