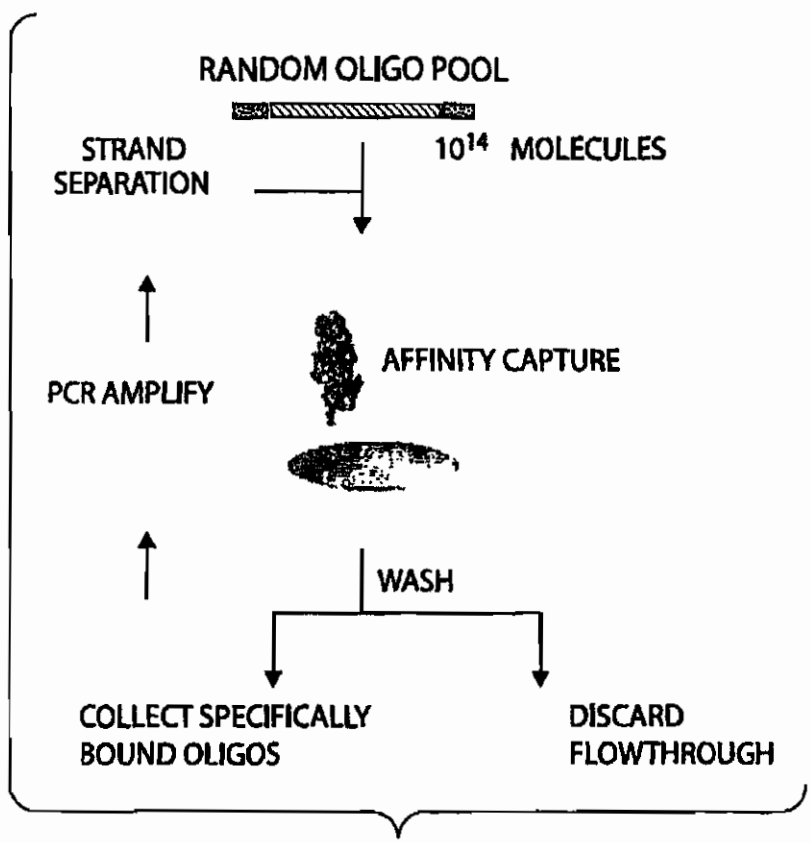
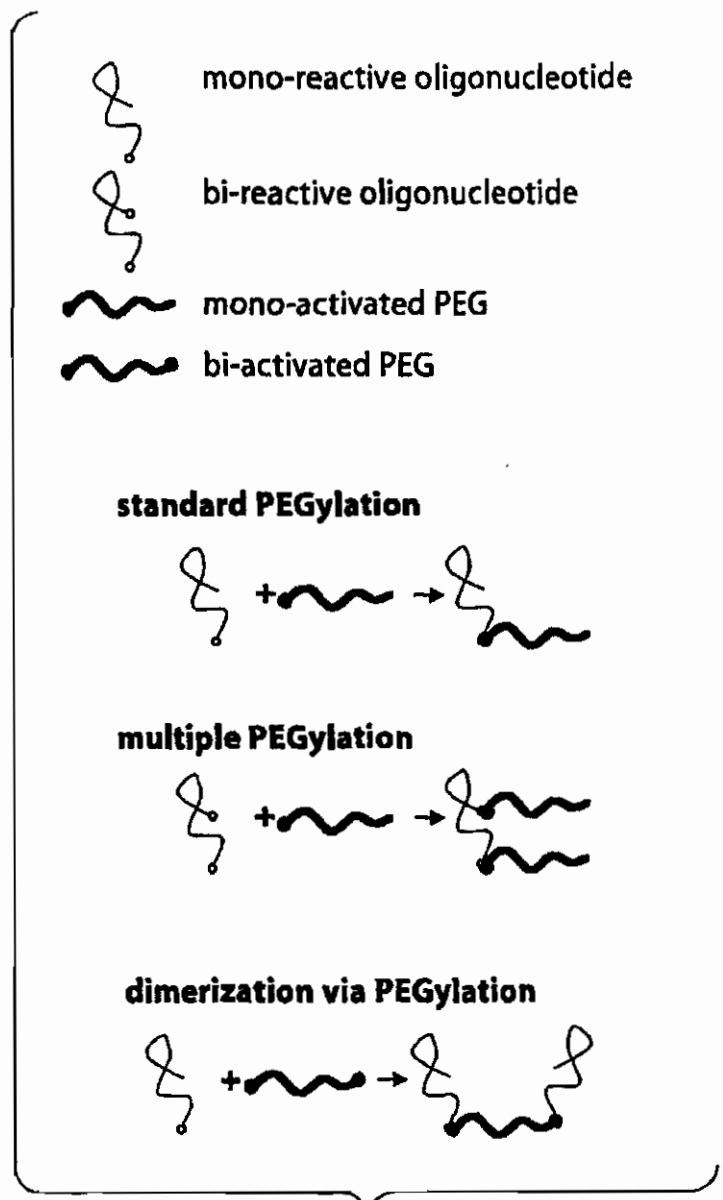

RANDOM OLIGO POOL
STRAND SEPARATION
10^{14} MOLECULES
PCR AMPLIFY
AFFINITY CAPTURE
WASH
COLLECT SPECIFICALLY BOUND OLIGOS
DISCARD FLOWTHROUGH

Fig. 1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bi-reactive oligonucleotide
mono-activated PEG
bi-activated PEG
standard PEGylation
multiple PEGylation
dimerization via PEGylation

Fig. 2

Amino Acid Sequence of Human vWF domain A1

MGHHHHHHEPPLHDFYCSRLLDLVFLLDGSSRLSEAEFEVLKAFVVDMMEQLRISQK
WVRVAVVEYHDGSHAYIGLKDRKRPSELRRIASQVKYAGSQVASTSEVLKYTLFQIFSK
IDRPEASRIALLLMASQEPQRMSRNFVRYVQGLKKKKVIVIPVGIGPHANLKQIRLIEKQ
APENKAFVLSSVDELEQQRDEIVSYLCDLAPEAPPPT (SEQ. ID. No. 4)

Amino Acid Sequence of Human vWF domain A1

MRGSHHHHHHGSQEPGGLVVPPTDAPVSPTTLYVEDISEPPLHDFYCSRLLDLVFLLD
GSSRLSEAEFEVLKAFVVDMMERLRISQKWVRVAVVEYHDGSHAYIGLKDRKRPSELR
RIASQVKYAGSQVASTSEVLKYTLFQIFSKIDRPEASRIALLLMASQEPQRMSRNFVRY
VQGLKKKKVIVIPVGIGPHANLKQIRLIEKQAPENKAFVLSSVDELEQQRDEIVSYLCDLA
PEAPPPTLPP (SEQ. ID. NO.5)

Amino Acid Sequence of Rabbit vWF domain A1

MGHHHHHHEPPLHDFYWSNLMDLVFLLDGSAQLSEAEFGVLKAFVVSVMERLHISQK
RIRVAVVEYHDGSHSYISLKDRKRPSELRRIASQVKYAGGPVASTSEVLKYTLFHIFSNV
DRPEASRIALLLSASQETPRMVRNLVRYAQGLKKEKVIVIPVGIGPHVSLRQIHLIEKQA
PENKAFVLSGVDELEQRRDEIISYLCDLGPEAPVPT (SEQ. ID. NO. 6)

Fig. 3

Amino Acid Sequence of Full Length Human vWF

MIPARFAGVLLALALILPGTLCAEGTRGRSSTARCSLFGSDFVNTFDGSMYSFAGYCSYLLAGG
CQKRSFSIIGDFQNGKRVSLSVYLGEFFDIHLFVNGTVTQGDQRVSMPYASKGLYLETEAGYYK
LSGEAYGFVARIDGSGNFQVLLSDRYFNKTCGLCGNFNIFAEDDFMTQEGTLTSDPYDFANSW
ALSSGEQWCERASPPSSSCNISSGEMQKGLWEQCQLLKSTSVFARCHPLVDPEPFVALCEKT
LCECAGGLECACPALLEYARTCAQEGMVLYGWTDHSACSPVCPAGMEYRQCVSPCARTCQS
LHINEMCQERCVDGCSCPEGQLLDEGLCVESRECPCVHSGKRYPPGTSLSRDCNTCICRNSQ
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GRGRLLVKLSPVYAGKTCGLCGNYNGNQGDDFLTPSGLAEPRVEDFGNAWKLHGDCQDLQK
QHSDPCALNPRMTRFSEEACAVLTSPTFEACHRAVSPLPYLRNCRYDVCSCSDGRECLCGAL
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SCRCERMEACMLNGTVIGPGKTVMIDVCTTCRCMVQVGVISGFKLECRKTTCNPCPLGYKEEN
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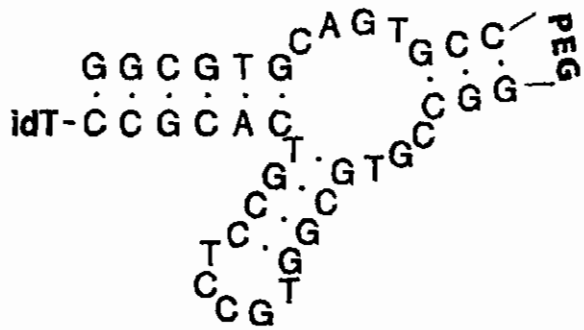
Fig. 4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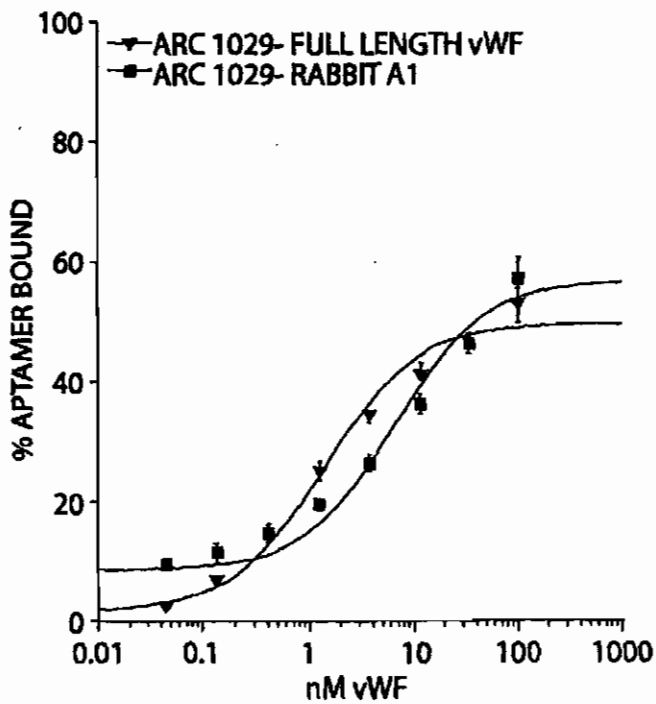
C C G T

Fig. 5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ARC 1029- RABBIT A1
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nM vWF
0
20
40
60
80
100
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0.1
1
10
100
1000

Fig. 6

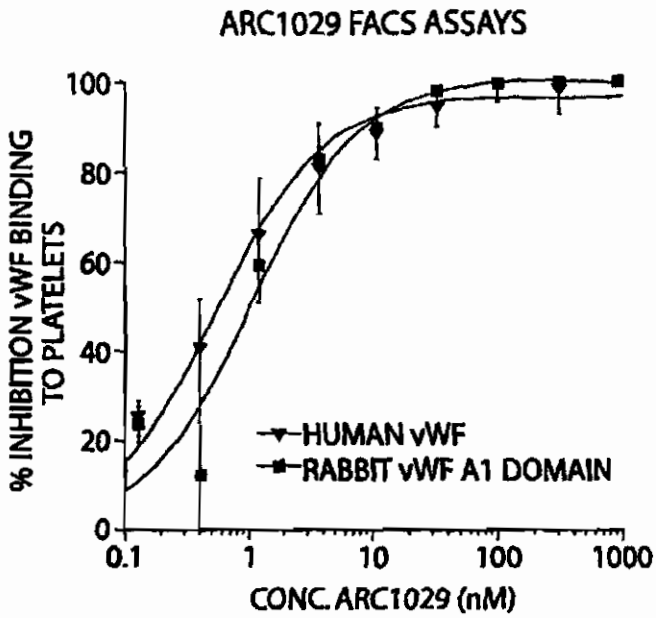
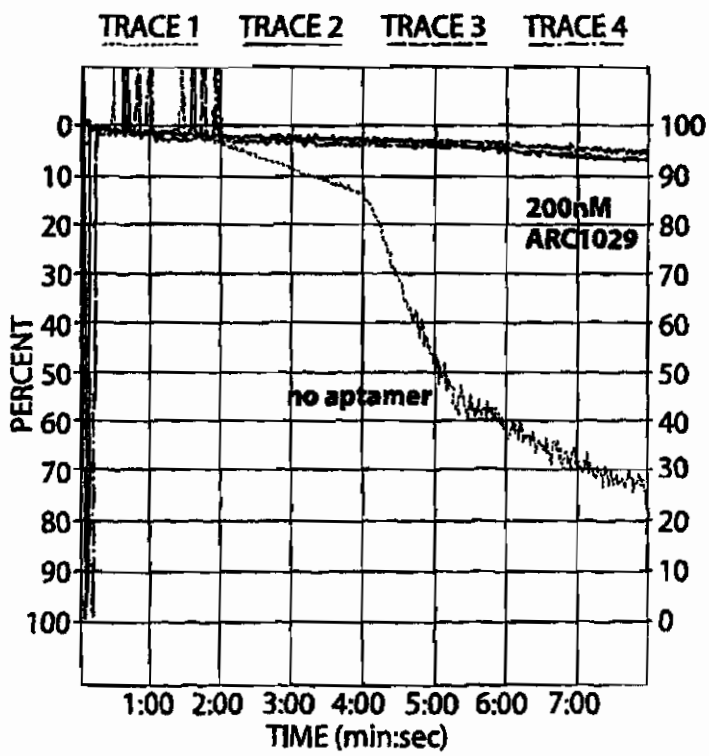

ARC1029 FACS ASSAYS
% INHIBITION vWF BINDING TO PLATELETS
100
80
60
40
20
0
0.1
1
10
100
1000
CONC. ARC1029 (nM)
HUMAN vWF
RABBIT vWF A1 DOMAIN

Fig. 7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TRACE 2
TRACE 3
TRACE 4
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50
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80
90
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2:00
3:00
4:00
5:00
6:00
7:00
TIME (min:sec)

Fig. 8

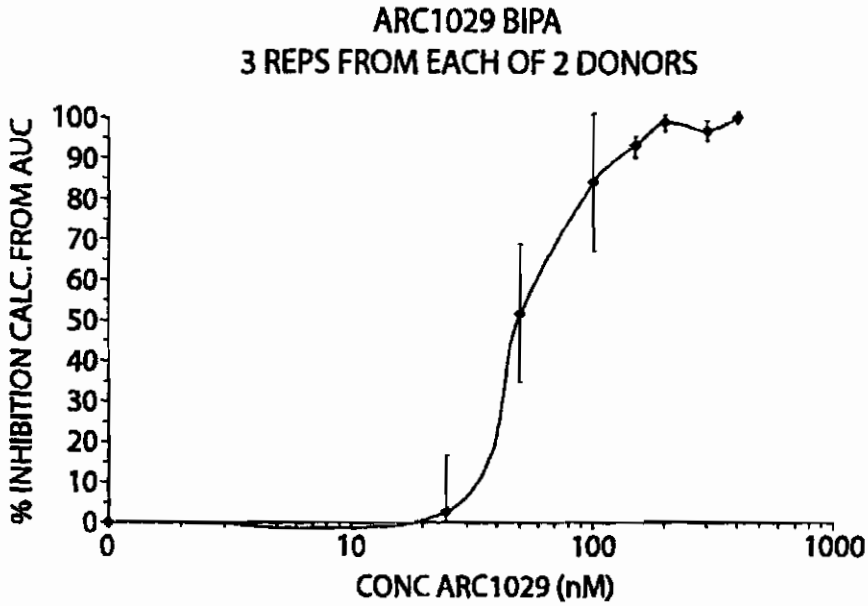
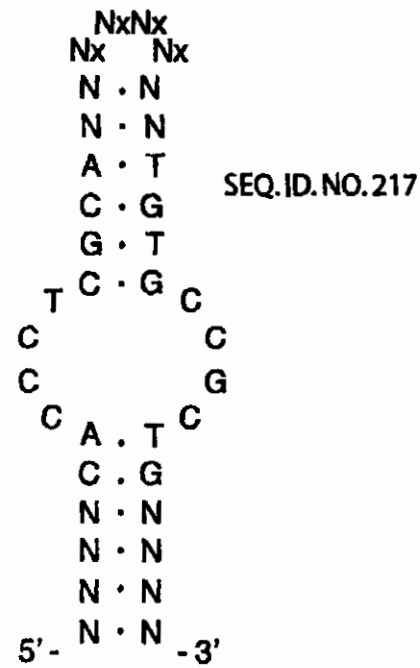


Fig. 9



SEQ. ID. NO. 217

Fig. 10

vWF rRdY SELEX FAMILY #1 SEQUENCE ALIGNMENT

```
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                                ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
Clone 70 min 3                1 ----------------GGGAC--G-GG-GTG--GG-TAGAC-GG--C-GG-GTAT--GTCCC------------------ 32
DL.159.87.70 (AMX203.G9)      1 GGAGCGCACT----CAGCCAC--G-GG-GTG--GG-TAGAC-GG--C-GG-GTAT--GTGGCTG--GTGTCGAAGGGTTT 60
DL.159.87.75 (AMX203.F9)      1 GGAGCGCACTCAGC--CACTG-AA-GG-GTAA-GG-ACGA--GG--A-GG-GTATA-CAGTG-----TGCGCGTGTATTT 61
DL.159.87.28 (AMX203.A6)      1 GGAGCGCACTCA-GCCACCAC-GG-GG-ACG--GG-TAG---GG--C-GG-GCGAG-GTGGTGGC-----ATTAGCGTTT 60

                                        90
                                ....|....|....|.
Clone 70 min 3               32 ---------------- 32
DL.159.87.70 (AMX203.G9)     61 CGACCTCTCTGCTAGC 76
DL.159.87.75 (AMX203.F9)     62 CGACCTCTCTGCTAGC 77
DL.159.87.28 (AMX203.A6)     61 CGACCTCTCTGCTAGC 76
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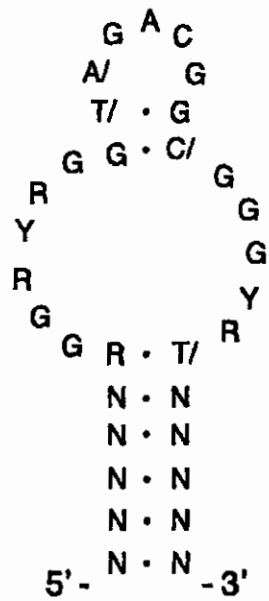
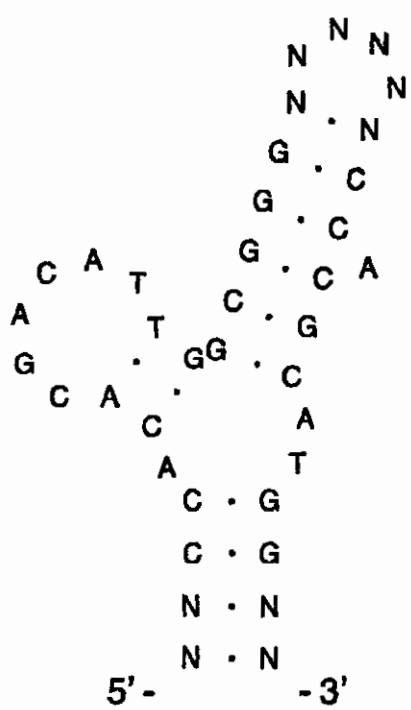
Fig. 11



SEQ. ID. NO. 218

Y = C or T
R = A or G
N = any nucleotide but in paired regions it assumes a Watson/Crick Base pair.

Fig. 12



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N = any nucleotide but in paired regions it assumes a Watson/Crick Base pair.

Fig. 13

vWF DNA SELEX 2, FAMILY 1 SEQUENCE ALIGNMENT

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                       ....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|....|
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AMX237.B11      1  CTACCTACGATCTGACT-AGCTC--CAGT-GTT-TTATCTAAT-AAC-CGTG-CGG-TG-CCT-CCG-T--GA-GCT-TACTCTCATGTAGTTCC 7
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AMX238.E7       1  CTACCTACGATCTGACT-AGCGTG-CAGT-GCC-TATTTTA---GGC-CGTG-CGG-TG-CCT-CCG-T-CAC-GCT-TACTCTCATGTAGTTCC 7
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AMX236.H2       1  CTACCTACGATCTGACT-AGCGTG-CAGT-GCC-TATCCCA---GGC-CGTG-CGG-TAGCCT-CCG-T-CAC-GCT-TACTCTCATGTAGTTCC 8
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Fig. 14

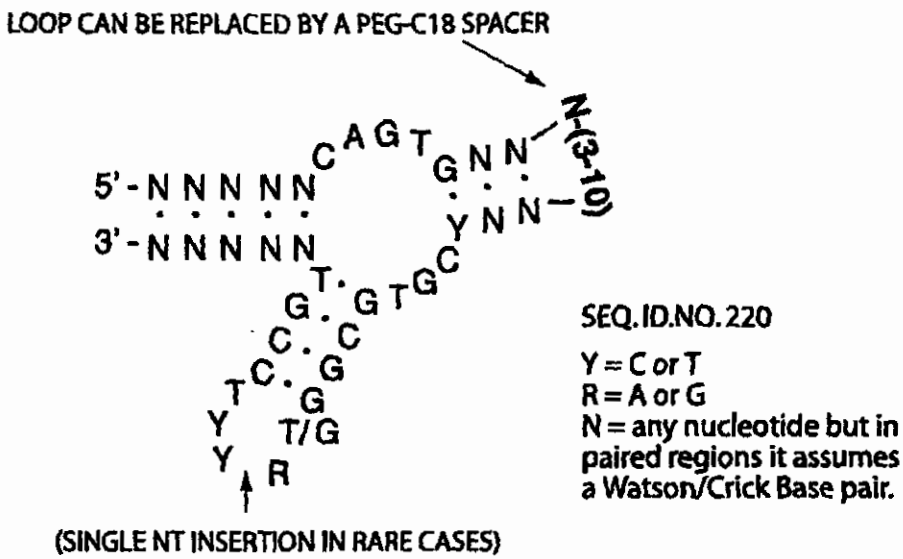
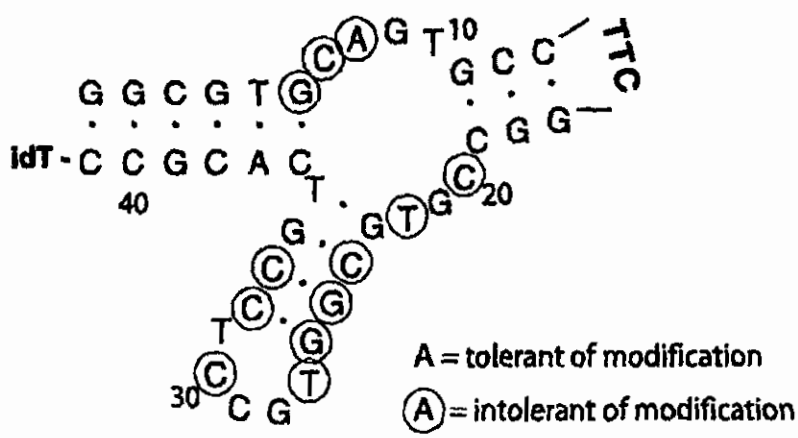


Fig. 15A



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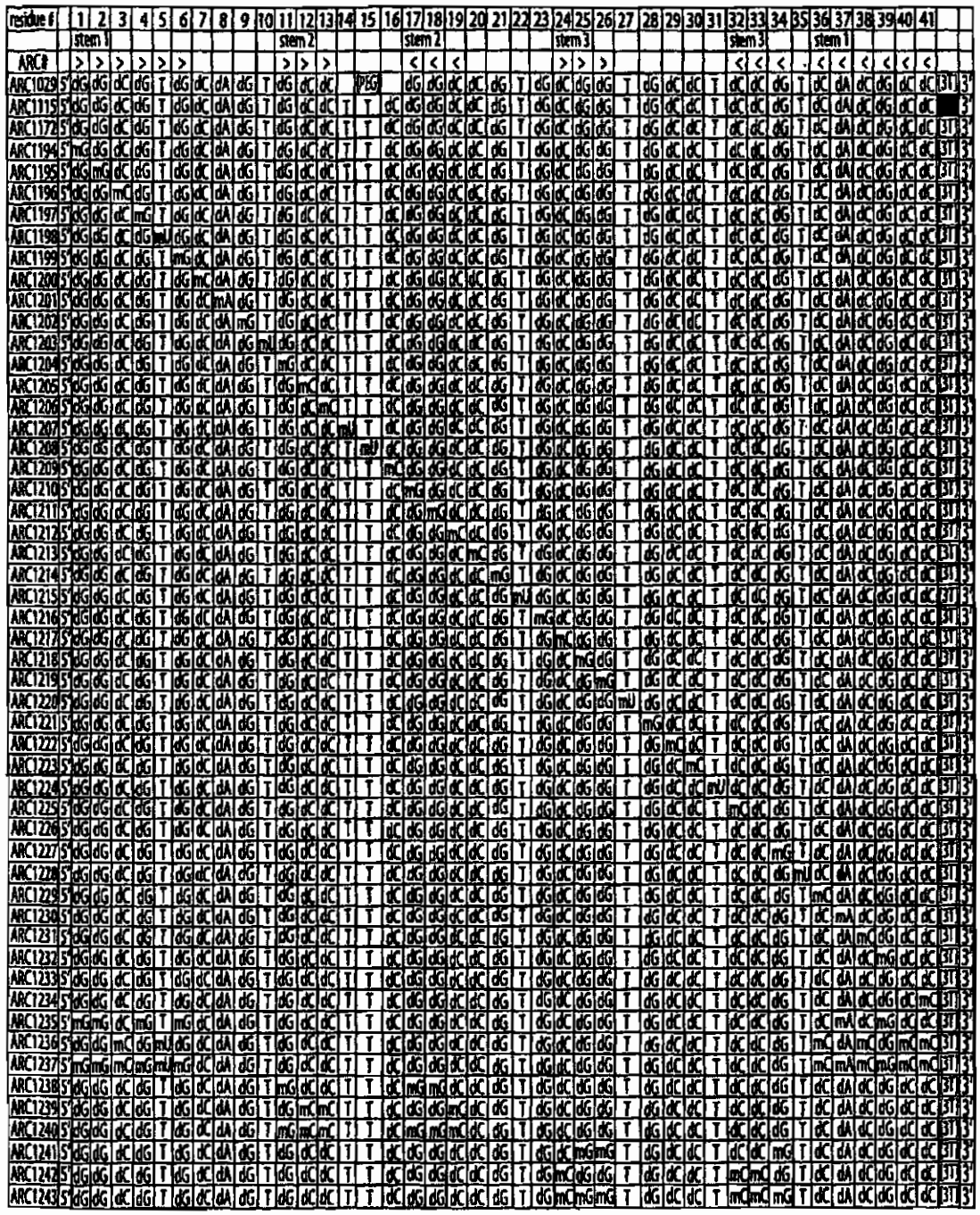

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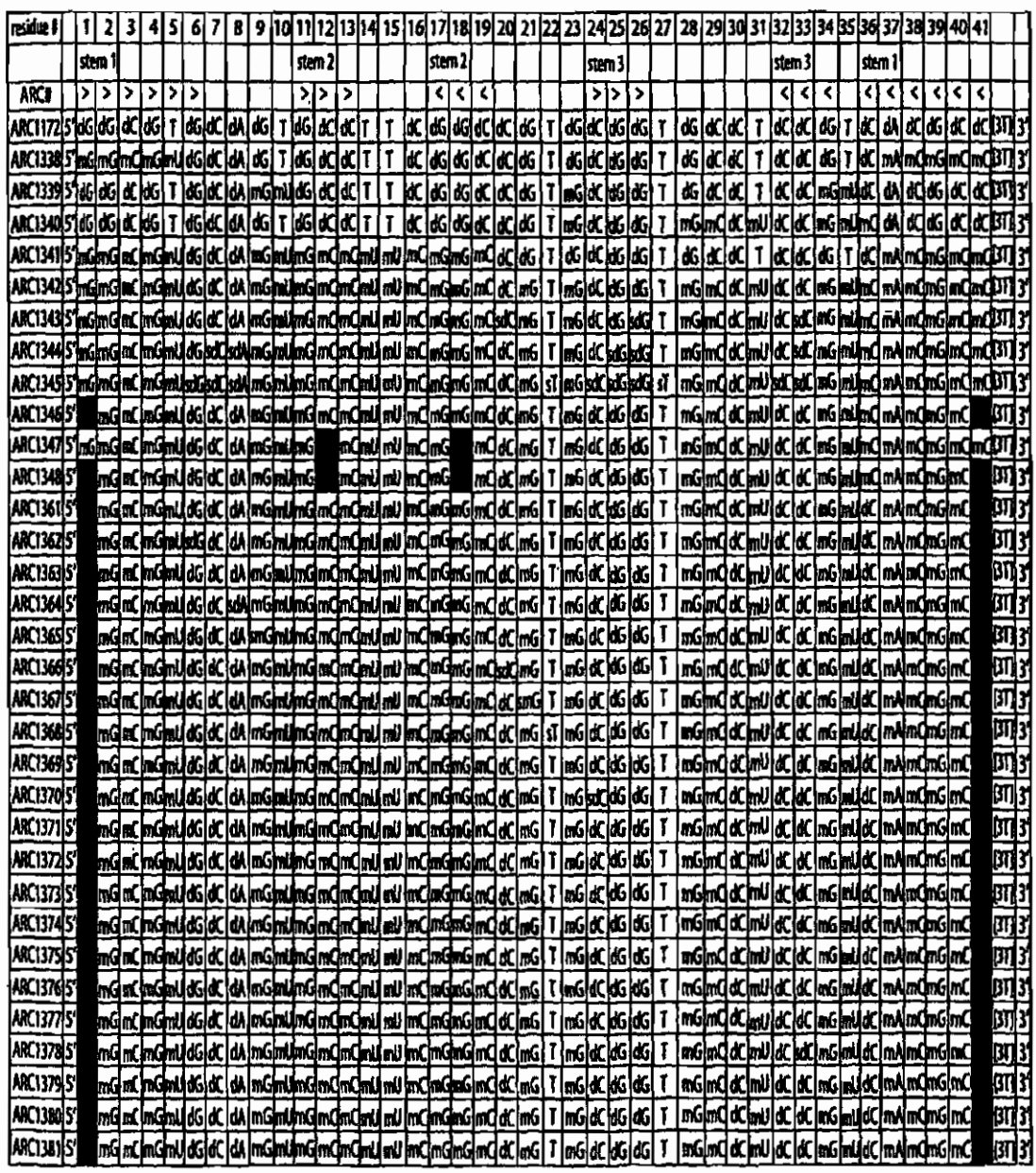

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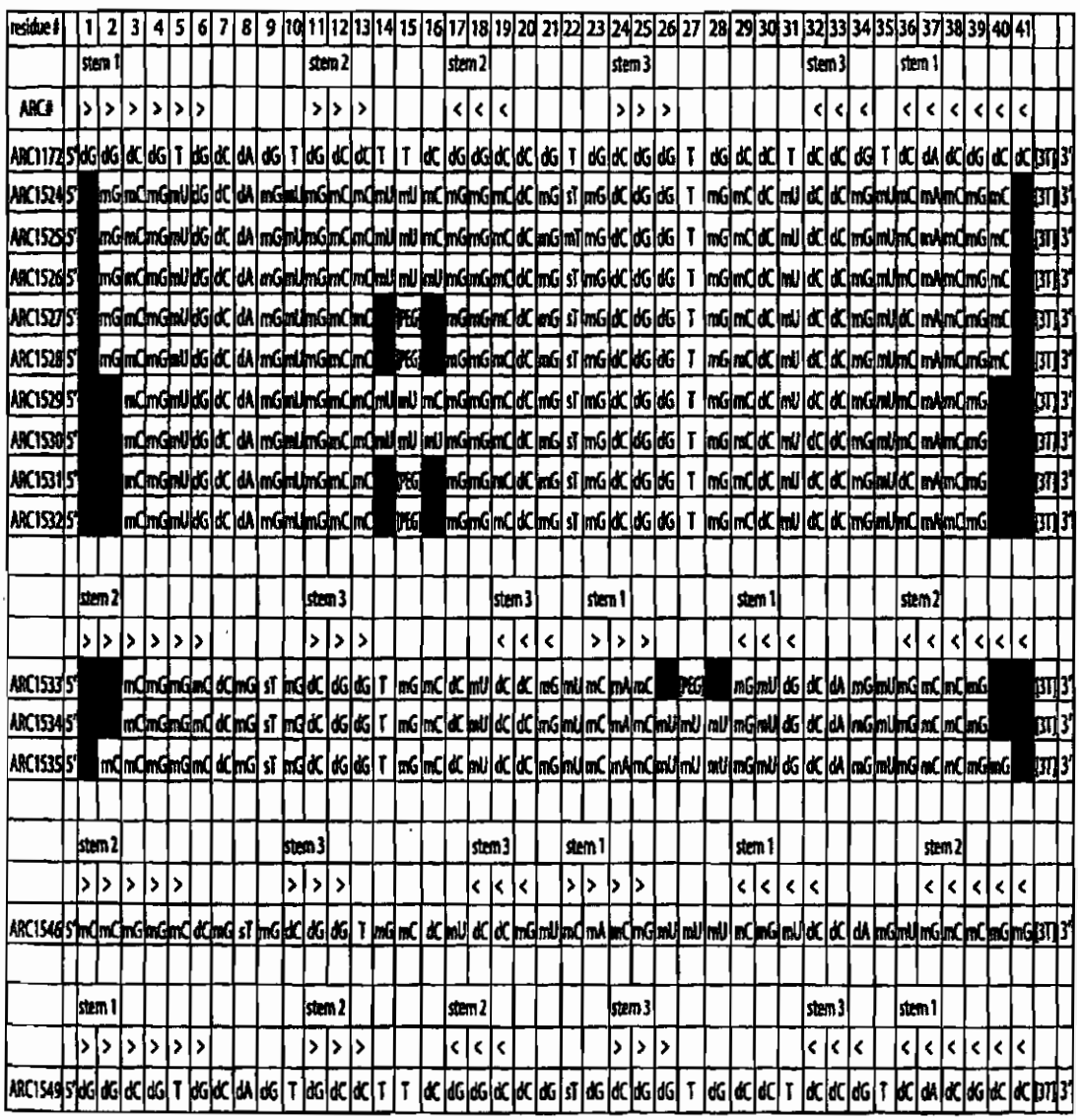

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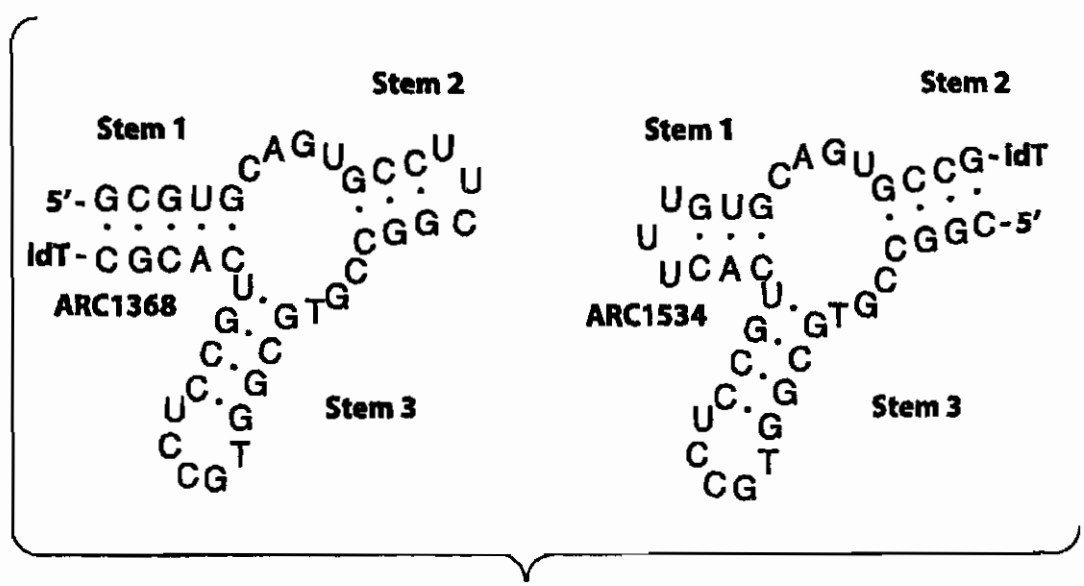
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Stem 2
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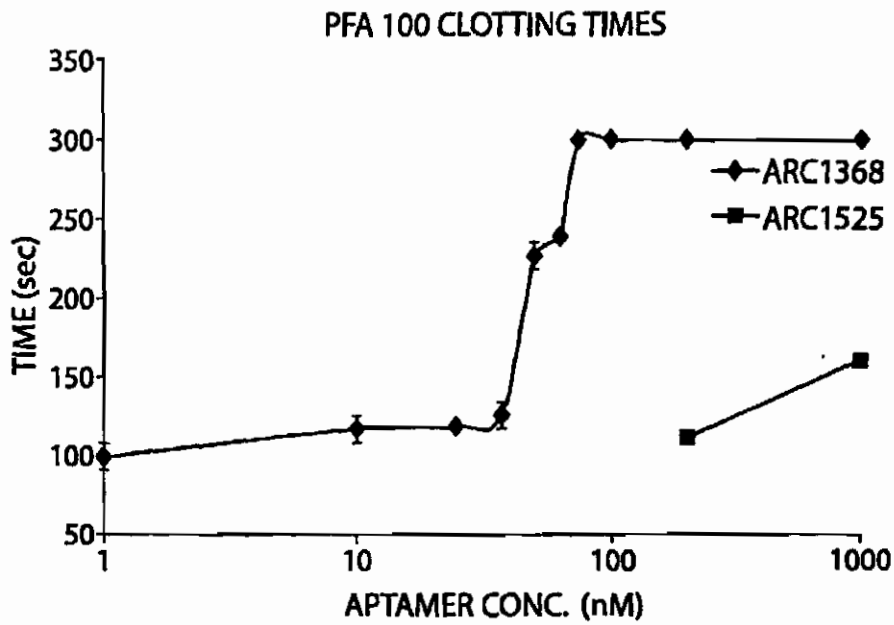
C-5'
Stem 3

Fig. 19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10
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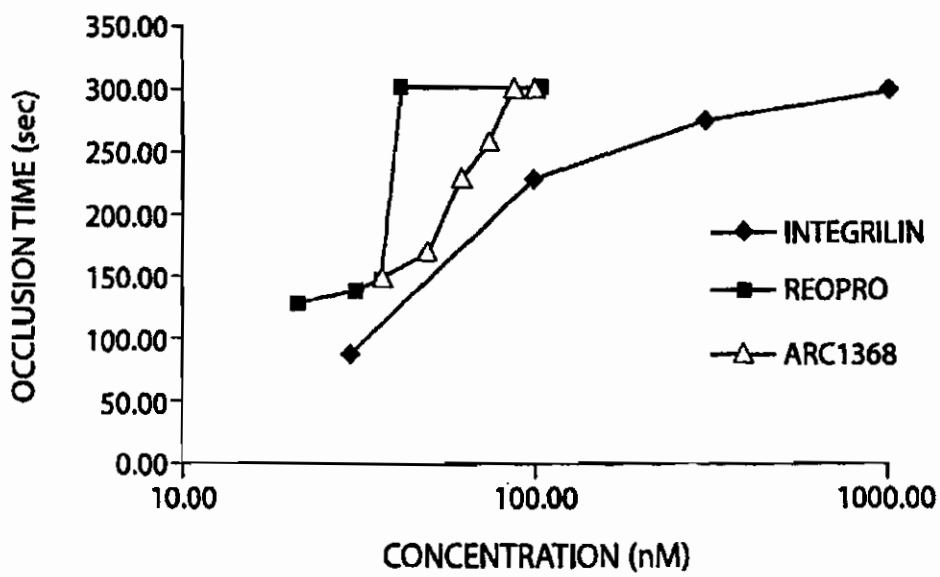
1000
APTAMER CONC. (nM)
ARC1368
ARC1525

Fig. 20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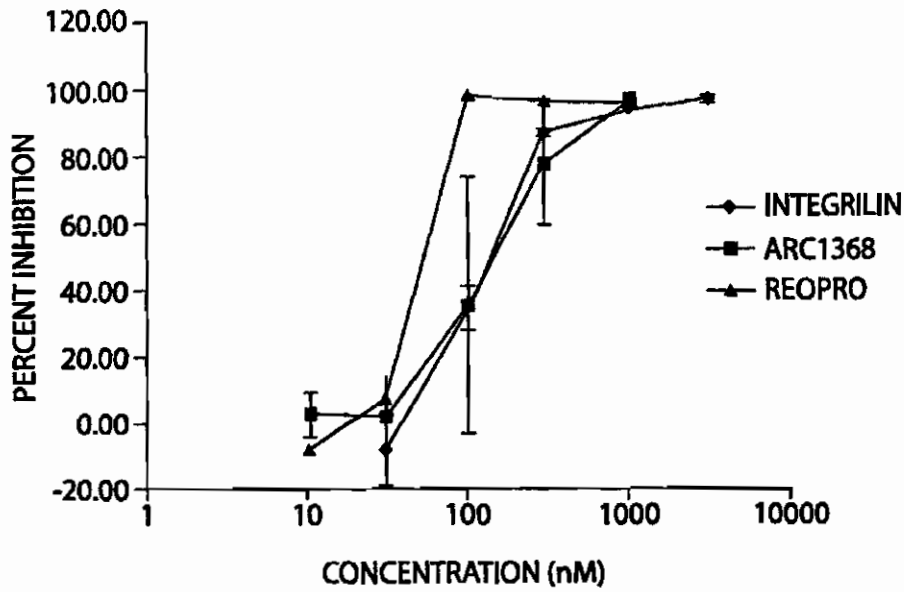
INTEGRILIN
REOPRO
ARC1368

Fig. 21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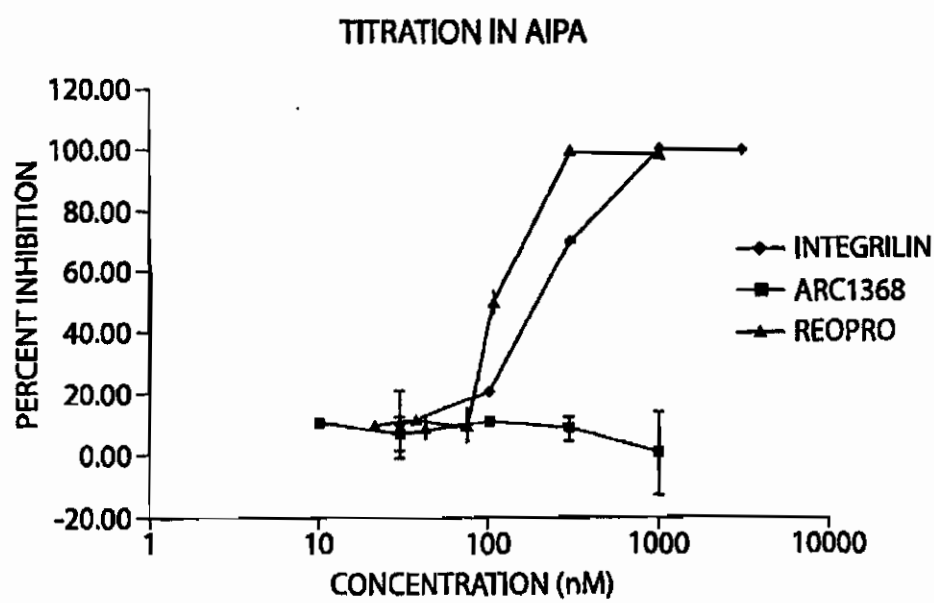
ARC1368
REOPRO

Fig. 22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ARC1368
REOPRO

Fig. 23

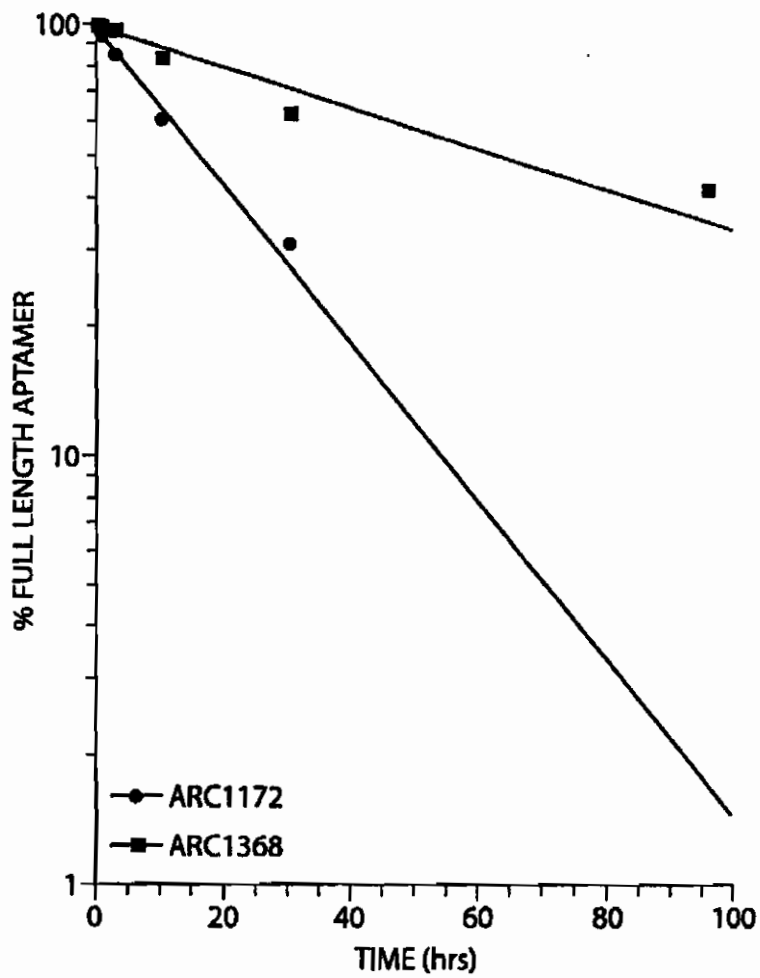
100
10
1
% FULL LENGTH APTAMER
0
20
40
60
80
100
TIME (hrs)
ARC1172
ARC1368

Fig. 24

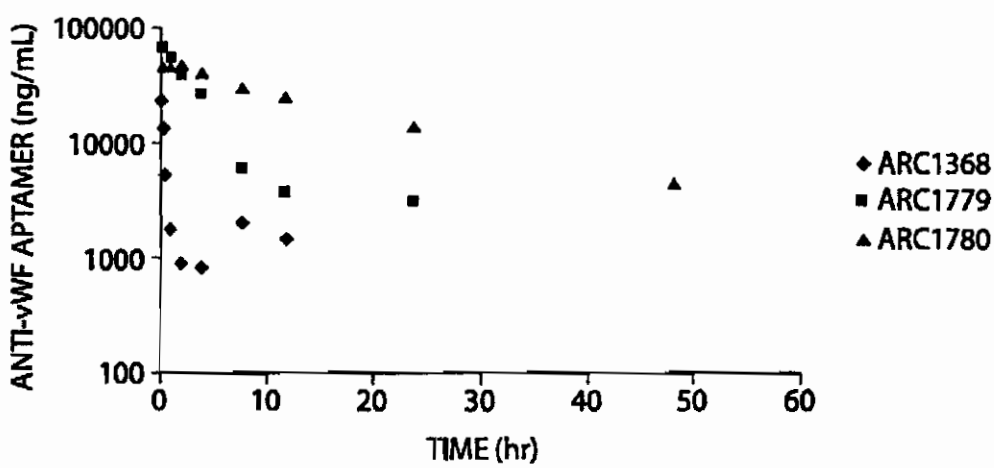
ANTI-vWF APTAMER (ng/mL)
100000
10000
1000
100
0
10
20
30
40
50
60
TIME (hr)
ARC1368
ARC1779
ARC1780

Fig. 25

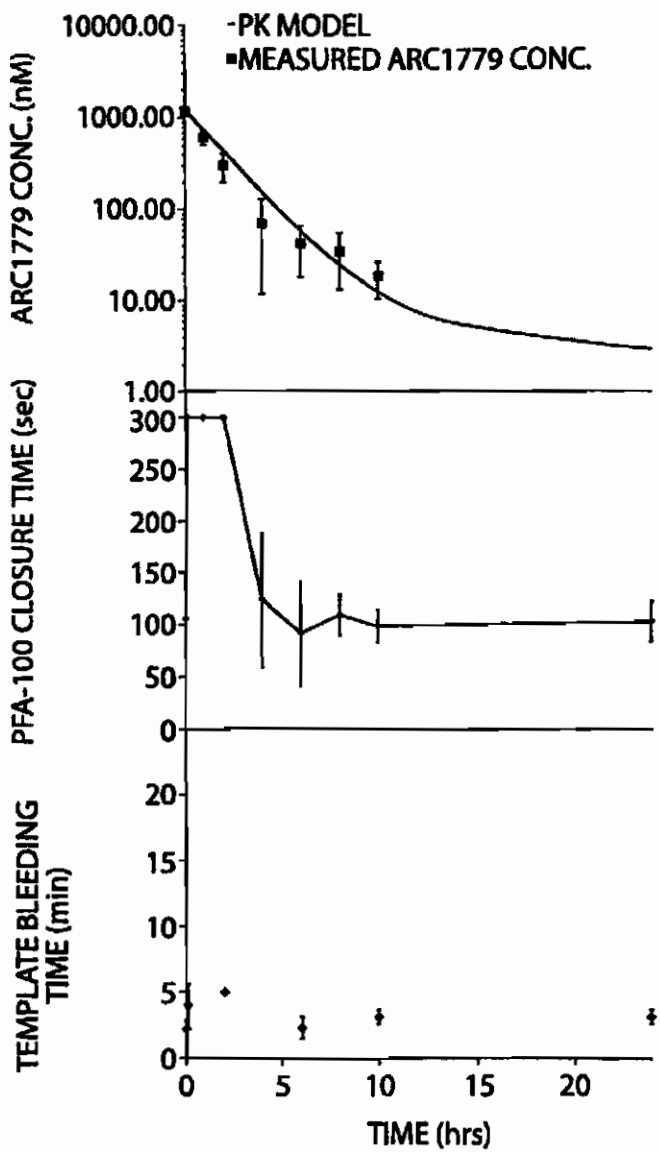
-PK MODEL
▪MEASURED ARC1779 CONC.
ARC1779 CONC. (nM)
10000.00
1000.00
100.00
10.00
1.00
PFA-100 CLOSURE TIME (sec)
300
250
200
150
100
50
0
TEMPLATE BLEEDING TIME (min)
20
15
10
5
0
0
5
10
15
20
TIME (hrs)

Fig. 26

	ANIMAL 1001			ANIMAL 1101			ANIMAL 1102		
	CBT	BIPA	PFA-100	CBT	BIPA	PFA-100	CBT	BIPA	PFA-100
Pre	1	30	79	3	36	124	2	34	120
5 min	3.2	>>	>>	6.8	>>	>>	4.8	>>	>>
6 hours	1		119	1.3		107	2.3		163
10 hours	2.4		99	3		107	3.5		155
24 hours	2.3	47	92	2.3	51	106	1.8	NA	NA

>> = 100% INHIBITION

Fig. 27

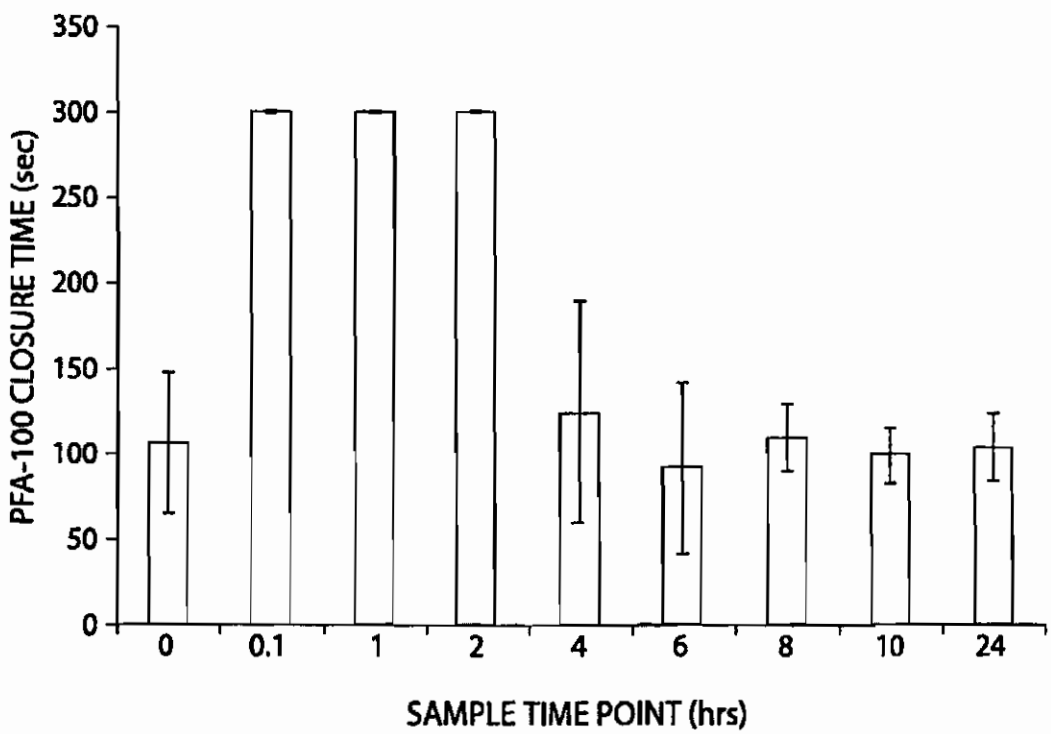

Fig. 28

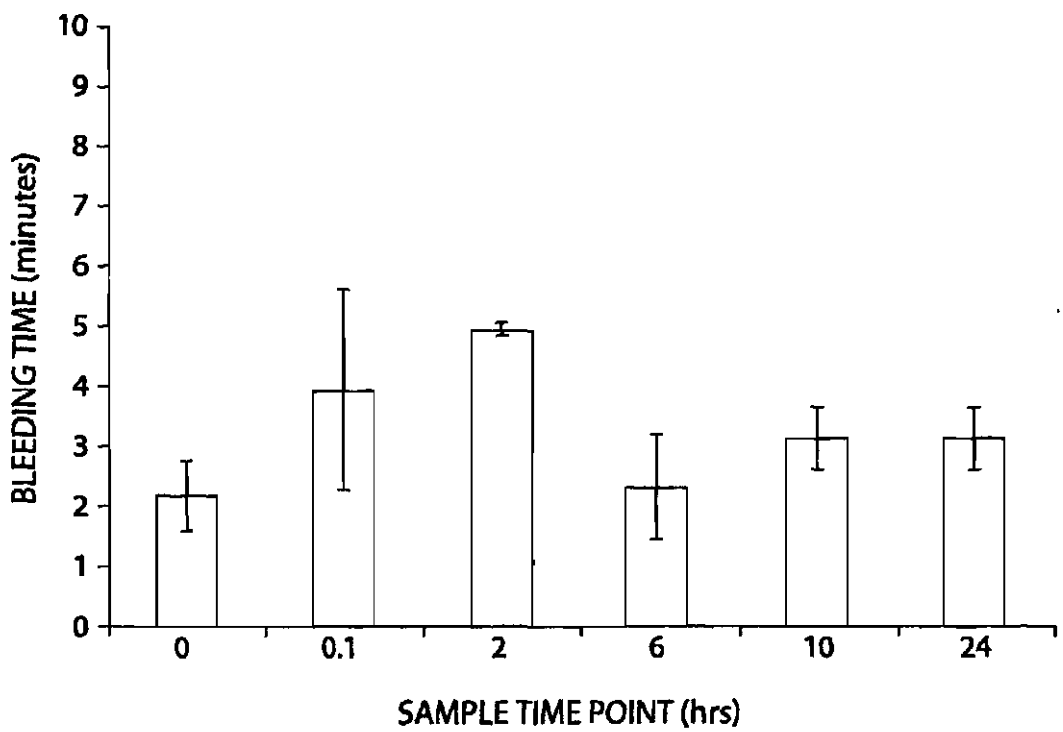
BLEEDING TIME (minutes)
10
9
8
7
6
5
4
3
2
1
0
0
0.1
2
6
10
24
SAMPLE TIME POINT (hrs)

Fig. 29

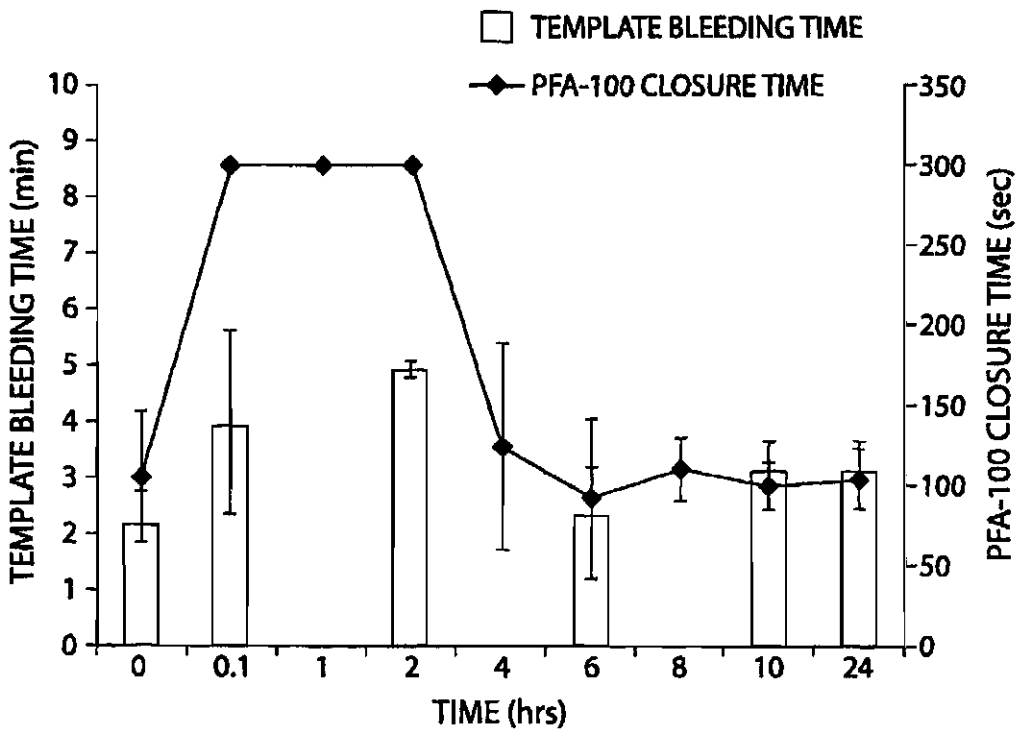
TEMPLATE BLEEDING TIME
PFA-100 CLOSURE TIME
TEMPLATE BLEEDING TIME (min)
PFA-100 CLOSURE TIME (sec)
TIME (hrs)
0
0.1
1
2
4
6
8
10
24
0
1
2
3
4
5
6
7
8
9
10
0
50
100
150
200
250
300
350

Fig. 30

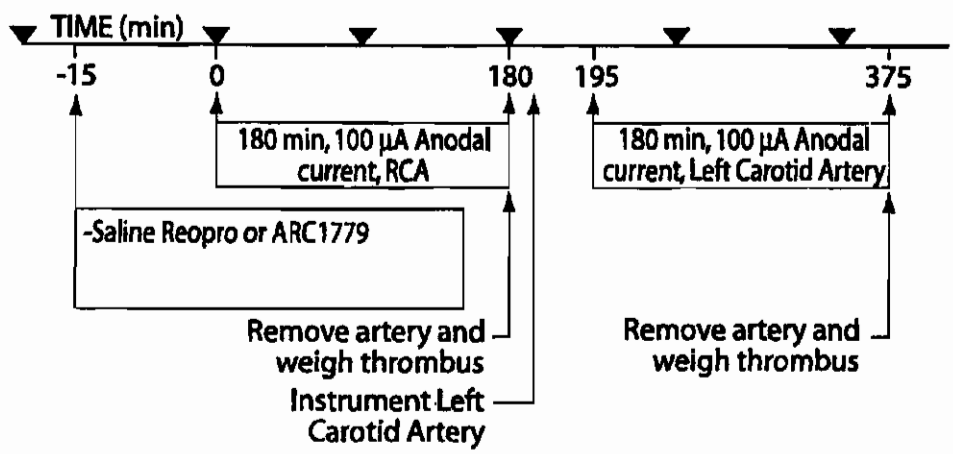
TIME (min)
-15
0
180
195
375
180 min, 100 µA Anodal current, RCA
180 min, 100 µA Anodal current, Left Carotid Artery
-Saline Reopro or ARC1779
Remove artery and weigh thrombus
Instrument Left Carotid Artery
Remove artery and weigh thrombus
▼ Sample time: ACT, BIPA, PFA-100, plasma, bleeding time

Fig. 31

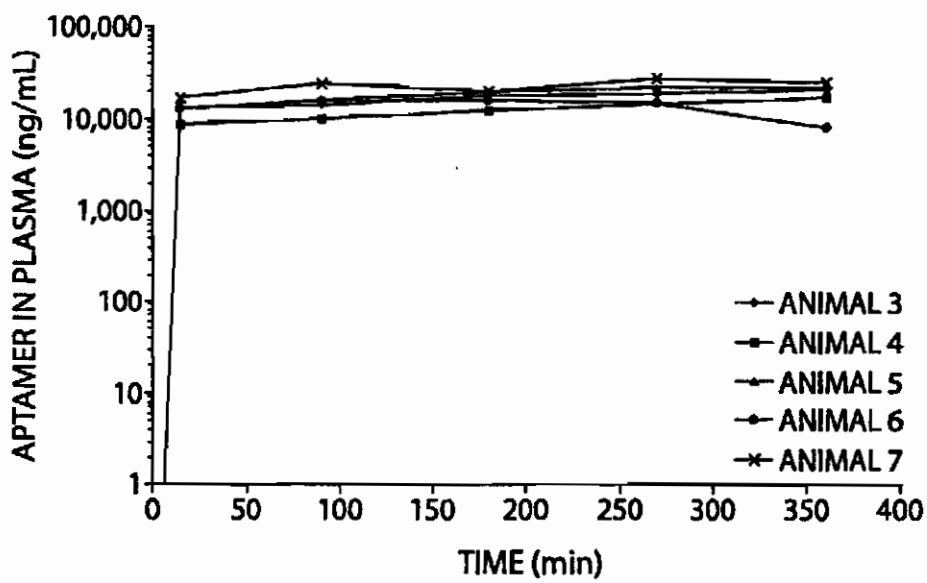
100,000
10,000
1,000
100
10
1
APTAMER IN PLASMA (ng/mL)
0
50
100
150
200
250
300
350
400
TIME (min)
ANIMAL 3
ANIMAL 4
ANIMAL 5
ANIMAL 6
ANIMAL 7

Fig. 32

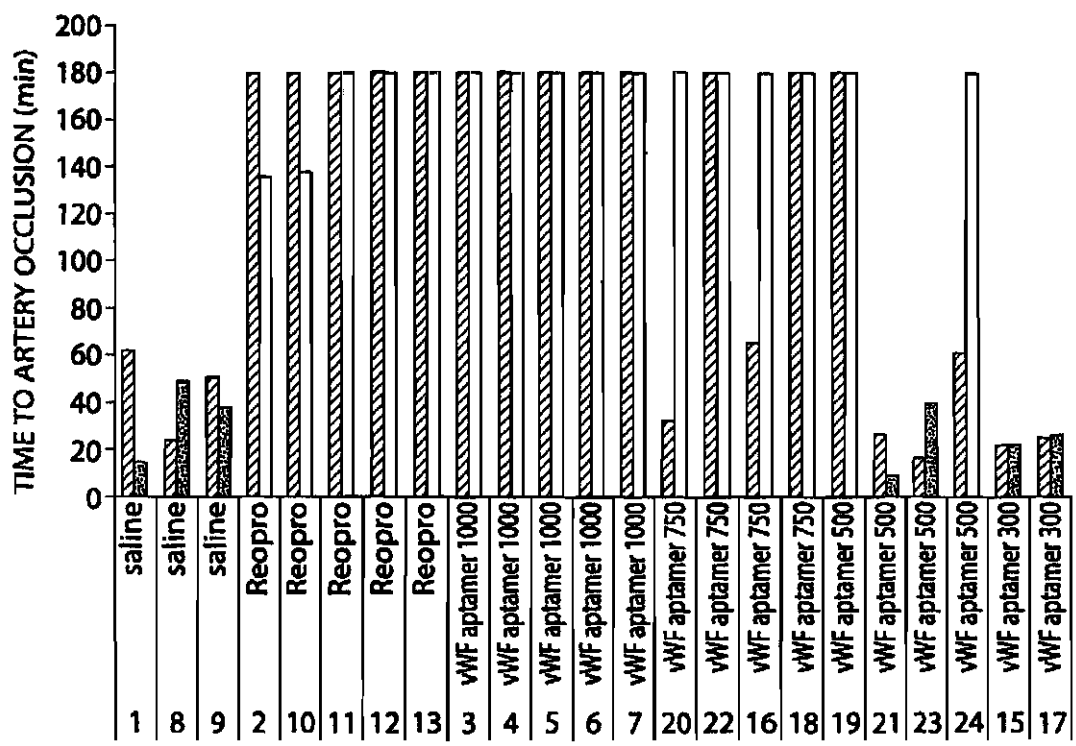
TIME TO ARTERY OCCLUSION (min)
200
180
160
140
120
100
80
60
40
20
0
saline
saline
saline
Reopro
Reopro
Reopro
Reopro
Reopro
vWF aptamer 1000
vWF aptamer 1000
vWF aptamer 1000
vWF aptamer 1000
vWF aptamer 1000
vWF aptamer 750
vWF aptamer 750
vWF aptamer 750
vWF aptamer 750
vWF aptamer 500
vWF aptamer 500
vWF aptamer 500
vWF aptamer 500
vWF aptamer 300
vWF aptamer 300
1 8 9 2 10 11 12 13 3 4 5 6 7 20 22 16 18 19 21 23 24 15 17

Fig. 33

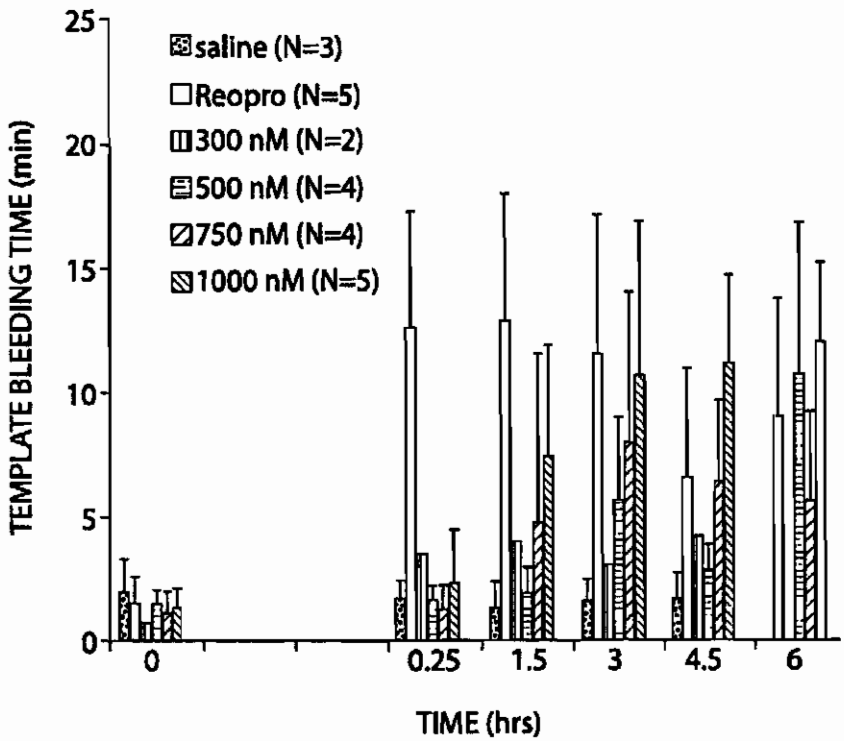
25
20
15
10
5
0
TEMPLATE BLEEDING TIME (min)
saline (N=3)
Reopro (N=5)
300 nM (N=2)
500 nM (N=4)
750 nM (N=4)
1000 nM (N=5)
0
0.25
1.5
3
4.5
6
TIME (hrs)

Fig. 34