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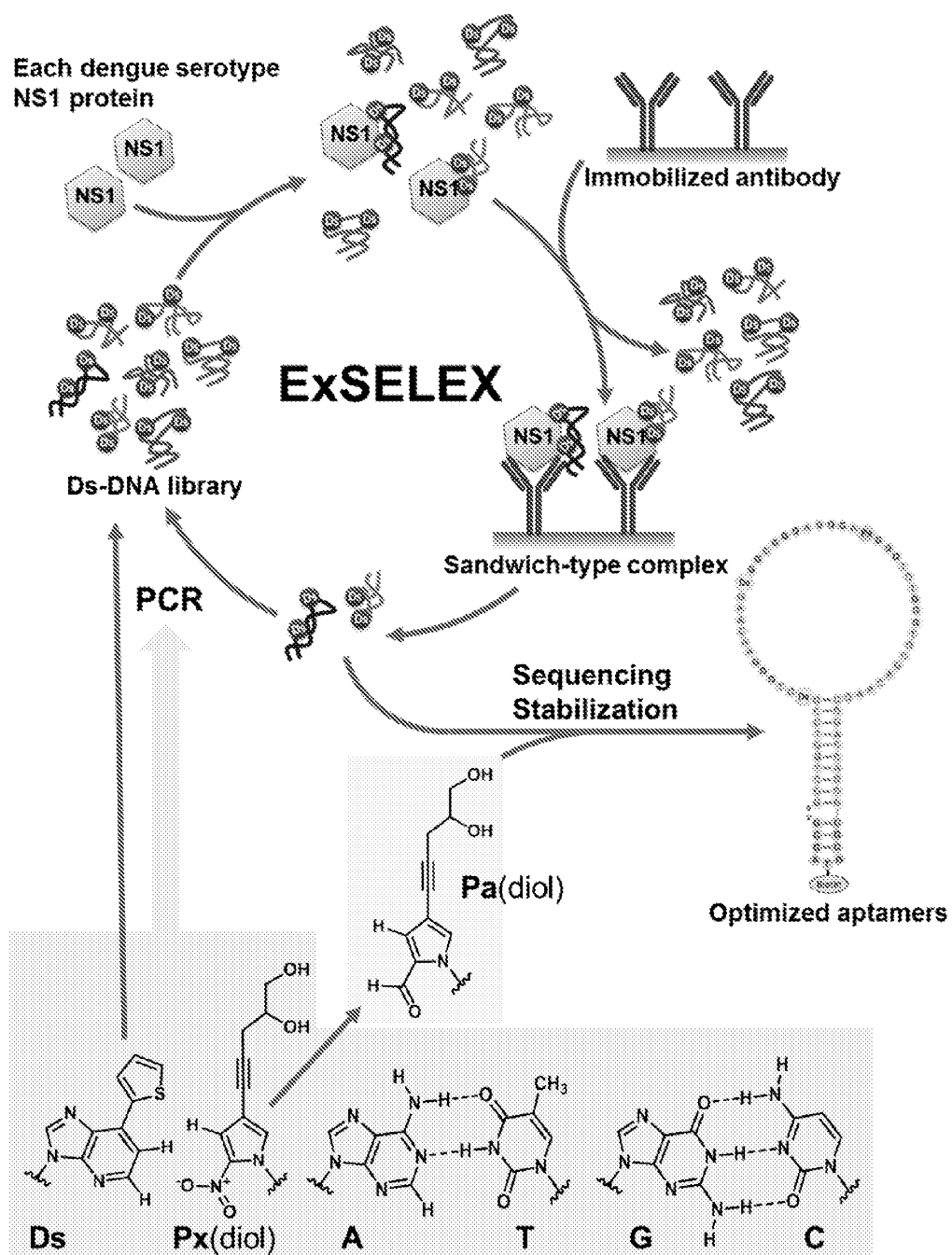


FIG. 1

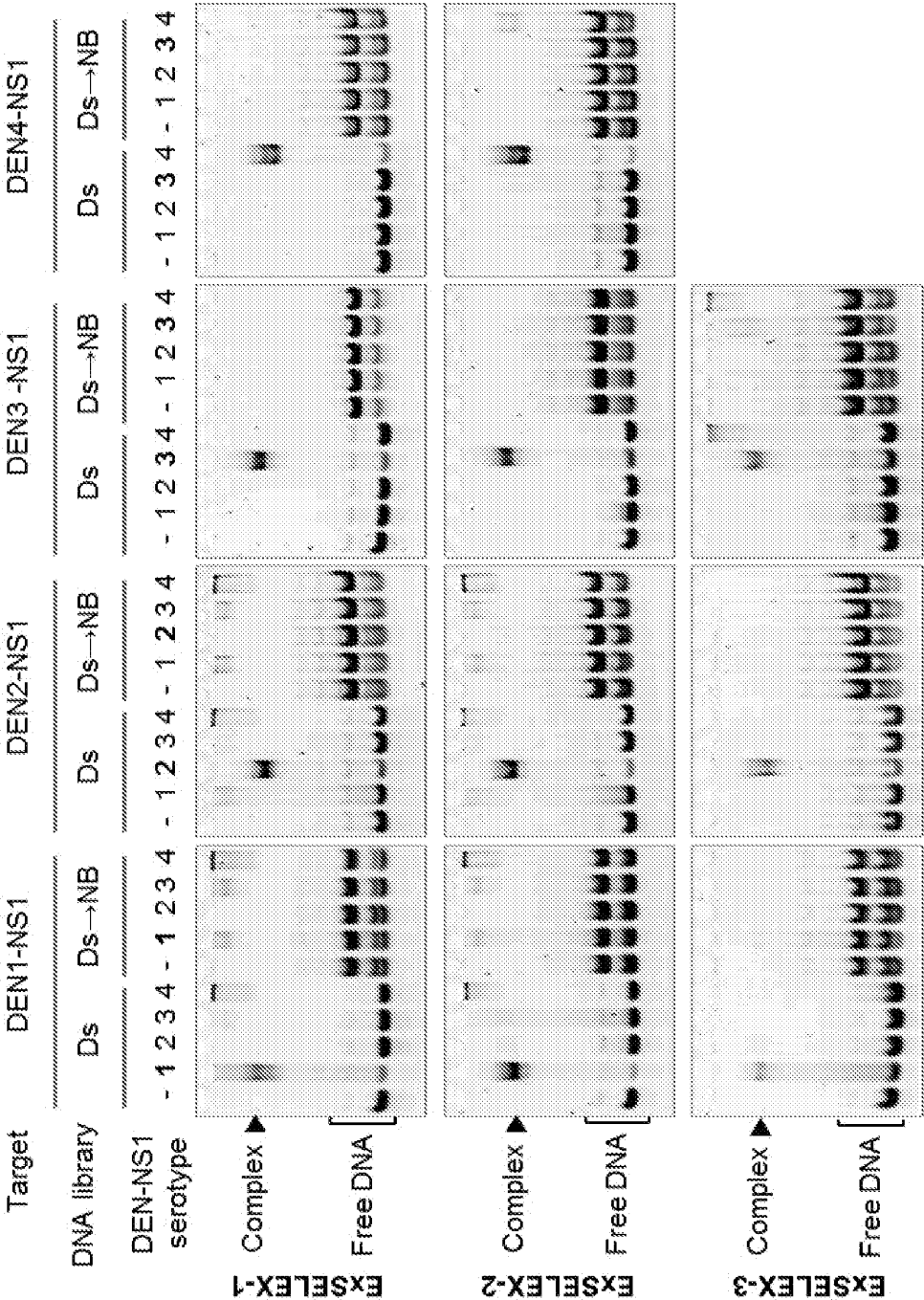


FIG. 2

			TTTGGCACTCCATGATATGGTCTACTG - [N ₄₂] - GACAAAGCGGAGTAGTATAGACCGTCAAA	
			Random	region
ExSELEX-Target	Family	Ratio (%)		
ExSELEX-1-D1	D1-1	10.01	TGTGAxGTCTTACAATGGACTGGTGTxCTCGGxATGGCCATT	
ExSELEX-1-D1	D1-1	8.79	GCAGCTATGCTCAAGATCCCTGGTGTxCTCGGxATGGGACTT	
ExSELEX-1-D1	D1-1	7.39	TCCGCTTAGCxAAGCTGCTGGTGTxCTCGGxATGATCTGTGC	
ExSELEX-1-D1	D1-1	2.63	CCGTAAAGGTCxGGTTGGCTGGTGTxCTCGGxATGGTATGCC	
ExSELEX-1-D1	D1-1	2.52	CACTGGTGTxCTCGGxATGGGAGTGACCATATTTCACTGGA	
ExSELEX-1-D1	D1-1	3.75	TACTGTCCGGCATGTCxGTGCTGGTGTxCTCGGxATGTACGGT	
ExSELEX-1-D1	D1-1	1.68	GAGAGxATGCGCTGGTGTxCTCGGxATGGCTCATTTCATTA	
ExSELEX-1-D1	D1-2	10.62	AGGAGCGCATGTGGAGATACCAAGCxCATCCCAATCxTTCTT	
ExSELEX-1-D1	D1-2	2.79	CAGCATGTACTGCGGCCAATCxCAGCCCAACCAAGCAAGT	
ExSELEX-1-D1	D1-2	2.46	GCTTGTGGTGGCGGCCAATCxCATCCCAACCAAGTCTGTAGG	
ExSELEX-2-D1	D1-3	54.58	ACGCCGGGCGGCTATxTCAGACGTATACxCATCAAGGACAT	
ExSELEX-2-D1	D1-4	22.71	CCTGCACCTGCTGTGxAGGCCCAAGCxCCTCATCCAAATGCTCA	
ExSELEX-2-D1	D1-4	11.73	TCTAAxGTCAATGAGCCCAAGCxCCTCATCCAAATGCGATTATA	
ExSELEX-2-D1	D1-4	2.14	GCCGGxAGTGGCTACCAATCTAC-CCAAACATGGCxCATGCCAC	
ExSELEX-2-D1	D1-4	1.75	CTGCTTTGTACAGGAGx-CAATCTAG-CCAAACCTGCCACTG	
ExSELEX-2-D1	D1-4	1.34	ATTGTCCATAxTGGTGGCAxTGGCAAGGTTxAGGTTATCGG	
ExSELEX-3-D1	D1-5	8.23	CAGCTAAGTCCCAAGCCAGCCCAATCxCAGCGCTGCxATGTA	
ExSELEX-3-D1	D1-5	7.88	GCGACxGGCGTGCATTGxCCAAATCTTAGCCCAACCAAAAT	
ExSELEX-3-D1	D1-6	7.05	ACGAGCTTAGACCTTGTACCAACCCCTCCCAATCxAATAGG	
ExSELEX-3-D1	D1-7	6.10	GACGGTTGTAAAGAGTGCACAGTCCCAATCxCAGATT	
ExSELEX-3-D1	D1-7	5.89	GGTAGCGCGGAGGCGTCCCAATCTAT-CCAAATCxCAGTCCG	
ExSELEX-3-D1	D1-7	4.11	GTCCATTGACTGAxACCCAATCCTTCAATCxAATGTAAG	
ExSELEX-3-D1	D1-7	3.31	TCCGTxAAGSTTGTCCACCCCAACAGCTCCCAATCTGTCACA	
ExSELEX-3-D1	D1-7	3.22	ATACGxATTGATAGAGCCxCCCAACAAA-CCAAATCCAGGCGG	
ExSELEX-3-D1	D1-7	3.20	CTCTGTTTGTAGGAGAGCCCAATCTAT-CCAAATCTCCACAAT	
ExSELEX-3-D1	D1-7	2.75	CTACGGTTGGCGGATxTTACCAATCTCTCCCAATCxAATGTC	

FIG. 3

			TTTCGCACTCCATGATATGGTCTACTG - [N ₄₂] - GACAAGCGGAGTAGTTAGACCGTCAAA	
			Random	region
ExSELEX-Target	Family	Ratio (%)		
ExSELEX-1-D2	D2-1	34.41	GTCCGxCTGGGAACAAGxGGGGGAGGGAxGGGT-GTGGGTGC	
ExSELEX-1-D2		7.66	AGGGAGTAGxGAGGACCAAGxG-C-GGA-GGAxGGGG-GGGGGTGG	
ExSELEX-1-D2		1.88	ATTATGGCTCAGTCAAGxGGCAGTTGGGAxGGGTGTGGGT	
ExSELEX-1-D2		17.36	TGGGAAGTCAxGGGGGCTGGTGTAGTCGGxAGACGGGAGT	
ExSELEX-1-D2		1.13	ACGTCAAGTTGGAAGAGxACGGCCGTAAATACATGCACAAG	
ExSELEX-1-D2		20.75	CTCTAACCAACAGAGGCCAGxCAAATCTTA-CCAAACCxCCCCG	
ExSELEX-1-D2		2.85	AGTGTGACGGGGAGxCAAATCCG-CCAAACCxCCCCCTA	
ExSELEX-1-D2		3.54	CTACGTGAAGTCCAATCTCTACCAACCTGT*TCACGAxAGT	
ExSELEX-1-D2		2.79	ATAGCCTGTCCGCTT*GTCCGCCAAACCCGTG*TCCAATCCAA	
ExSELEX-1-D2		1.40	AAAGGGGGT*GTAACTGTCCAATCCGG*TCCAACCTACGA	
ExSELEX-1-D2		23.26	GAATAACAAGTCCGTGxGTGGCCAAATCCGTG*TCCAACCCC	
ExSELEX-2-D2	D2-2	21.67	GTCTACAxGCAACGCTTTCGxCAAACxCGTG*TCCAATCCCA	
ExSELEX-2-D2	D2-3	11.97	CTTCACGAGTCAAGGxCTCCAATCCGTG*TCCAACCAAGTTT	
ExSELEX-2-D2	D2-4	6.97	ACCGCGAAGTAGGxTCAAACxCGTG*TCCAATCCGGCCGA	
ExSELEX-2-D2		10.59	GGCTCGGCTCGGGxTCAATCCGTG*TCCAATCCGGCCGA	
ExSELEX-2-D2	D2-5	11.63	TGGCTGGGCCAxCGTGTCAACCTTACCAATCTGxCAAGGG	
ExSELEX-2-D2	D2-6	8.27	TAGAT*TTGTGAGAxGCACCAACCAACCAATCTGxCTTGA	
ExSELEX-2-D2		4.16	ACCGTGGACCTCTCACCCAAACCTTCCCAATC*AGCAATAGA	
ExSELEX-3-D2	D2-1	65.94	GTCCGxCTGGGAACAAGxGGGGGAGGGAxGGGTGTGGGTGC	
ExSELEX-3-D2	D2-2	1.53	GAATAACAAGTCCGTGCAAGTCCCAATCCGTG*TCCAACCCC	
ExSELEX-3-D2		7.99	AGACGCGCAGGACTAxGACCAATCTTACCAACCA*CTCAAGG	
ExSELEX-3-D2		2.96	CCCGA*TTGCCTGCCCCxCAAACCAAGCCCAATCCATGGGGCG	
ExSELEX-3-D2		2.84	CCTTG*ATATGTCTTCTACCAACCAACCAATCTAxGAGACA	
ExSELEX-3-D2		2.65	CTGGC*GGGGGAGGGCCAAACAGACCAATCC*CGAGACCA	
ExSELEX-3-D2		1.76	CACGGAGT*GGGAAGxCAAACCTACCAATCTTACCT	
ExSELEX-3-D2		1.56	TATTCAAG*TTGTACCGxCAAATCACCAACCAACAGAGGTA	

FIG. 4

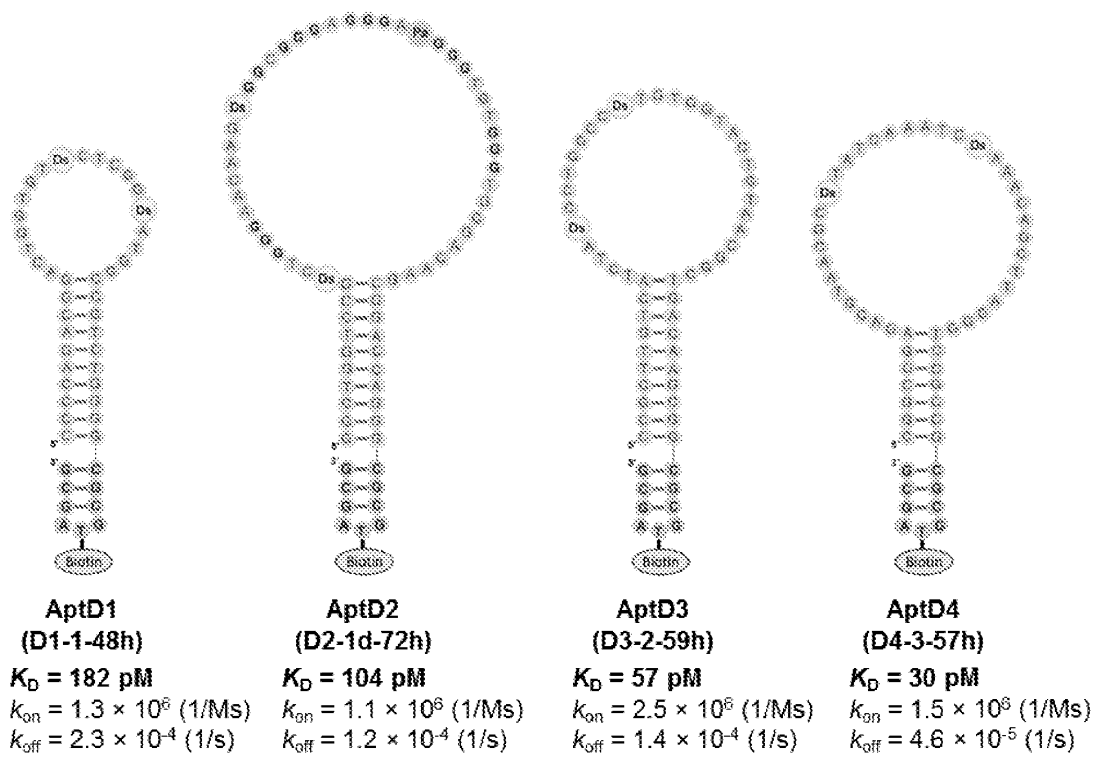
TTTCGCACTCCATGATATGGTCTACTG - [N ₂] - GACAAGCGGAGTAGTTAGACCGTCAAA				Random region	
ExSELEX-Target	Family	Ratio (%)			
ExSELEX-1-D3	D3-1	89.07	ATAGTACTCCxGTTTAACTCTGAxACTTGACGTCCAATTCATA		
ExSELEX-1-D3		3.09	CTGAAGCTCCGGTGGxCCCC-GGGTTTGTAAAxCCCTTTA		
ExSELEX-1-D3		2.64	CTTGCxCCCCCGGGTTTGTAAAGGxAGAATTCTGTTAA		
ExSELEX-1-D3		2.00	GTCGCTTGGCxCCTCGTCGGTGAAGTAAATxCAAGTCAG		
ExSELEX-2-D3	D3-2	81.23	AAGTGTGTCANCAxCTGGCCxTGTGTACTGTAAACGGCT		
ExSELEX-2-D3	D3-3	15.56	GGGCTxGGTCTTCCGTxTGCAGATTAACTTGGTGCCAGTAA		
ExSELEX-3-D3	D3-1	34.13	ATAGTACTCCxGTTTAACTCTGAxACTTGACGTCCAATTCATA		
ExSELEX-3-D3		27.21	TACCACCTTGAATGGACGCGxCGTATGTTGGxTCGGGGAAATG		
ExSELEX-3-D3		8.17	GTGTAATCCGGTTGTGAGACGGCGGAATGxATTGGAAAGGC		
ExSELEX-3-D3		8.07	CGCGCTTGGGxGACGAATTGTACAGCGTATATCCxCGACG		
ExSELEX-3-D3		4.85	CTCTGTGCCGTCGAGxGACCCCTTAGGTTxGAGTGTCTAACC		
ExSELEX-3-D3		2.83	CGTGGTCGAGxGGGCGTGTAAACGCAATCACAGCCGTAGCC		
ExSELEX-3-D3		3.14	ACACCGTCTxTGTATGTGCGCATTCCTGACTCTAxCCCCGACA		
ExSELEX-3-D3		1.45	CTCTGCGCGTGGTGCxAAACTCGGGCxTTGTAAATCAACTTTT		

FIG. 5

TTTTGCACTCCATGATATGGTCTACTG - [N ₄] - GACAAGCGGAGTAGTTAGACCGTCAAA				Random region	
ExSELEX-Target	Family	Ratio (%)			
ExSELEX-1-D4	D4-1	39.19	TCTCAACGGTGTCAAA	ACGGxTATCA	CGGCxACA
ExSELEX-1-D4		13.74	ACTTTGGCGGAAAACAGCTTTATCATATATAA	ACGCxTATCA	CG
ExSELEX-1-D4		2.38	CGGTAAxCGCTAAAGG	ACGGxTATCAAA	TTTAAACACCTCCTT
ExSELEX-1-D4		9.18	TAAGAACAGCGCTGTGA	ACGCxTATCAAA	TCxAAACAGCTTC
ExSELEX-1-D4		2.88	TCCTCTAAAGCTGTCCGCGC	xTATCAAA	GGAxAAACAGCCGA
ExSELEX-1-D4	D4-2	23.92	TCACAATCGCCGTAAAGx	CGAAGAGCTG	GGGAATCTAAGGT
ExSELEX-1-D4		4.40	TGGGGxGCGTGAGCTTGGCA	AAAGxTTGGxTAA	GGCCCTGACAA
ExSELEX-1-D4		1.29	GTCCCTCGTCCAAACCGTGC	CACTCTCACTx	GAGAACCCAAATC
ExSELEX-2-D4		21.96	GAGGAGACGTAACGCxTATCAAA		
ExSELEX-2-D4		17.04	TTGGCGCGAGGGAATC	xACGCxTATCAAA	TATxAAACAGCTTAGGGTCC
ExSELEX-2-D4	D4-3	8.60	TCGCACGTTAAACGCx	ACGGxTATCAAA	TATxAAACAGCTAAT
ExSELEX-2-D4		1.43	GGCACCCATTGTCTCA	ACGCxTATCAAA	TATxAAACAGCTGA
ExSELEX-2-D4		23.35	TATAATCCGCxTTTCGT	CATGTGxTTGGATCT	GGGTCTGGCA
ExSELEX-2-D4		7.28	CATAGCGGCx	CGGTGGTGGxTTGGC	xTTGGCTGGCAC
ExSELEX-2-D4		3.50	CCCAAxCTTGTCTGTAA	GGGxTTGGxTAA	GGCTGGCAAAAA
ExSELEX-2-D4	D4-5	2.09	GTCTGTGGGGx	CTTGAAGGGxTTGGxTAA	GGCTGGCAACAA
ExSELEX-2-D4		1.51	GTTTTxGGTTAGTTCTTTTGGG	xTTGGCAxCGGG	CCCTGGCGTG
ExSELEX-2-D4		1.00	CGACGGCTTAx	ACGTCAATGGGxTTGGCT	GGGGGTCTGGCCT

FIG. 6

a



b

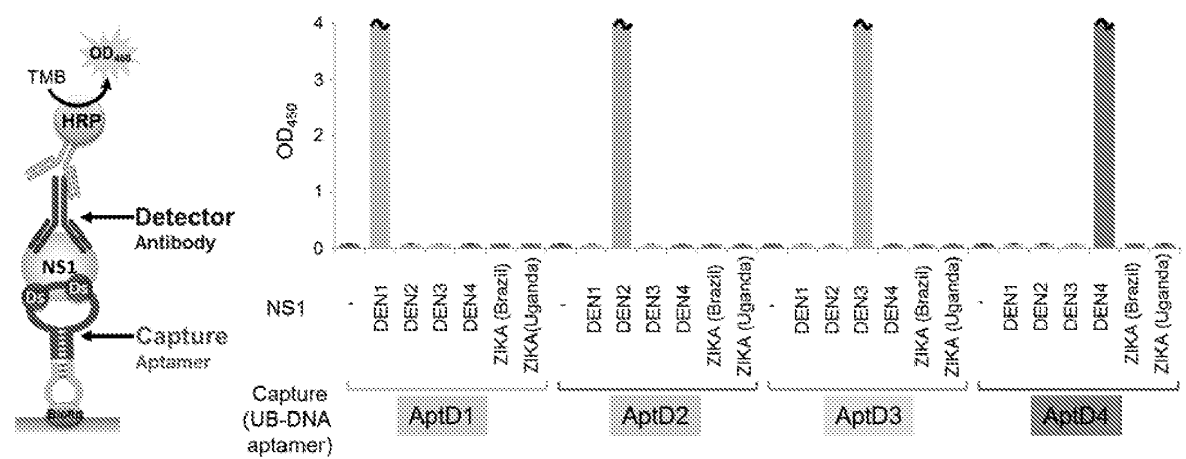


FIG. 7

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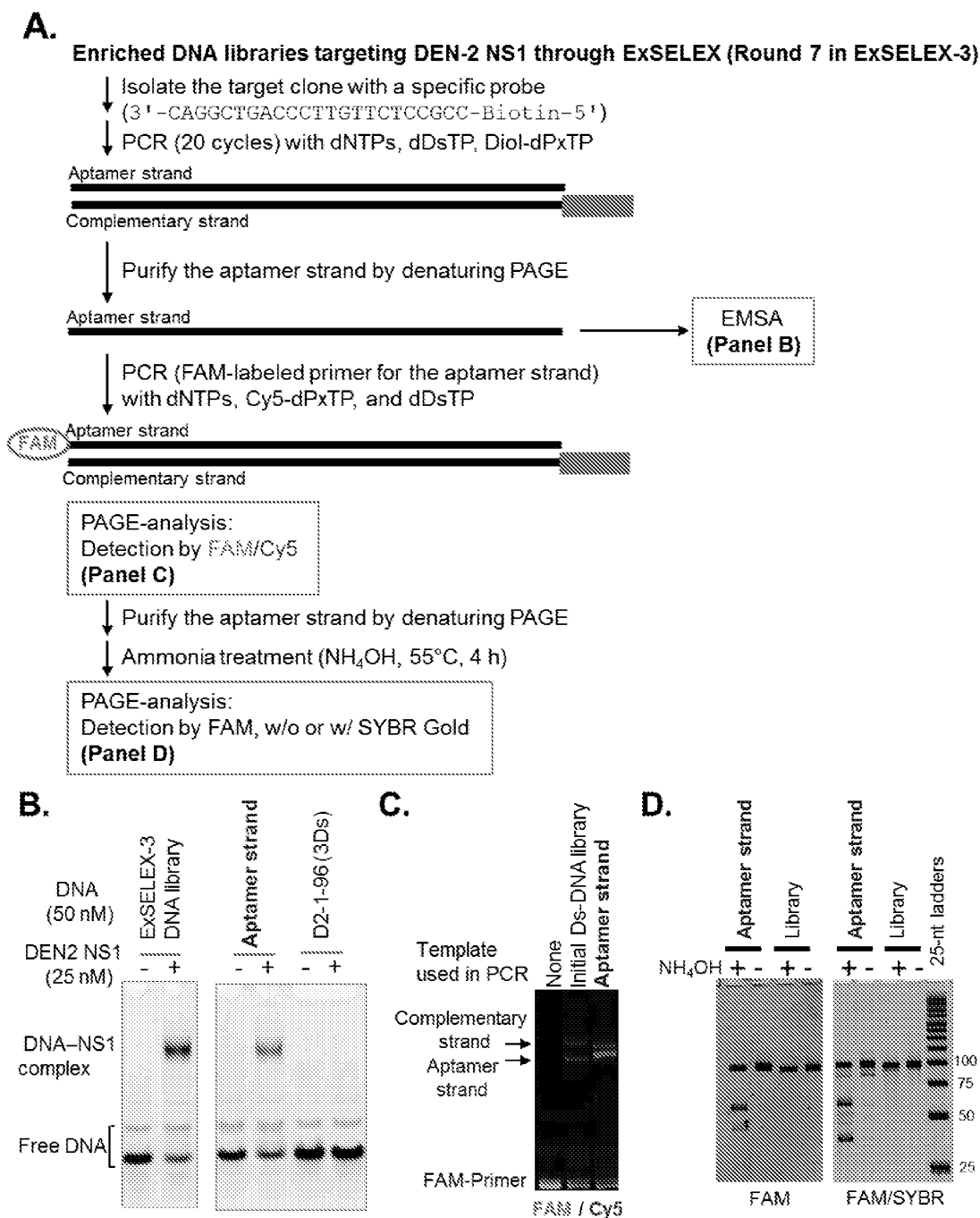


FIG. 8

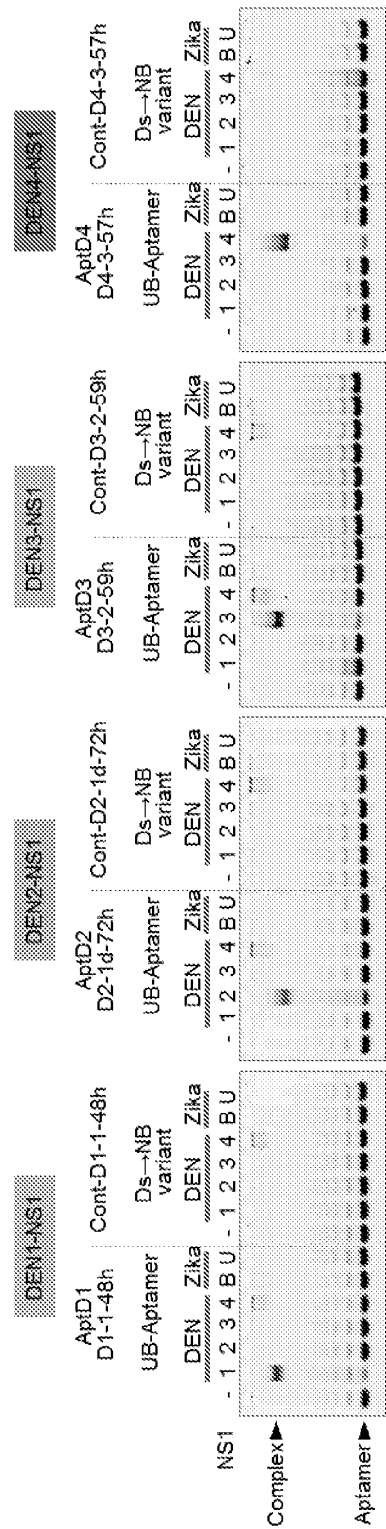


FIG. 9

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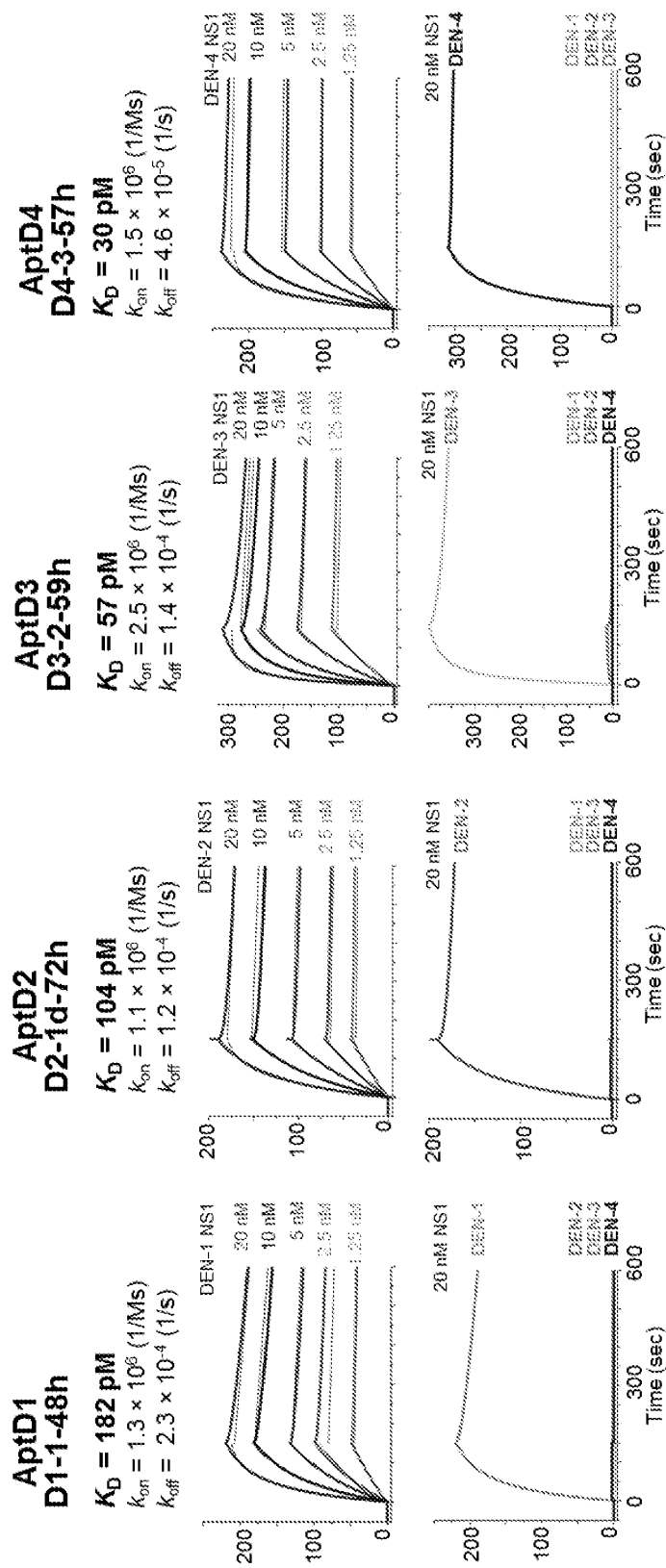
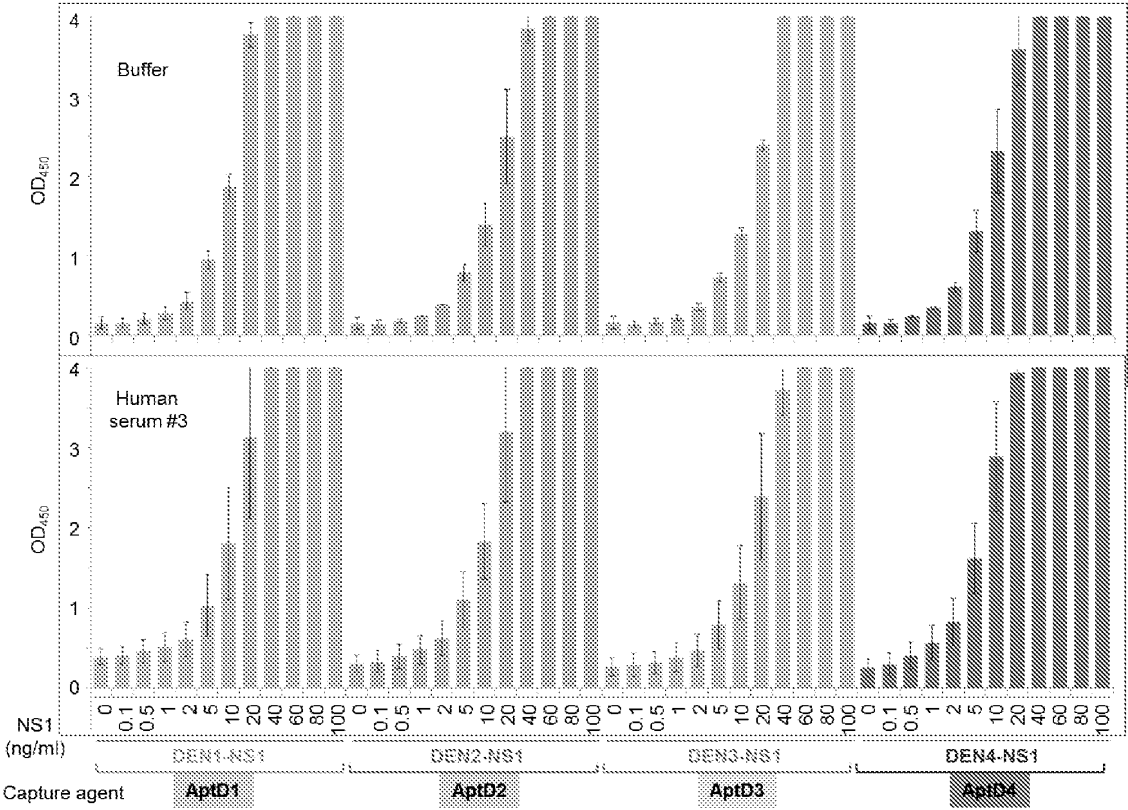


FIG. 10

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10 ul in assays	DEN1-NS1 (ng/ml)		DEN2-NS1 (ng/ml)		DEN3-NS1 (ng/ml)		DEN4-NS1 (ng/ml)	
	Buffer	HS	Buffer	HS	Buffer	HS	Buffer	HS
LOD (blank+ 3σ)	1.60	2.22	1.86	1.99	2.36	3.31	1.19	1.14
LOQ (blank+ 10σ)	4.77	6.97	5.84	6.91	7.34	11.06	3.92	4.10

FIG. 11

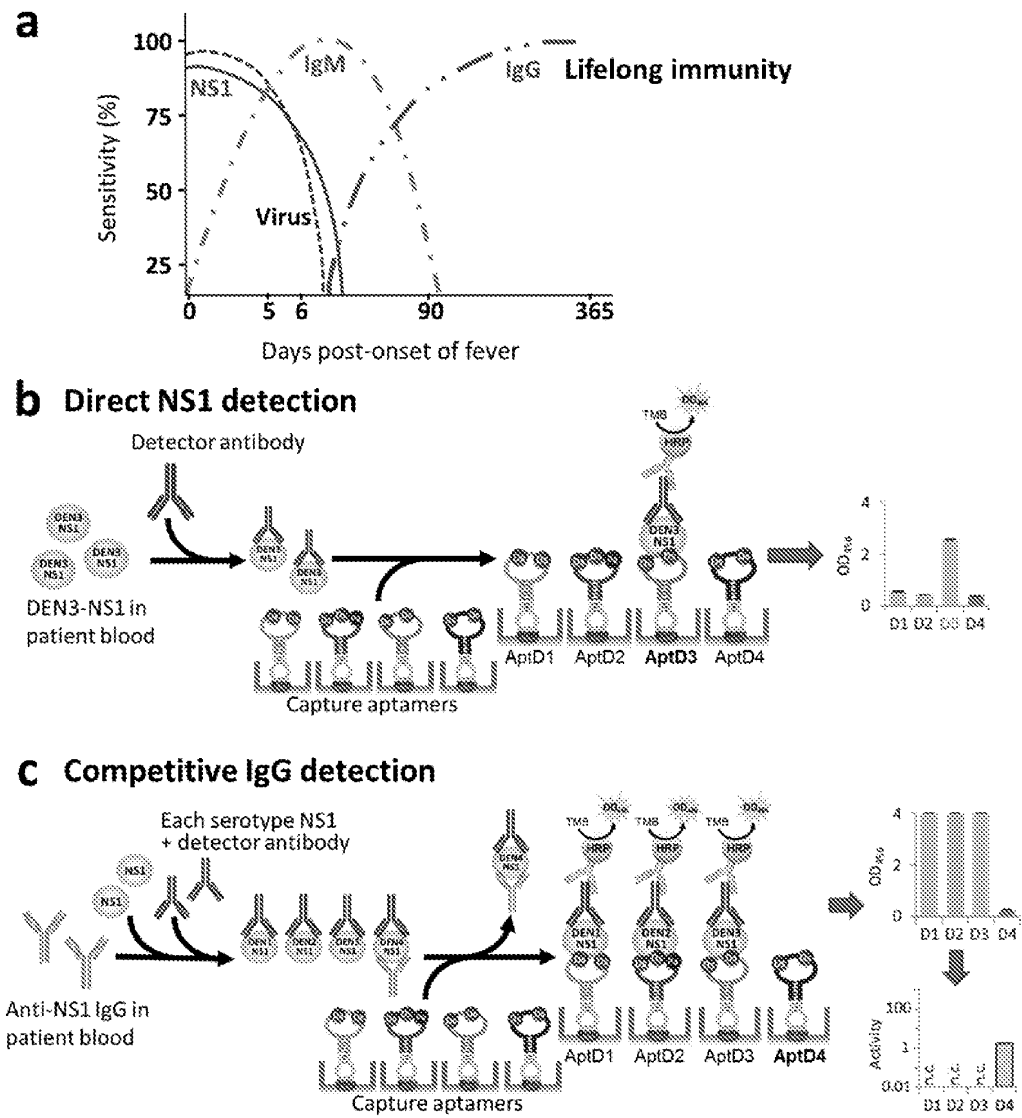


FIG. 12

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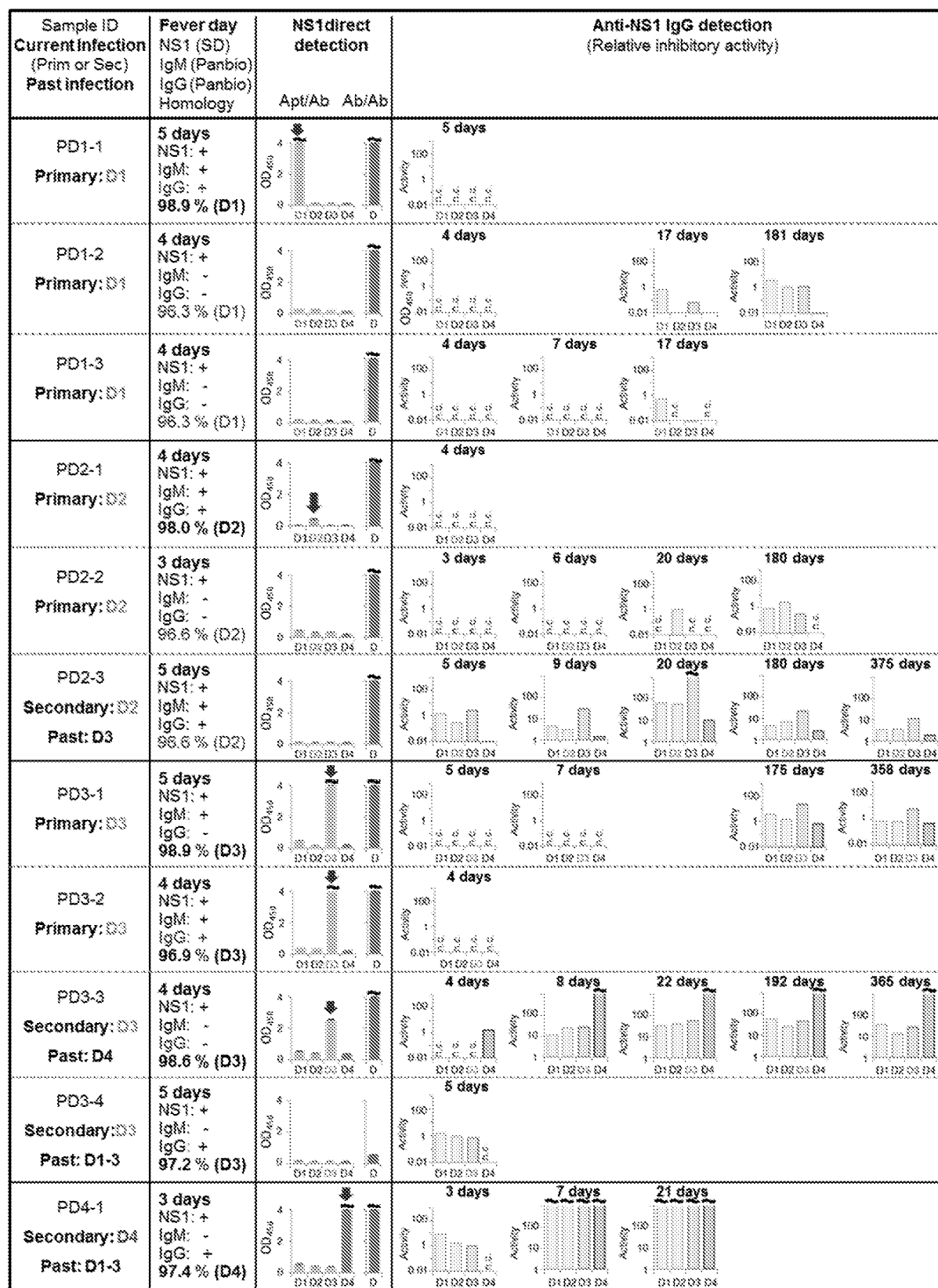


FIG. 13

FIG. 14

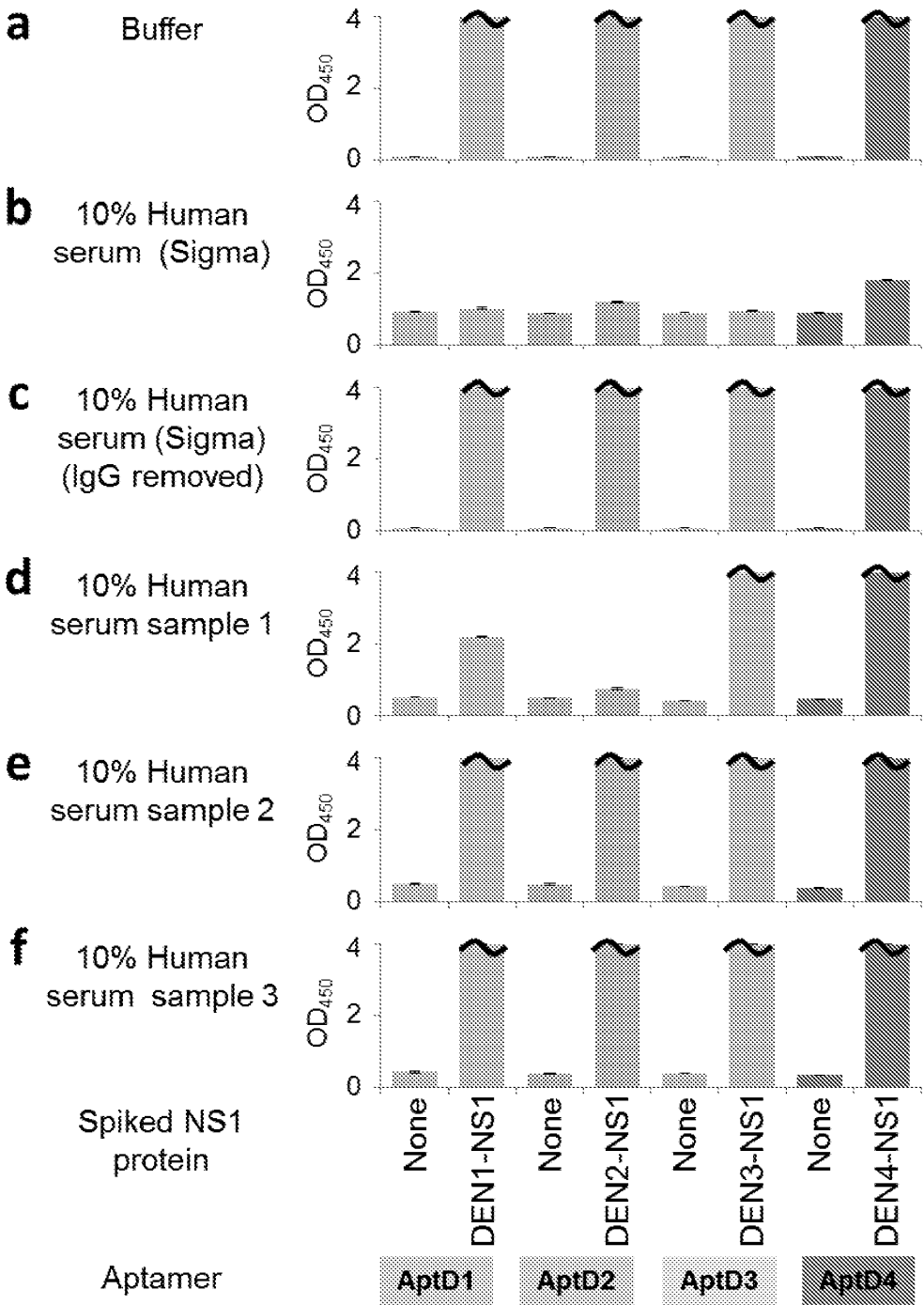


FIG. 15

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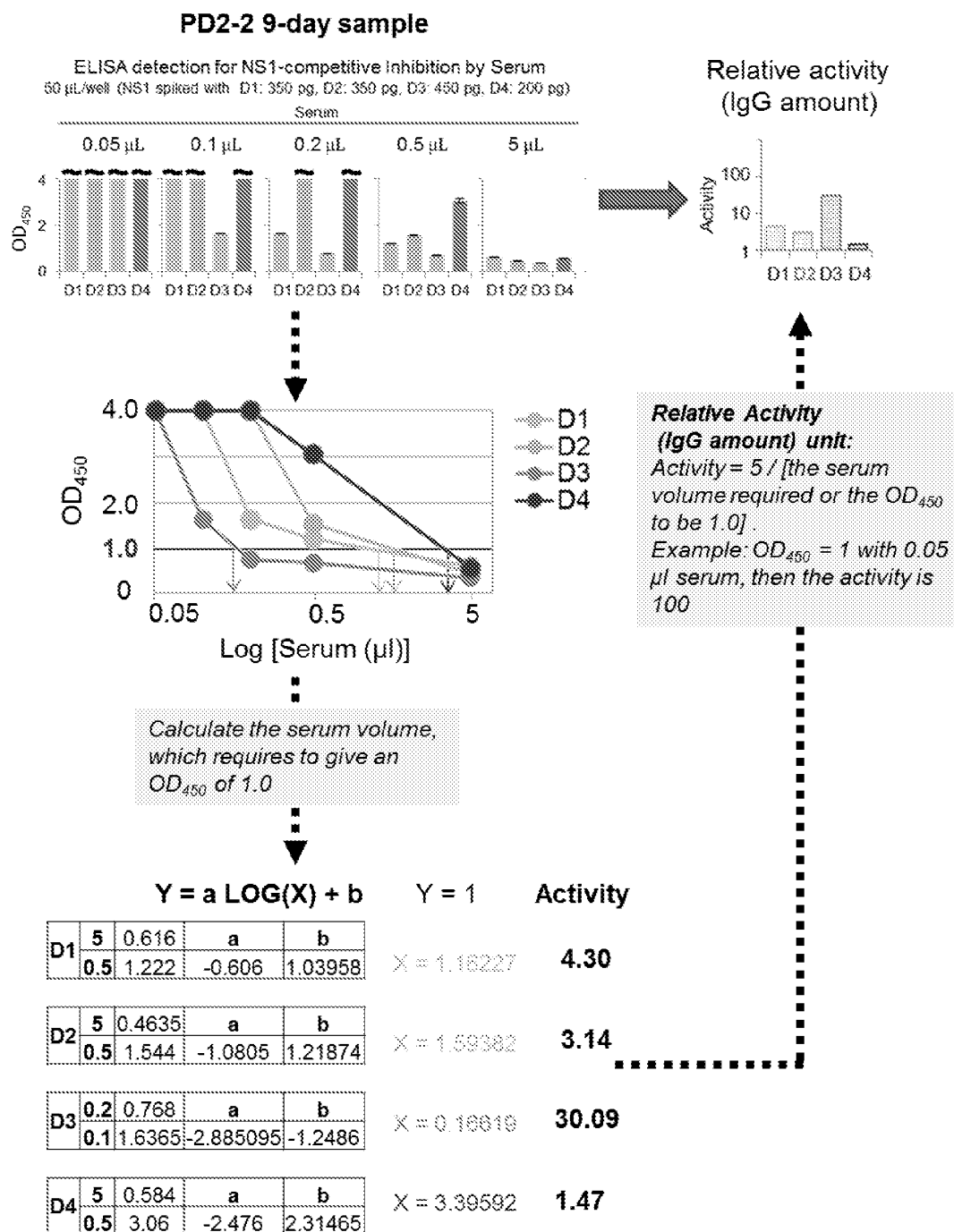


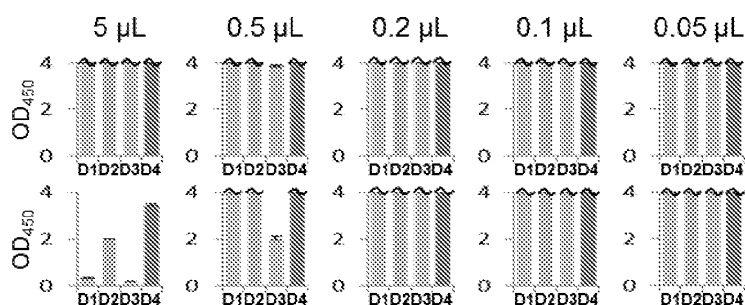
FIG. 16

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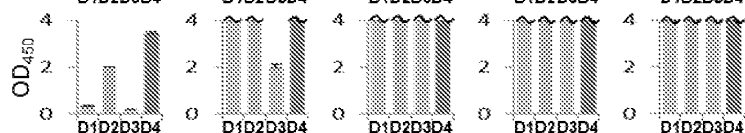
PD2-2

Fever day 5

Antibody/Antibody

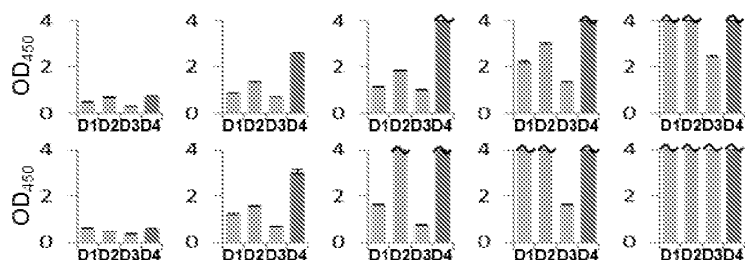


Aptamer/Antibody

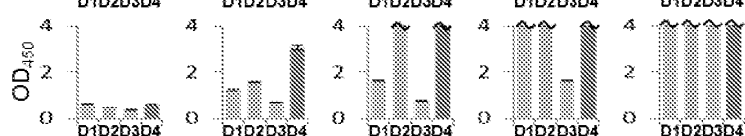


Fever day 9

Antibody/Antibody

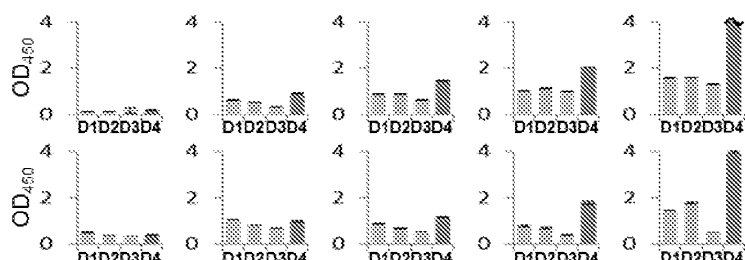


Aptamer/Antibody

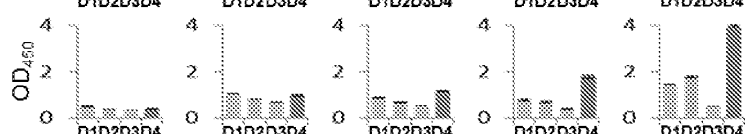


Fever day 20

Antibody/Antibody

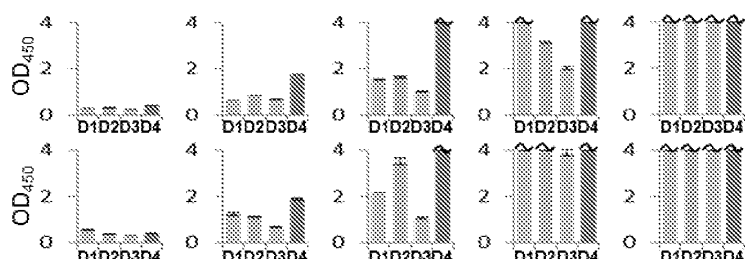


Aptamer/Antibody



Fever day 180

Antibody/Antibody

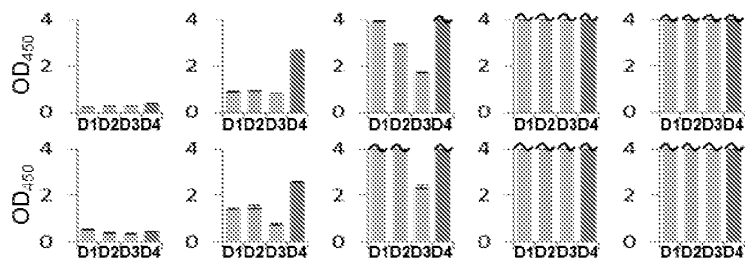


Aptamer/Antibody



Fever day 375

Antibody/Antibody



Aptamer/Antibody

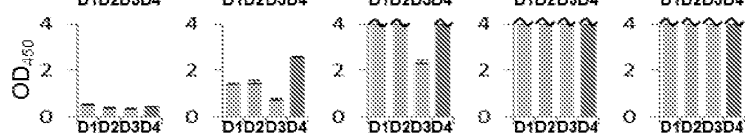
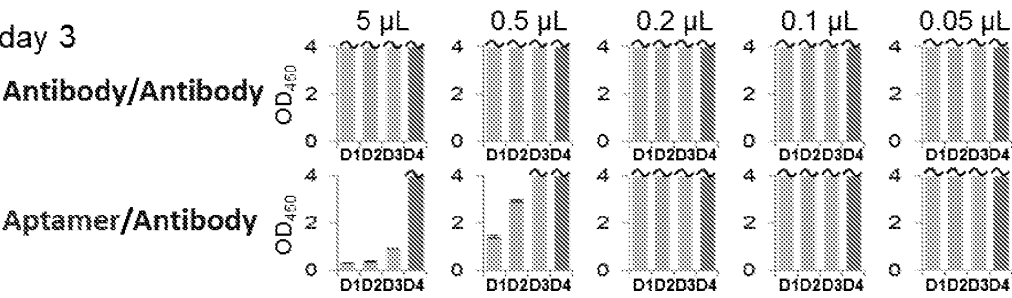


FIG. 17

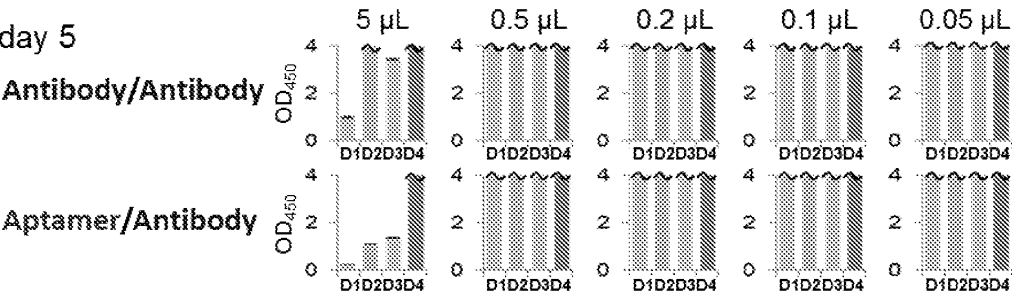
PD4-1

Fever day 3



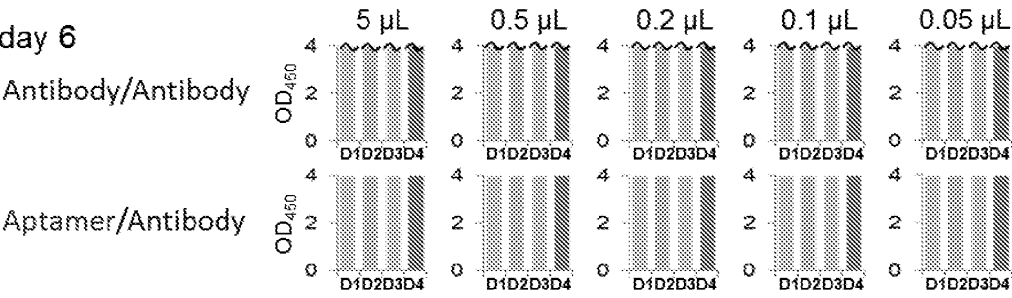
PD3-4

Fever day 5

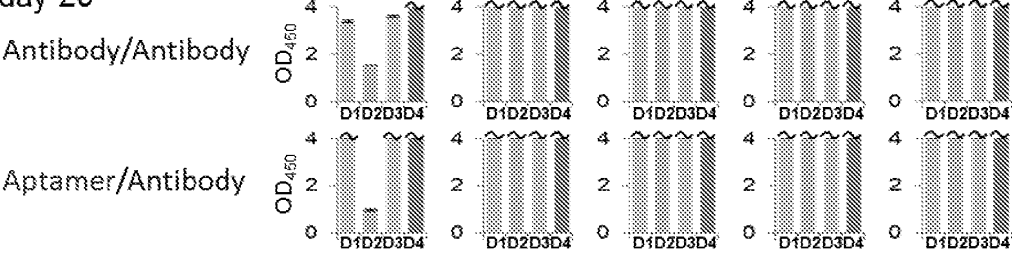


PD2-1

Fever day 6



Fever day 20



Fever day 180

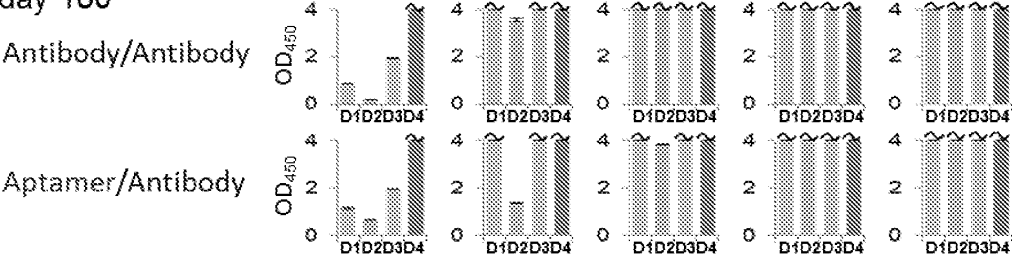


FIG. 18

50 80 93/94 98 117
 D1 target DSCVNMGRKCCSCITVMEVHTWE QYFQADSPFLSAIAINAMWCVGGRSA TRLNINMKNQSNELNHLNOMPTVVV GVVSILQCKKRIPOPHNYSWISCKR 120
 PD1-1 S·VIN·KG·····VTNE····· S·AD·KA·SA·CK·HEE·V·····A ·L·IM···SN···HI·L·NEMAF·VVV ·VA·ILQ·AMIR·QPEH·····S··· 120
 PD1-2/PD1-3 S·VIN·KG·····VTNE····· K·AD·KB·SA·CK·HEE·V·····A ·L·IM···SN···HI·L·NEMAF·VVV ·VA·ILQ·AMIR·QPEH·····S··· 120
 D2 target S·VVS·KN·····ITNM····· K·EE·SK·AS·CK·HEE·I·····V ·L·LM···TP···HI·S·NEVL·IMT ·IK·IMQA·ASLR·QPEL·····T··· 120
 PD2-1 S·VVS·KN·····ITNM····· K·EE·SK·AS·CK·QPE·I·····V ·L·LM···TP···HI·S·NEVL·IMT ·IK·IMQA·ASLR·QPEL·····T··· 120
 PD2-2/PD2-3 S·VVS·KN·····ITNM····· K·EE·SK·AS·CK·AS·CK·HEE·I·····V ·L·LM···TP···HI·S·NEVL·IMT ·IK·IMQA·ASLR·QPEL·····T··· 120
 128 131 139 146 162 174 177/178 222 227
 D1 target ALICADVHTTIDGWTDEEDKQAN NINEVDGCGTITNTLWLDSTYQD HNLSSALIKOSNAYHADMCTWESNHTV KLADSTFVTCVTHNSHTLHNGCTSESZ 240
 PD1-1 ALICADVQ·TT·I·····N·F···DDQ··· IN·····I·····L·L·RDSTYQ··· HR·····I·SK·····EK·ET·····EK·ET·····I·EKS·····S·····E 240
 PD1-2/PD1-3 ALICADVQ·TT·I·····N·F···DDQ··· IN·····I·····L·L·RDSTYQ··· HR·····I·SK·····EK·ET·····EK·ET·····I·EKS·····S·····E 240
 D2 target KULSTESH·QT·L·····E·A···VTR··· SL·····V·····V·····L·L·KXQDV··· SK·····I·SK·····AL·DE·KIEK·F·····N·H·EKS·····S·····E 240
 PD2-1 KULSTESH·QT·L·····E·A···VTR··· SL·····V·····V·····L·L·KXQDV··· SK·····I·SK·····AL·DE·KIEK·F·····N·H·EKS·····S·····E 240
 PD2-2/PD2-3 KULSTESH·QT·L·····E·A···VTR··· SL·····V·····V·····L·L·KXQDV··· SK·····I·SK·····AL·DE·KIEK·F·····N·H·EKS·····S·····E 240
 247 264/265 272 278 281 286 293 307/308 324 347
 D1 target MIPKICGPFISQHNRCYFTYACFWHL CULLEPDLCECTVTVVDEHCHNCRCPSLRT TTVTCNTHCCRCSTPFLKPCDCGW YCNELNFMENLKNYSVSA 352
 PD1-1 I·KING·I·····P·F···TA····· K·L·DL·E·····VVD·H·GN····· VV···I·HE·····L·····E·····VK·····L·K·S··· 352
 PD1-2/PD1-3 I·KING·I·····P·F···TA····· K·L·DL·E·····VVD·H·GN····· VV···I·HE·····L·····E·····VK·····L·K·S··· 352
 D2 target K·KLA·V·····Y·P···H···TT····· K·M·DF·D·····VT·D·GN····· AS·LITE·····L·····VR····· VK·····L·N·L·T··· 352
 PD2-1 I·KMLA·V·····Y·P···H···TT····· K·M·DF·D·····VT·D·GN····· AS·LITE·····L·····VR····· VK·····L·N·L·T··· 352
 PD2-2/PD2-3 I·KMLA·V·····Y·P···H···TT····· K·M·DF·D·····VT·D·GN····· AS·LITE·····L·····VR····· VK·····L·N·L·T··· 352

FIG. 19A

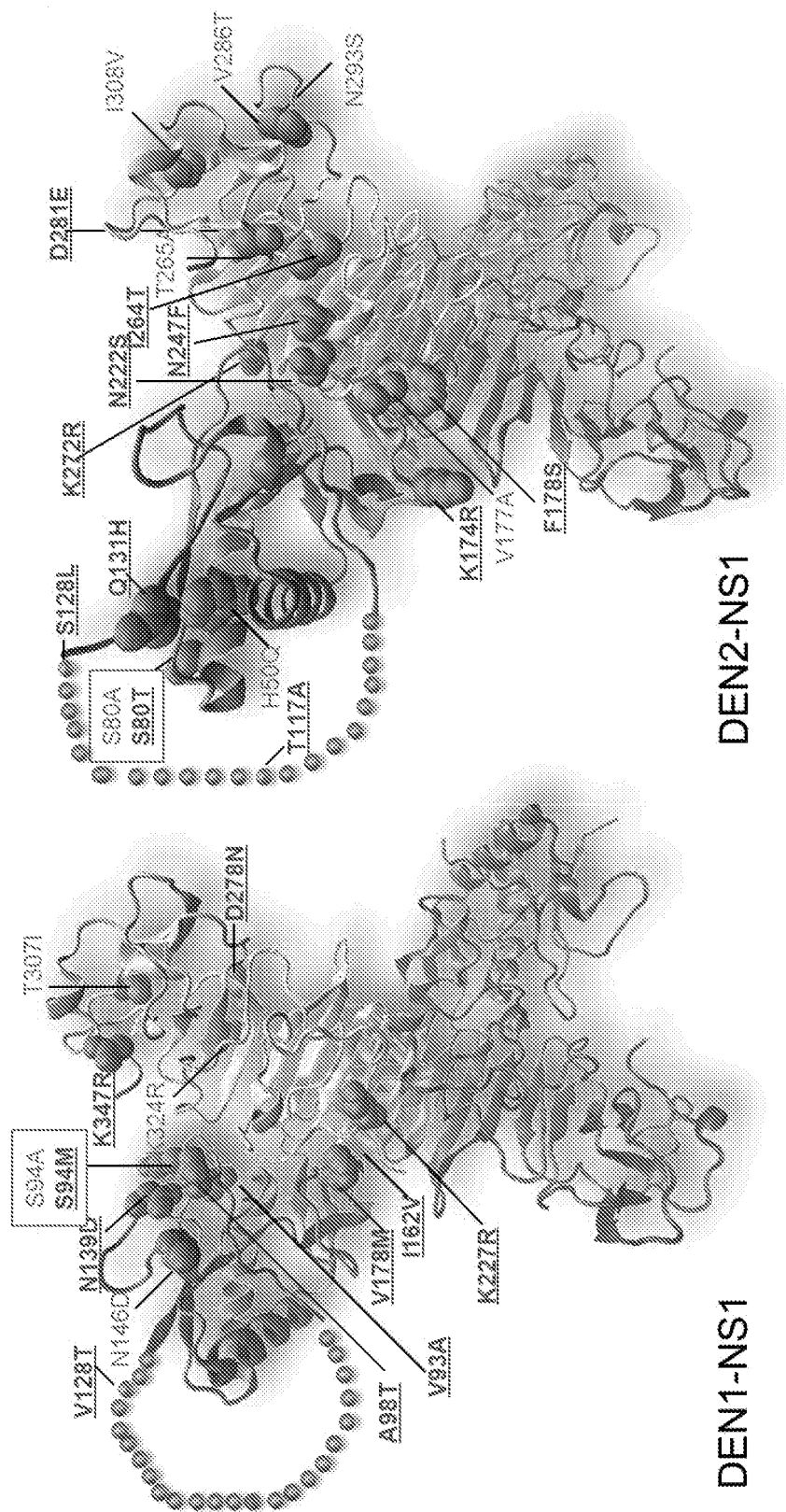


FIG. 19B

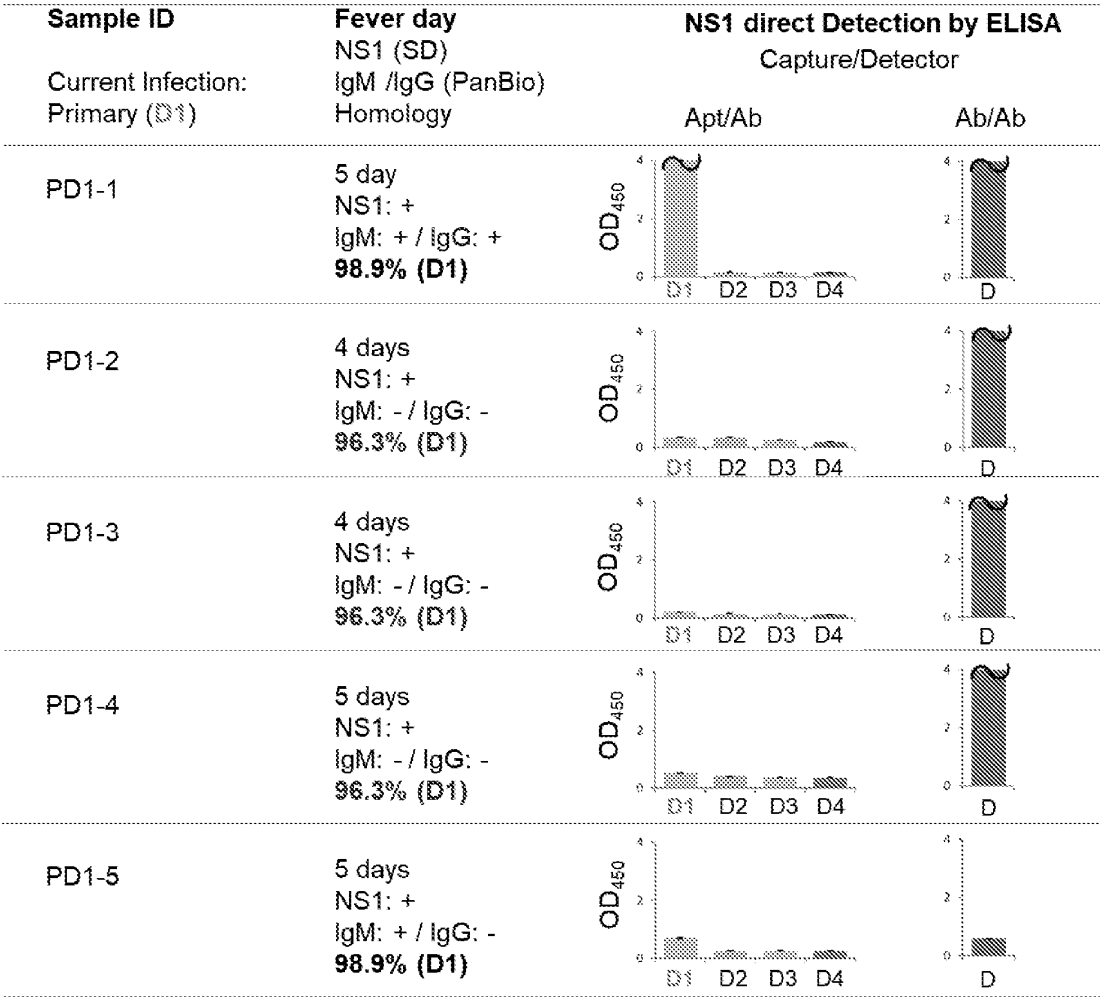


FIG. 20

A

NA DEN1-NS1	DSGCVINWKGRELKCGSGIFVTNEVHTWTEQYKFQADSPKRLSAAIGKAWEEGVCGIRSA	60
PD1-1/1-5	DSGCVINWKGRELKCGSGIFVTNEVHTWTEQYKFQADSPKRLSAAIGKAWEEGVCGIRSA	
PD1-2/1-3/1-4	DSGCVINWKGRELKCGSGIFVTNEVHTWTEQYKFQADSPKRLSAAIGKAWEEGVCGIRSA	
NA DEN1-NS1	TRLENIMWKQISNELNHILLENDMKFTTVVVGDVSGILAQCKKMIRPQPMEHKYSWKSWGK	120
PD1-1/1-5	TRLENIMWKQISNELNHILLENDMKFTTVVVGDVAGILAQCKKMIRPQPMEHKYSWKSWGK	
PD1-2/1-3/1-4	TRLENIMWKQISNELNHILLENDMKFTTVVVGDAAGILTQGGKMIRPQPMEHKYSWKSWGK	
NA DEN1-NS1	AKIIGAEVQNTTFEIIDGPNTPCEPDNQRAWNIWEVEDYGFGIFTTNIWLKLRDSYTVQCD	180
PD1-1/1-5	AKIIGAEVQNTTFEIIDGPNTPCEPDQRAWNIWEVEDYGFGIFTTNIWLKLRDSYTVQCD	
PD1-2/1-3/1-4	AKIIGAEVQNTTFEIIDGPDTPCEPDQRAWNIWEVEDYGFGVFTTNIWLKLRDSYTVQCD	
NA DEN1-NS1	HRLMSAAIKDSKAVHADMGYWIESEKNETWKLARASFIEVKTCIWPKSHTLWNGVLESE	240
PD1-1/1-5	HRLMSAAIKDSKAVHADMGYWIESEKNETWKLARASFIEVKTCIWPKSHTLWNGVLESE	
PD1-2/1-3/1-4	HRLMSAAIKDSKAVHADMGYWIESEKNETWKLARASFIEVKTCIWPFRSHTLWNGVLESE	
NA DEN1-NS1	MIIPKIYGGPISQHNYPGYFTQTAGPWHLGKLELDFDLCEGTTVVVDEHCGNRGPSLRT	300
PD1-1/1-5	MIIPKIYGGPISQHNYPGYFTQTAGPWHLGKLELDFDLCEGTTVVVDEHCGNRGPSLRT	
PD1-2/1-3/1-4	MIIPKIYGGPISQHNYPGYFTQTAGPWHLGKLELDFNLCEGTTVVVDEHCGNRGPSLRT	
NA DEN1-NS1	TTVTGKTIHEWCCRSCTLPPLRFRGEDGCGWYGMETRPVKEKEENLVKSMVSA	352
PD1-1/1-5	TTVTGKIHEWCCRSCTLPPLRFRGEDGCGWYGMETRPVKEKEENLVKSMVSA	
PD1-2/1-3/1-4	TTVTGKIHEWCCRSCTLPPLRFRGEDGCGWYGMETRPVKEKEENLVKSMVSA	

B

Identiy %	Native antigen D1	PD1-1 PD1-5	PD1-2 PD1-3 PD1-4
Native antigen D1	100		
PD1-1 PD1-5	98.9	100	
PD1-2 PD1-3 PD1-4	96.3	97.2	100

C

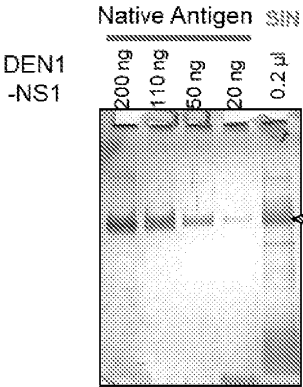


FIG. 21

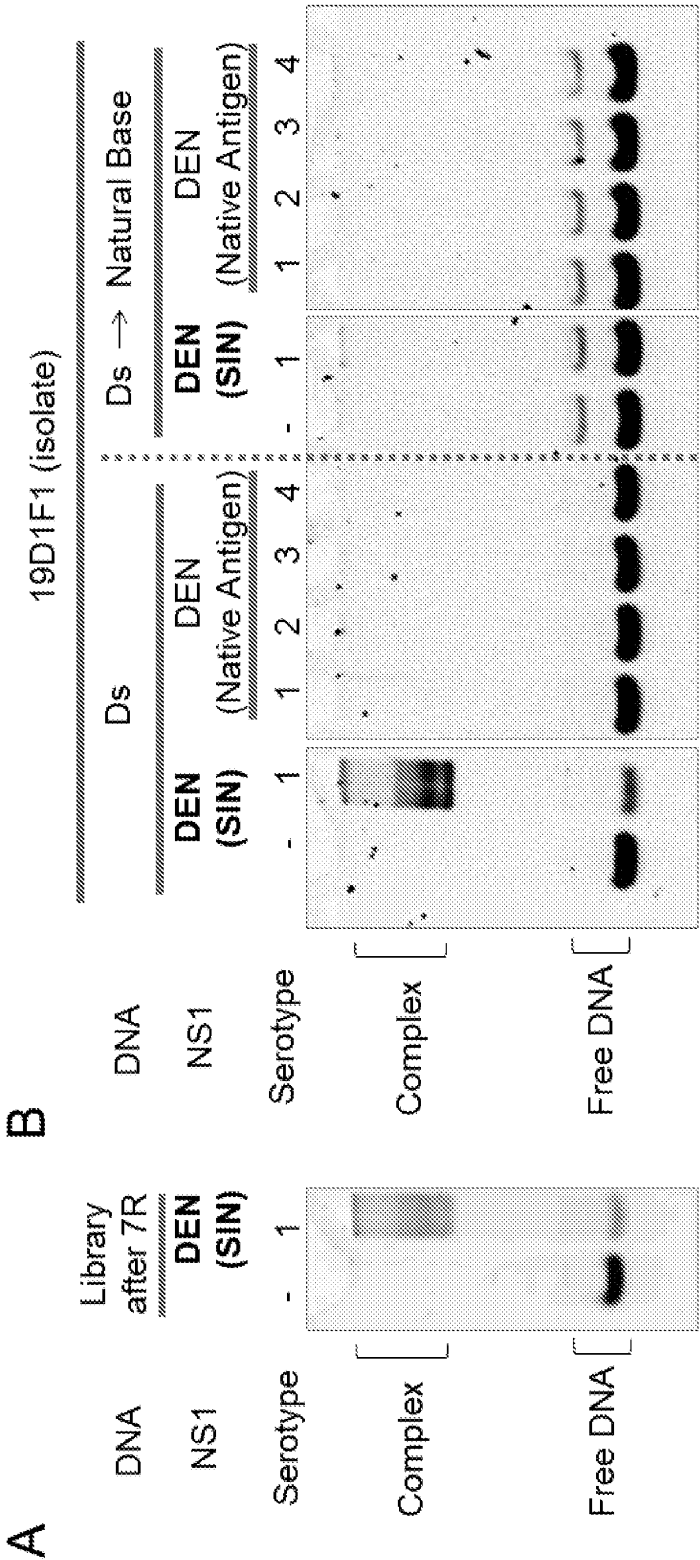


FIG. 22

FIG. 23

FIG. 23

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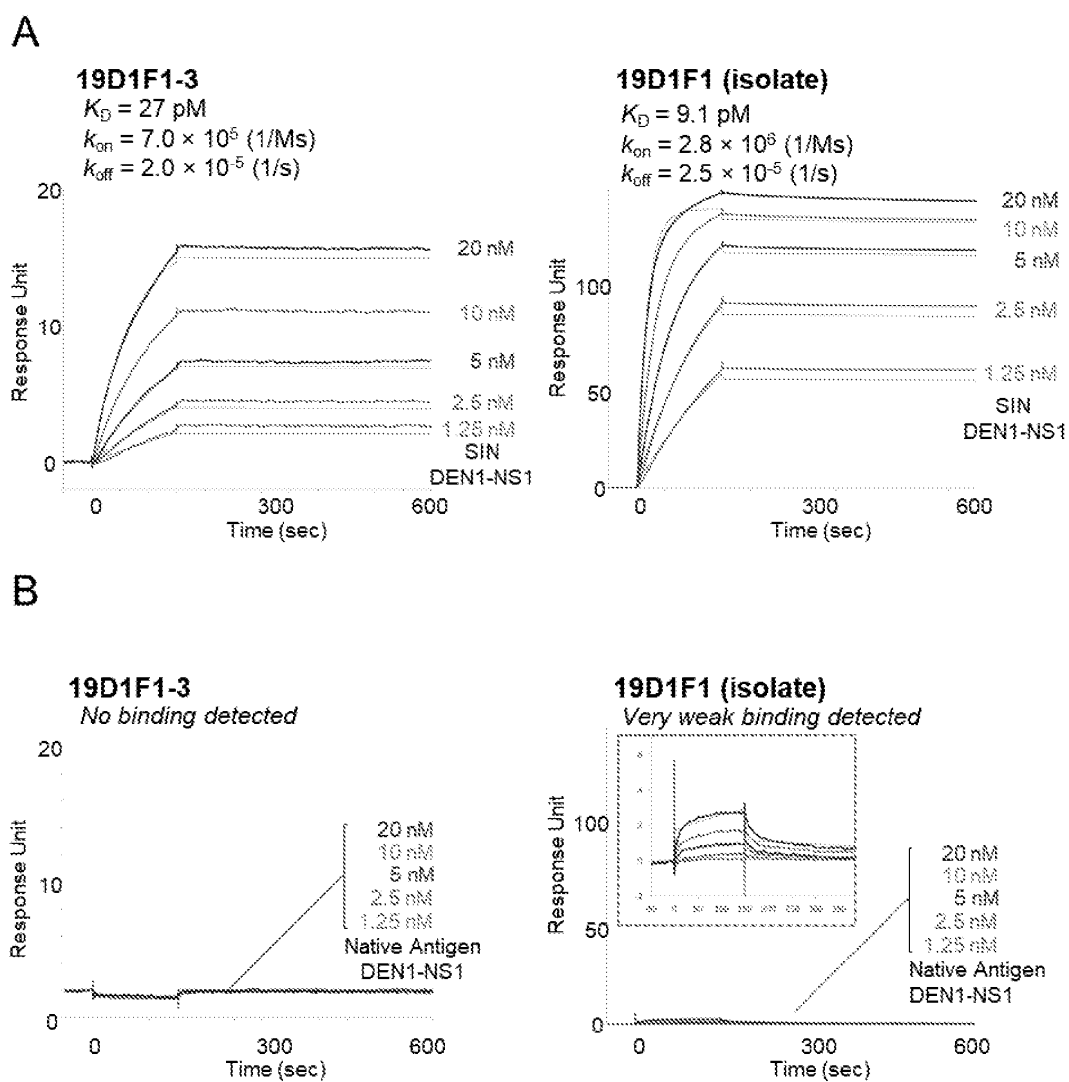
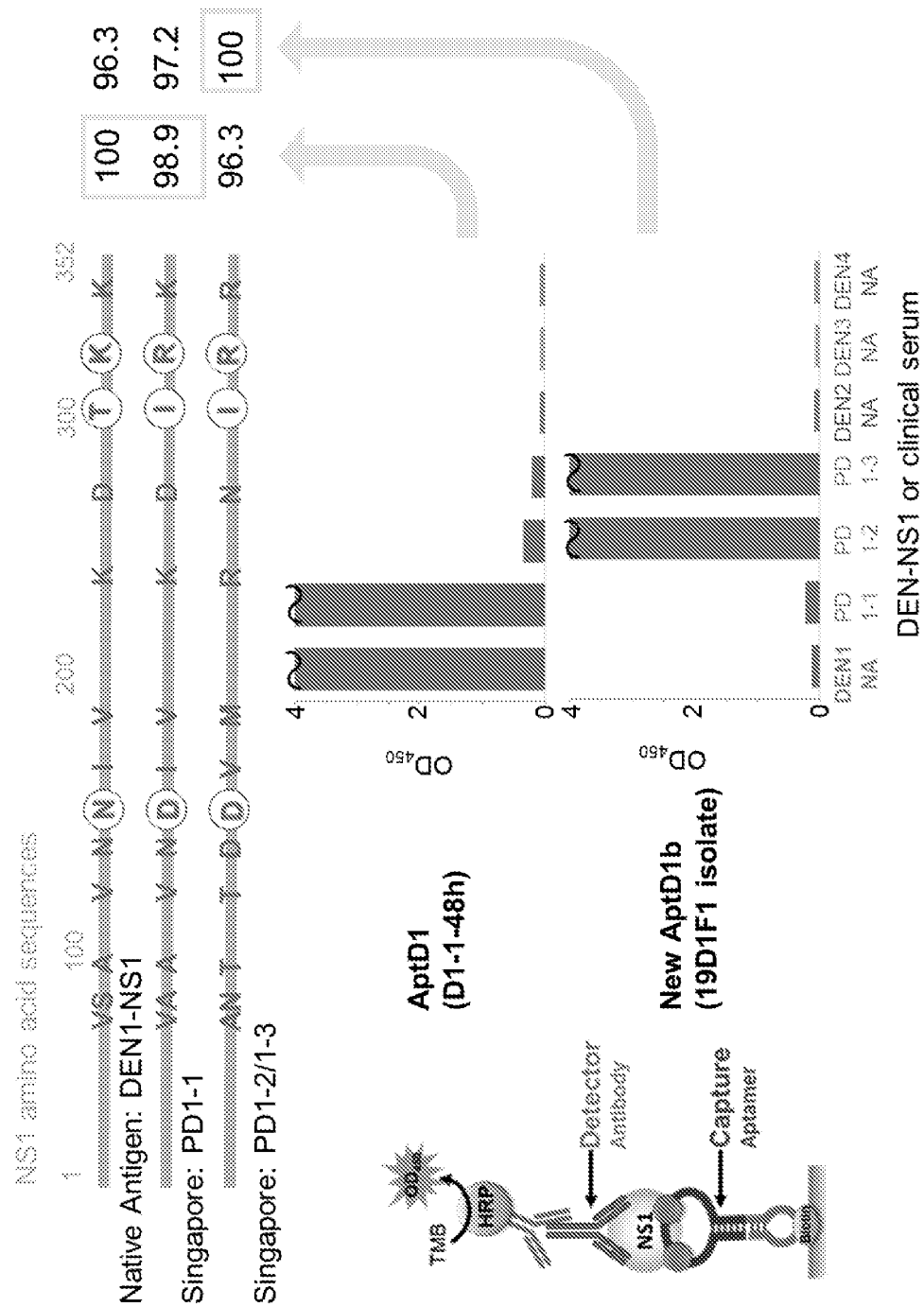
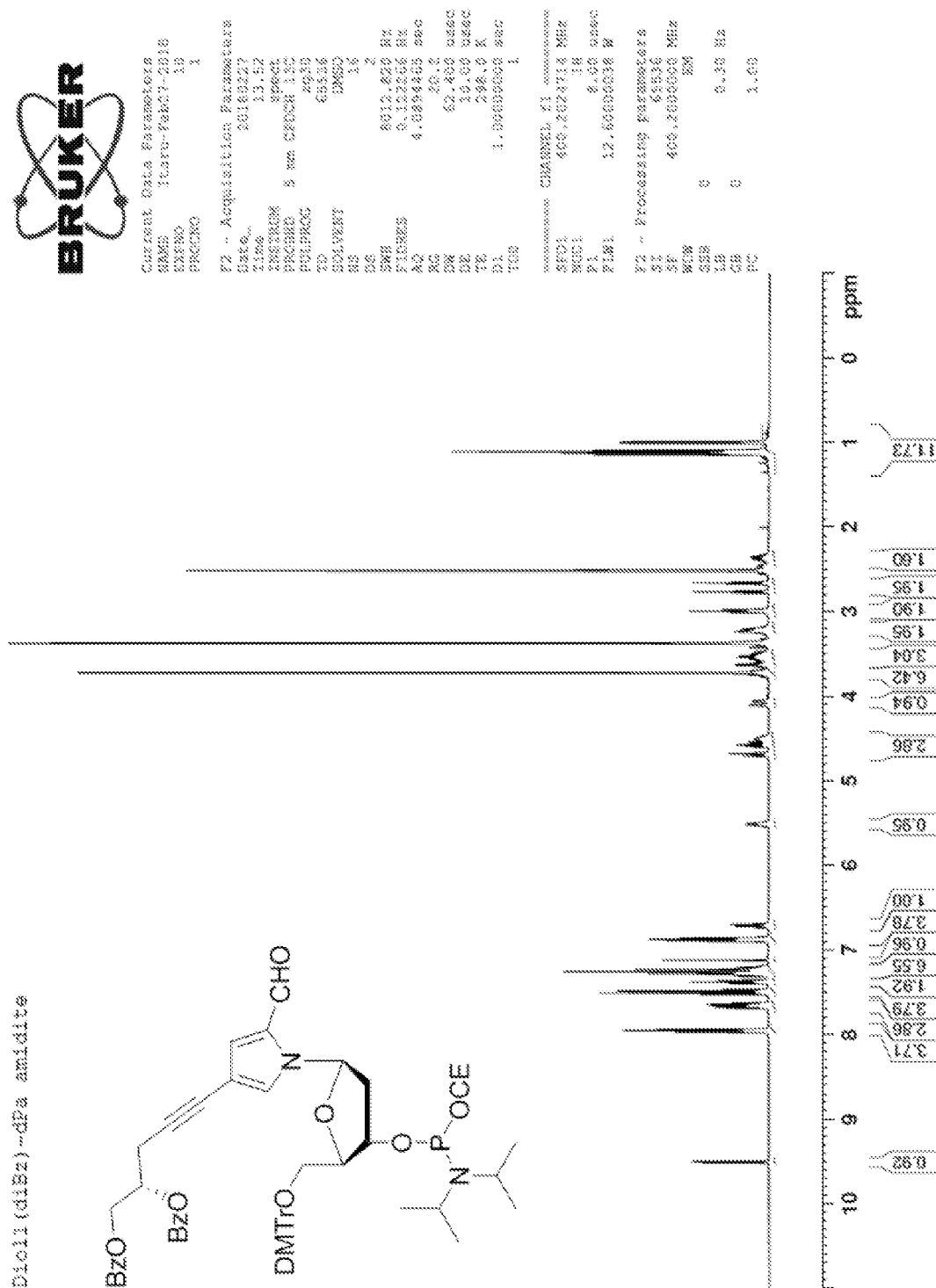


FIG. 24



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Current Data Parameters
NAME Item-Mar14-2019
EXPNO 4
PROCNO 1
F2 ~ Acquisition Parameters
Date_ 20190316
Time 20.47
INSTRUM spect
PROBHD 5 mm PABBO BBO-
PULPROG zgpg30
TD 32768
SOLVENT DMSO
NS 1024
DS 0
SWH 49019.608 Hz
FIDRES 1.495960 Hz
AQ 0.3362336 sec
RG 198.36
DM 10.200 usec
DE 6.50 usec
TE 301.2 K
G1 2.0000000 sec
TD0 1
----- CHANNEL f1 -----
NUC1 13C
P1 12.55 usec
PL1 16.0000000 W
F2 ~ Processing parameters
SI 32768
SF 161.975000 MHz
WDW 0
SSB 0
LB 5.00 Hz
GB 0
PC 1.40

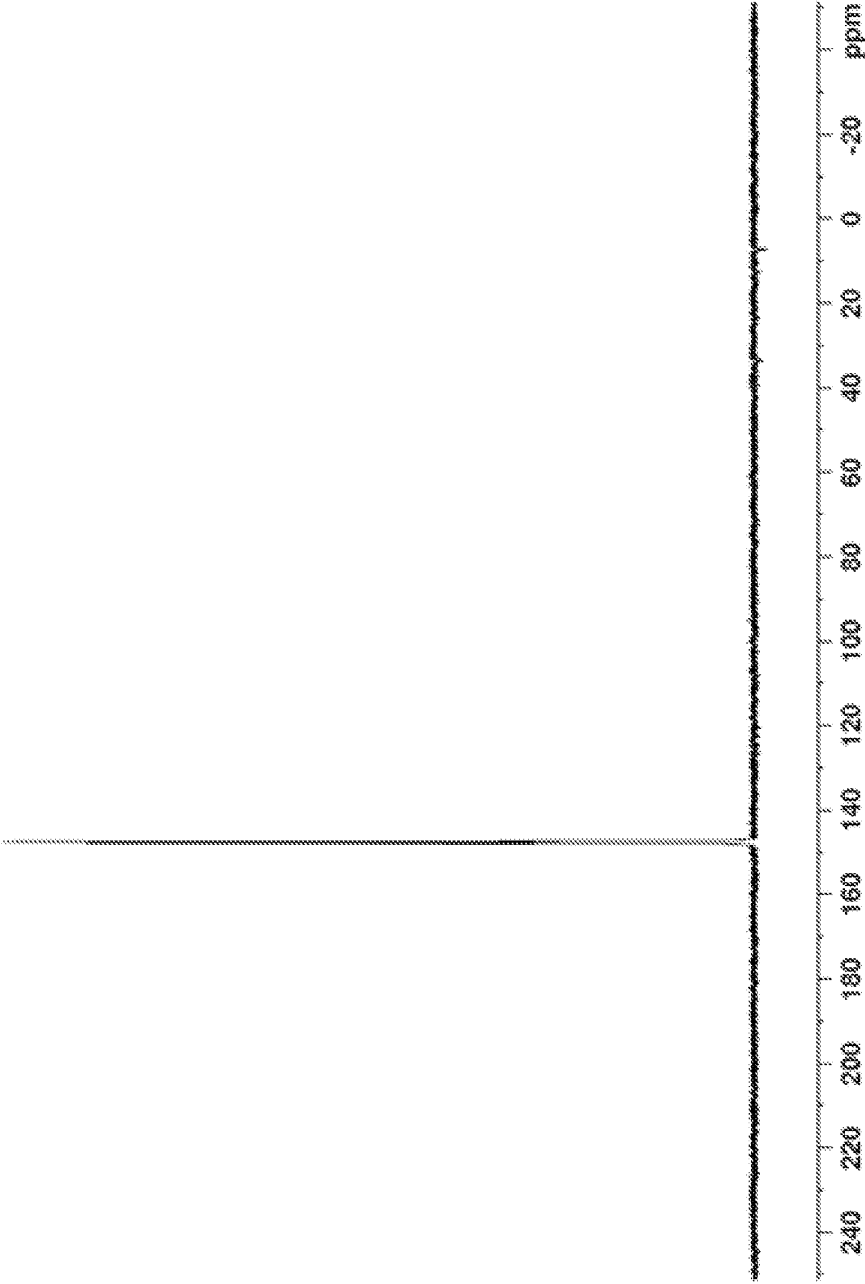


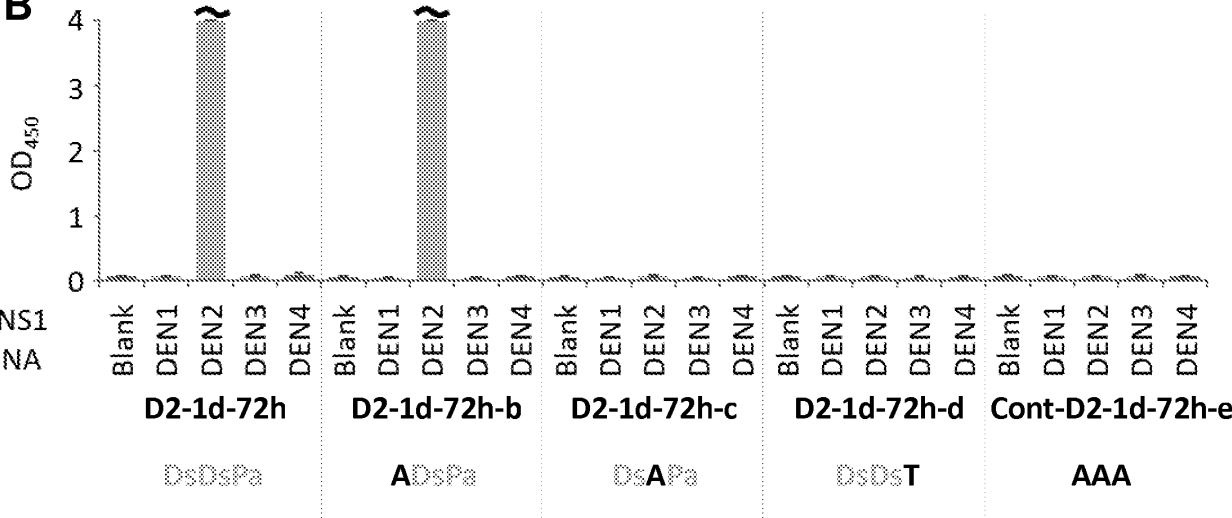
FIG. 27

A

x:Ds, d:Diol-Pa, L:Biotin-T

D2-1d-72h	GGCTGGTCCGxCTGGGAACAAGxGGCGGGAGGGAdGGGTGTGGGTGCGACAAGCGGACCAGCCCGCGLAGCG
D2-1d-72h-b	GGCTGGTCCGACTGGGAACAAGxGGCGGGAGGGAdGGGTGTGGGTGCGACAAGCGGACCAGCCCGCGLAGCG
D2-1d-72h-c	GGCTGGTCCGxCTGGGAACAAGAGGGCGGGAGGGAdGGGTGTGGGTGCGACAAGCGGACCAGCCCGCGLAGCG
D2-1d-72h-d	GGCTGGTCCGxCTGGGAACAAGxGGCGGGAGGGATGGGTGTGGGTGCGACAAGCGGACCAGCCCGCGLAGCG
Cont-D2-1d-72h-e	GGCTGGTCCGACTGGGAACAAGAGGGCGGGAGGGAdGGGTGTGGGTGCGACAAGCGGACCAGCCCGCGLAGCG

B



C

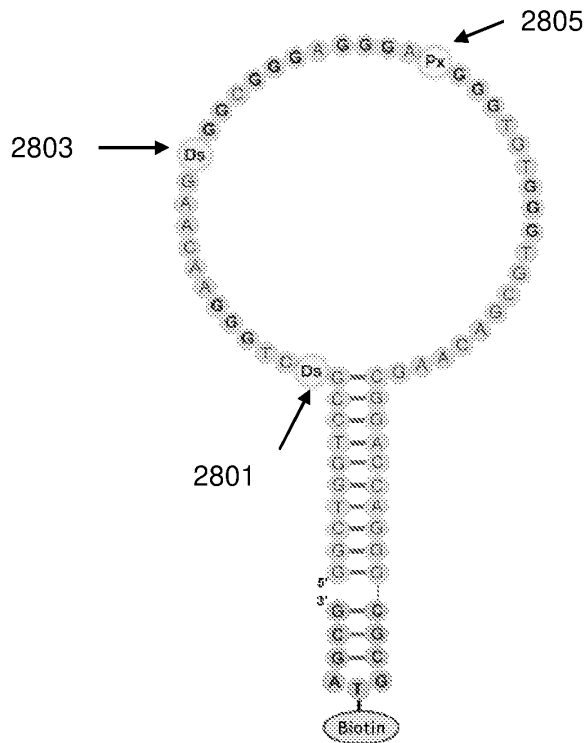


FIG. 28