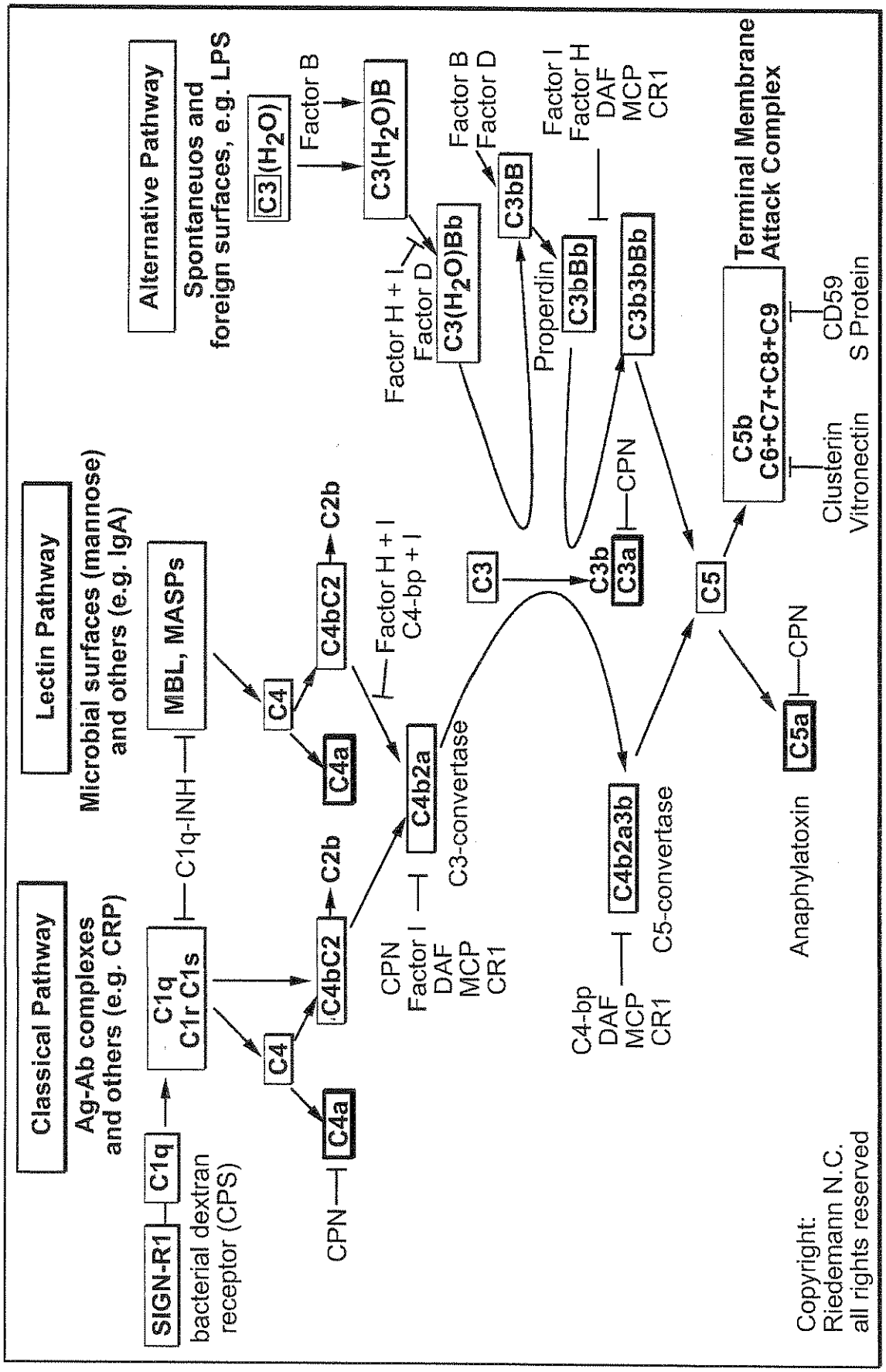

Classical Pathway
Lectin Pathway
Alternative Pathway
Ag-Ab complexes and others (e.g. CRP)
Microbial surfaces (mannose) and others (e.g. IgA)
Spontaneuos and foreign surfaces, e.g. LPS
SIGN-R1
C1q
C1r C1s
C1q-INH
MBL, MASPs
bacterial dextran receptor (CPS)
C4
C4a
C4bC2
C2b
CPN
Factor I
DAF
MCP
CR1
C4b2a
C3-convertase
Factor H + I
C4-bp + I
C3
C3b
C3a
C4b2a3b
C5-convertase
C5
C5b
C6+C7+C8+C9
Terminal Membrane Attack Complex
Clusterin
Vitronectin
CD59
S Protein
Anaphylatoxin
C5a
C3(H2O)
Factor B
C3(H2O)B
Factor H + I
Factor D
C3(H2O)Bb
Factor B
Factor D
C3bB
Properdin
C3bBb
Factor I
Factor H
DAF
MCP
CR1
C3b3bBb
C4-bp
DAF
MCP
CR1
Copyright:
Riedemann N.C.
all rights reserved

Figure 1

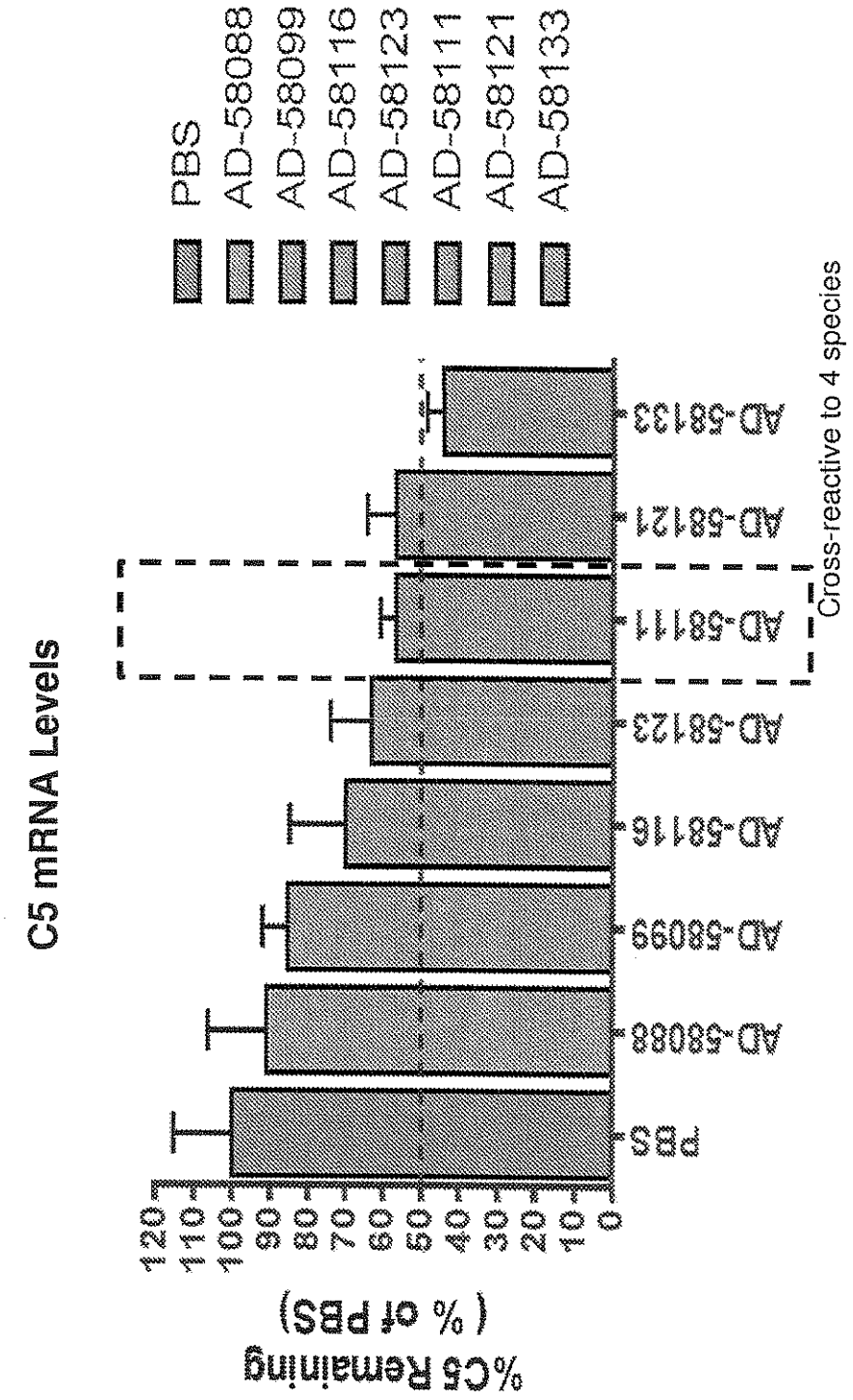

C5 mRNA Levels
%C5 Remaining
(% of PBS)
120
110
100
90
80
70
60
50
40
30
20
10
0
PBS
AD-58088
AD-58099
AD-58116
AD-58123
AD-58111
AD-58121
AD-58133
Cross-reactive to 4 species

Figure 2

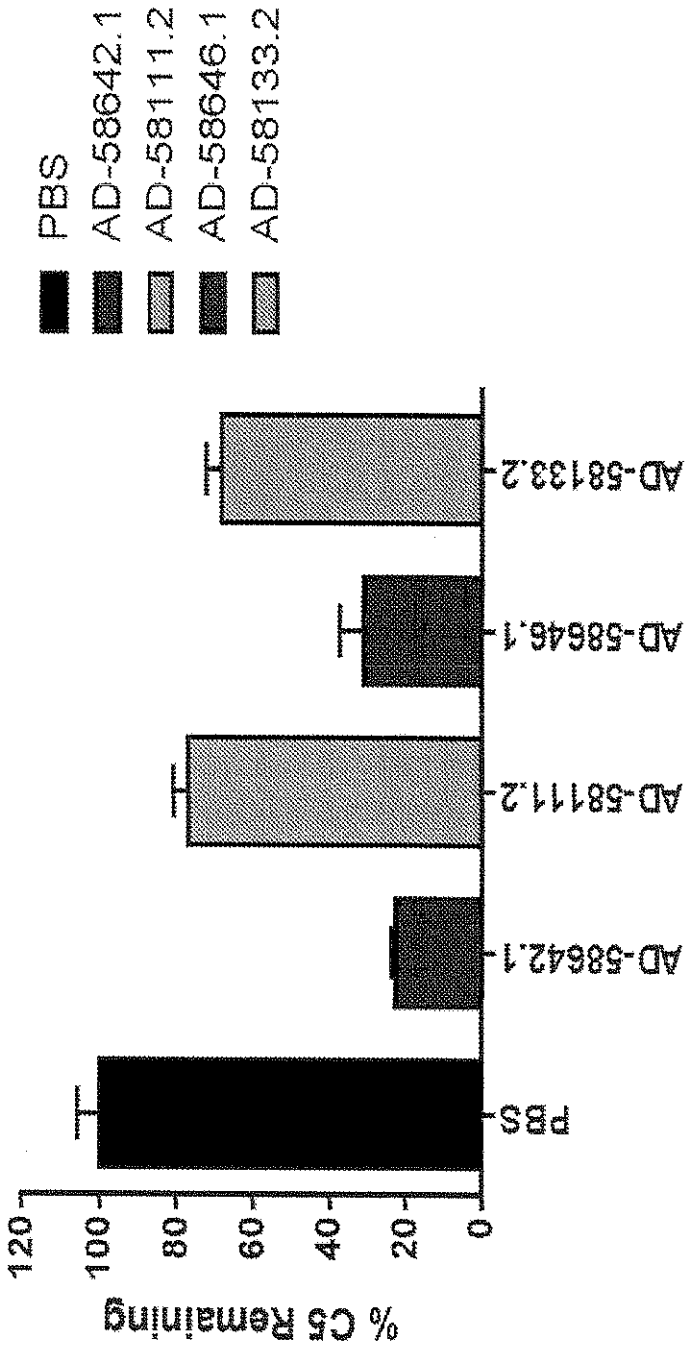

PBS
AD-58642.1
AD-58111.2
AD-58646.1
AD-58133.2
% C5 Remaining
120
100
80
60
40
20
0
PBS
AD-58642.1
AD-58111.2
AD-58646.1
AD-58133.2

Figure 3

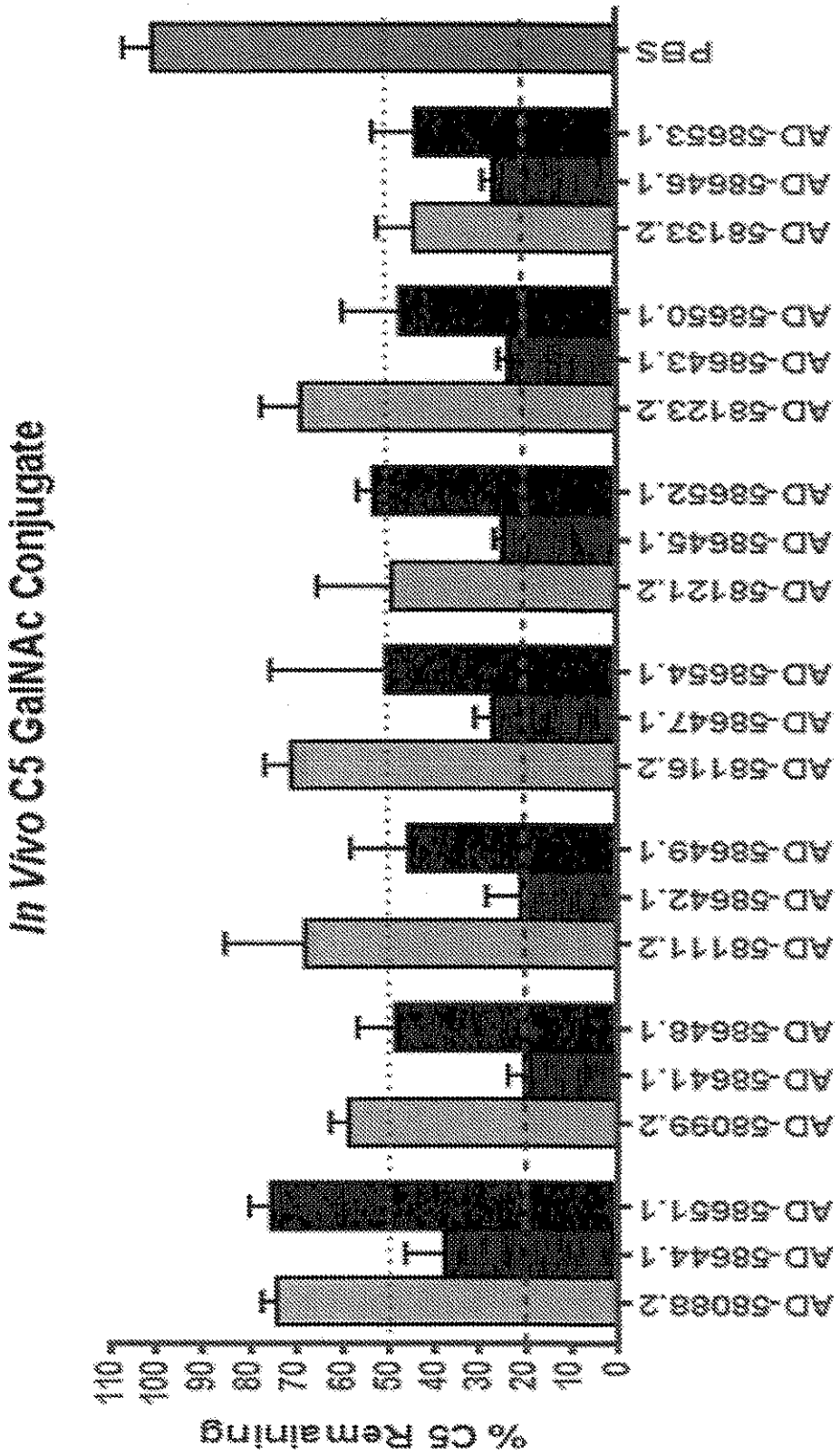
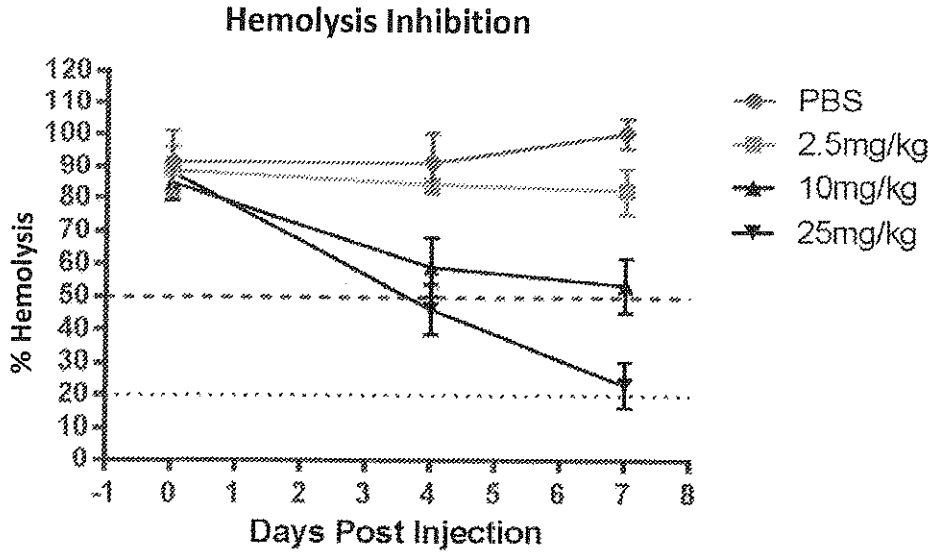

In Vivo C5 GalNAc Conjugate
% C5 Remaining
110
100
90
80
70
60
50
40
30
20
10
0
AD-580862
AD-586441
AD-586511
AD-580992
AD-586411
AD-586481
AD-581112
AD-586421
AD-586491
AD-581162
AD-586471
AD-586541
AD-581212
AD-586451
AD-586521
AD-581232
AD-586431
AD-586501
AD-581332
AD-586461
AD-586531
PBS

Figure 4

A.


Hemolysis Inhibition
% Hemolysis
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
0
1
2
3
4
5
6
7
8
Days Post Injection
PBS
2.5mg/kg
10mg/kg
25mg/kg

B.

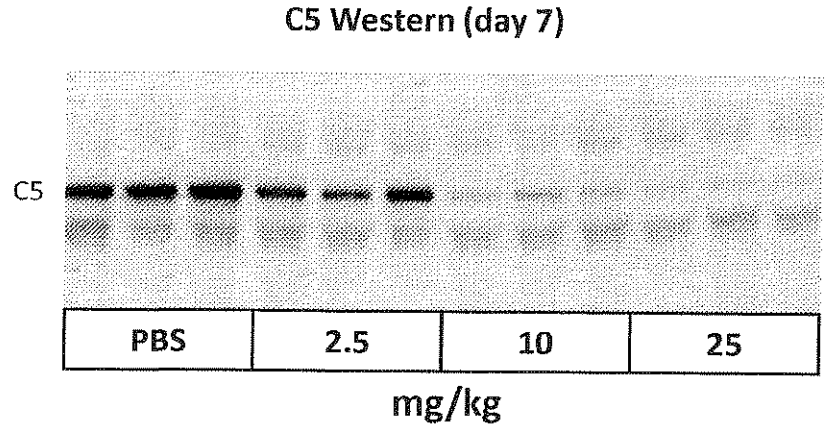

C5 Western (day 7)
C5
PBS
2.5
10
25
mg/kg

Figure 5

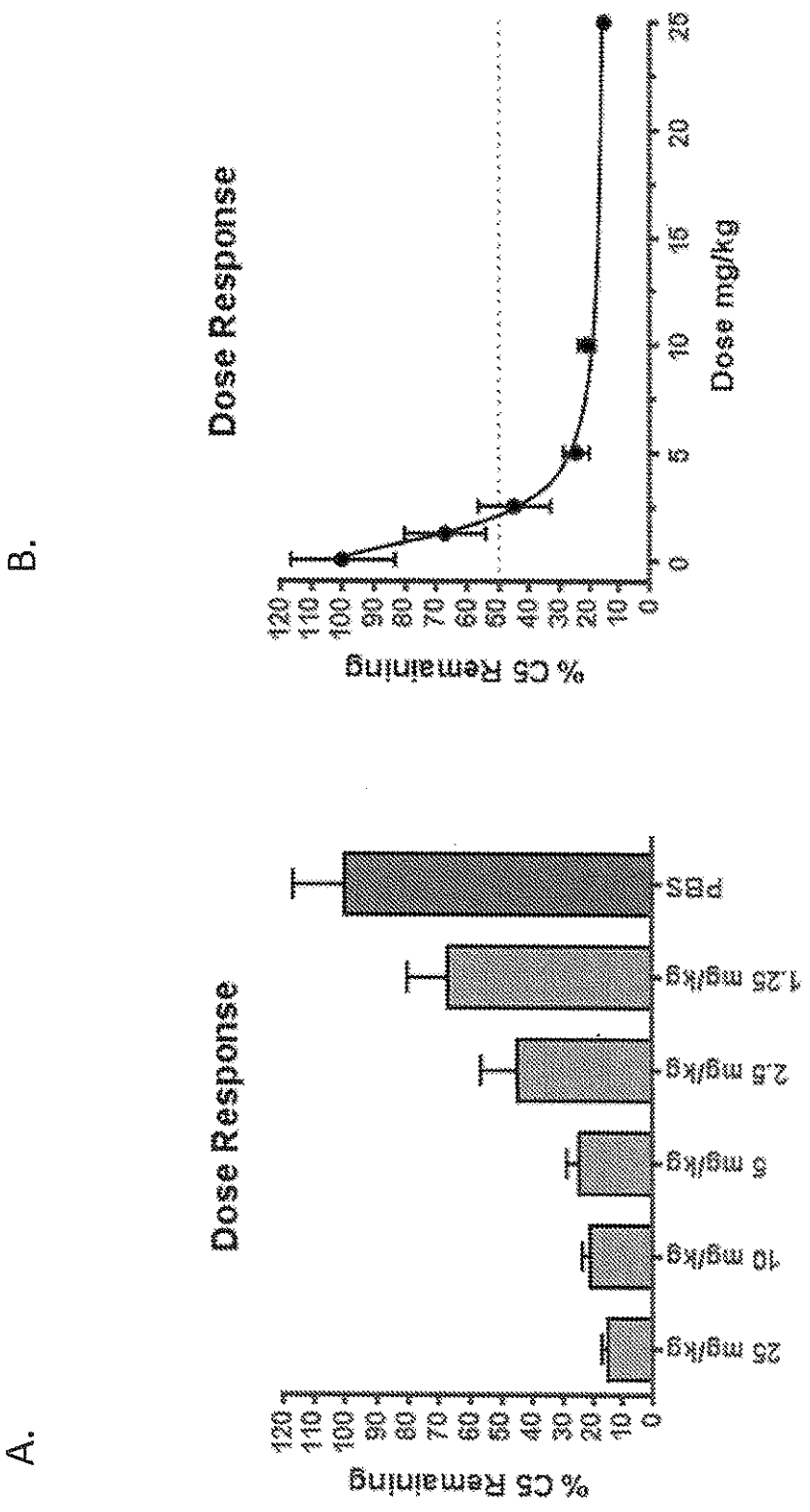

A.
Dose Response
% C5 Remaining
120
110
100
90
80
70
60
50
40
30
20
10
0
25 mg/kg
10 mg/kg
5 mg/kg
2.5 mg/kg
1.25 mg/kg
PBS
B.
Dose Response
% C5 Remaining
Dose mg/kg
0
5
10
15
20
25

Figure 6

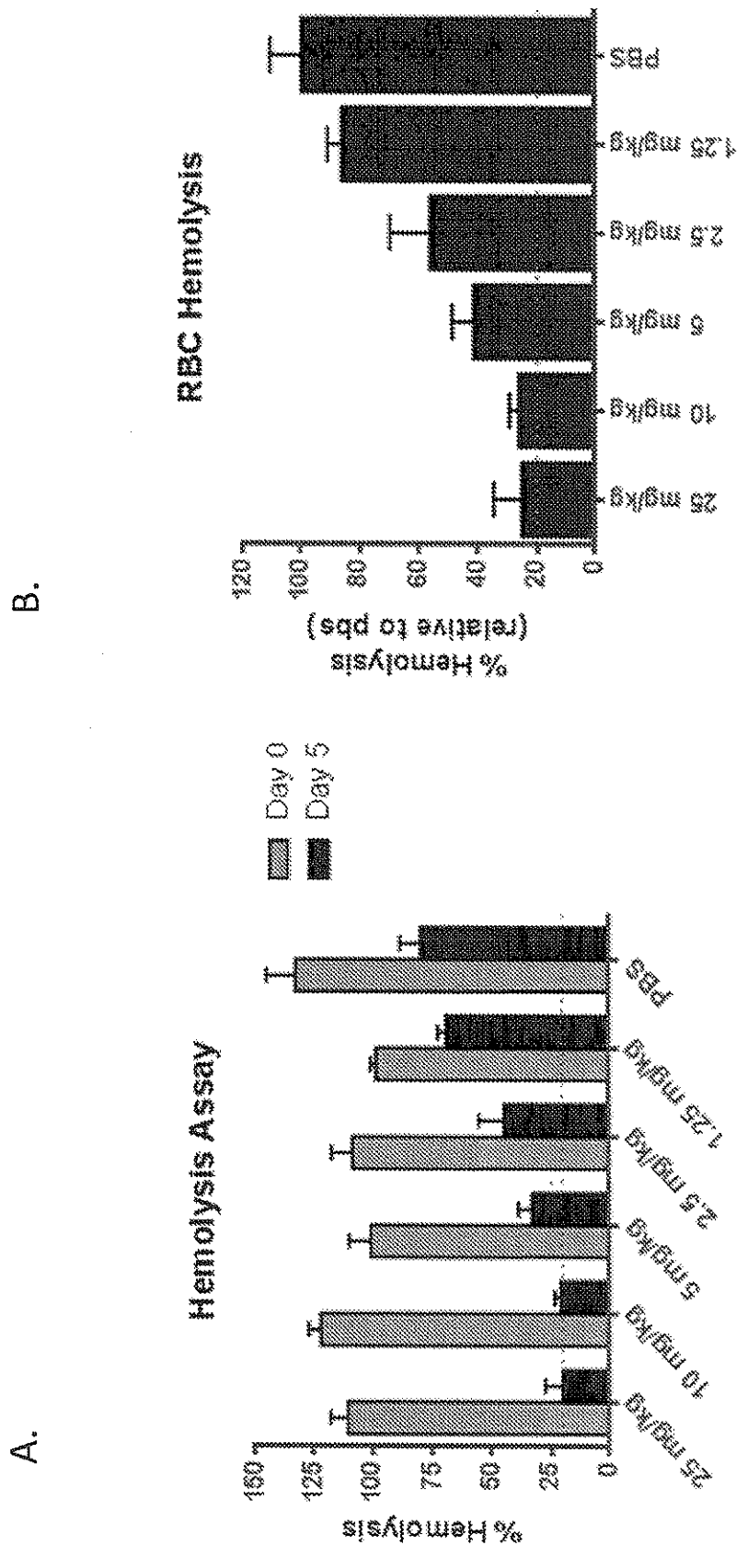
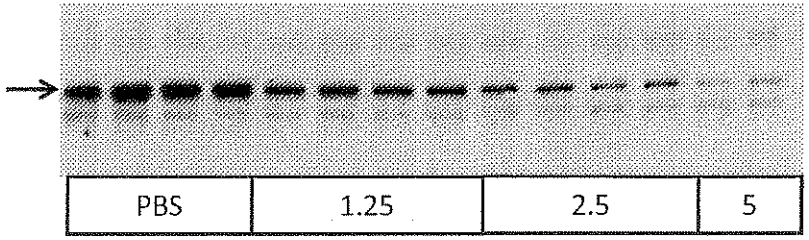
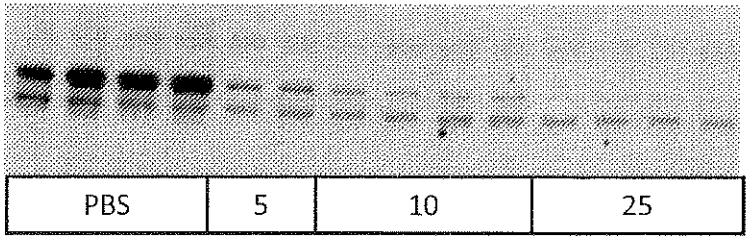

A.
Hemolysis Assay
% Hemolysis
160
125
100
75
50
25
0
Day 0
Day 5
25 mg/kg
10 mg/kg
5 mg/kg
2.5 mg/kg
1.25 mg/kg
PBS
B.
RBC Hemolysis
% Hemolysis
(relative to pbs)
120
100
80
60
40
20
0
25 mg/kg
10 mg/kg
5 mg/kg
2.5 mg/kg
1.25 mg/kg
PBS

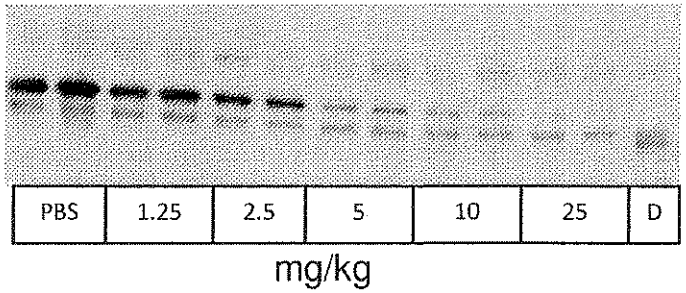
Figure 7

C5 protein silencing (4 mice from each group)
Day 5 samples





C5 protein silencing (2 mice from each group)



D – C5 deficient serum (DBA/2)

Figure 8

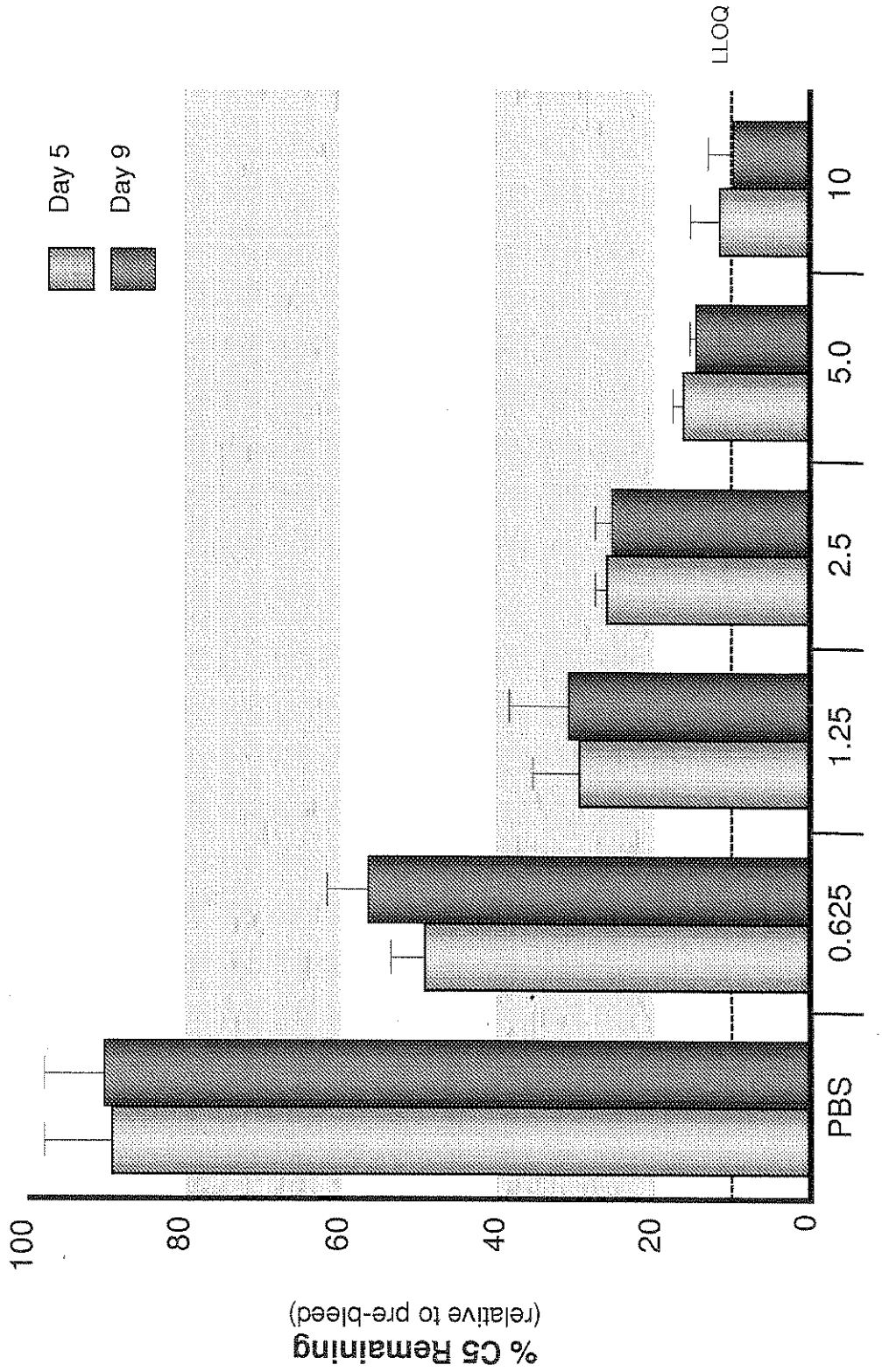

% C5 Remaining
(relative to pre-bleed)
100
80
60
40
20
0
Day 5
Day 9
LLOQ
PBS
0.625
1.25
2.5
5.0
10

Figure 9

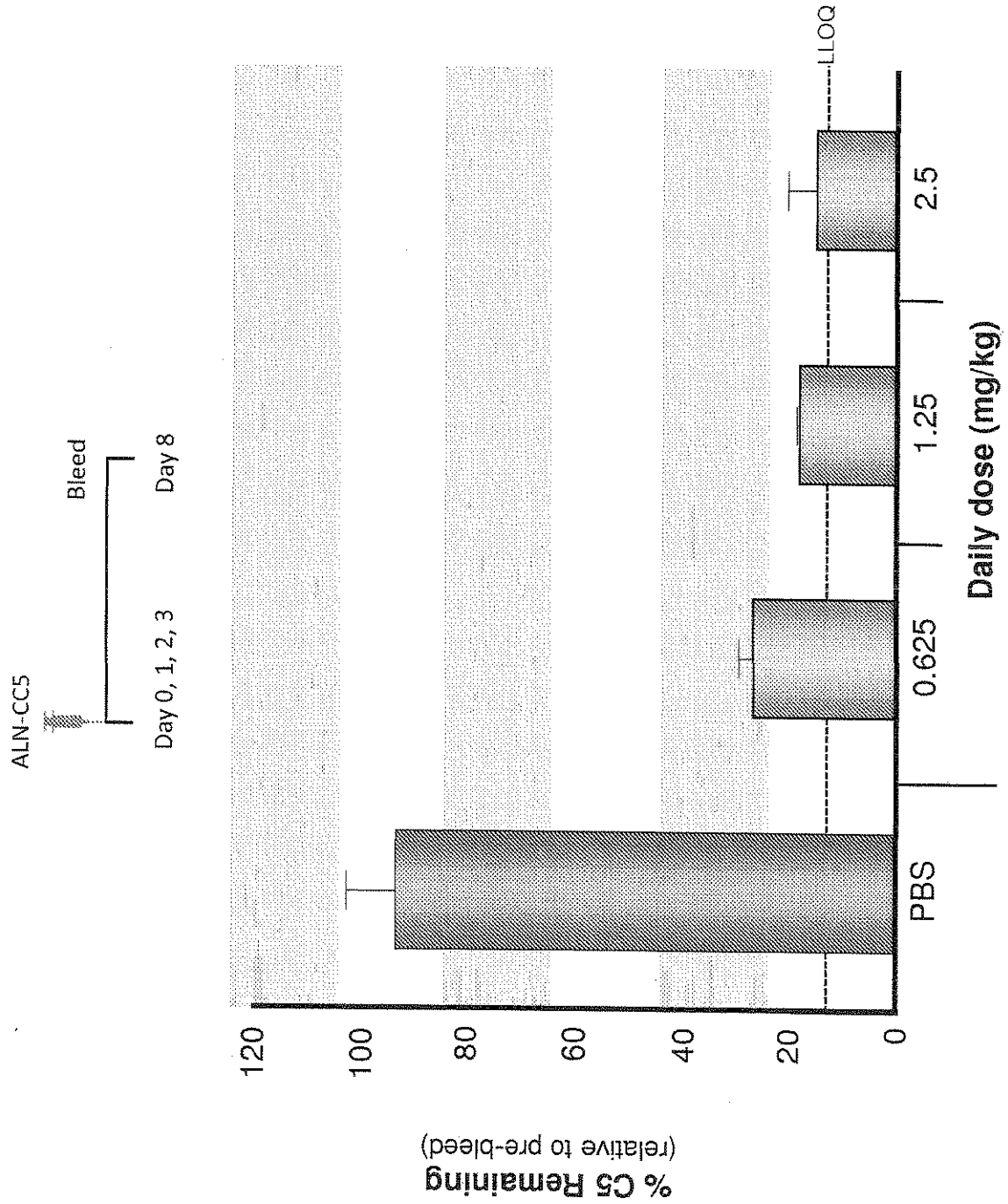
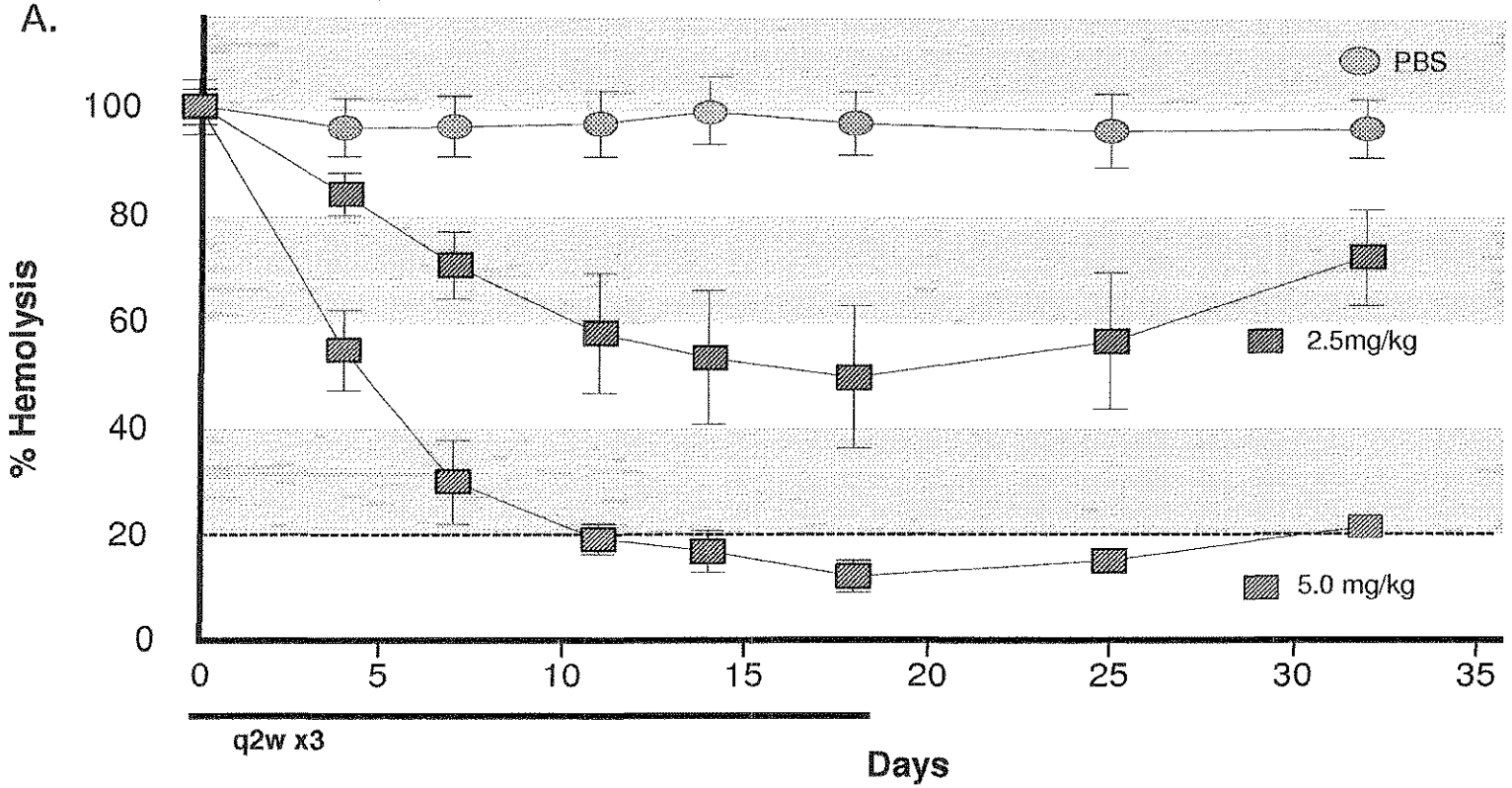

ALN-CC5
Bleed
Day 0, 1, 2, 3
Day 8
% C5 Remaining
(relative to pre-bleed)
120
100
80
60
40
20
0
LLOQ
PBS
0.625
1.25
2.5
Daily dose (mg/kg)

Figure 10


A.
PBS
2.5mg/kg
5.0 mg/kg
% Hemolysis
100
80
60
40
20
0
0
5
10
15
20
25
30
35
q2w x3
Days

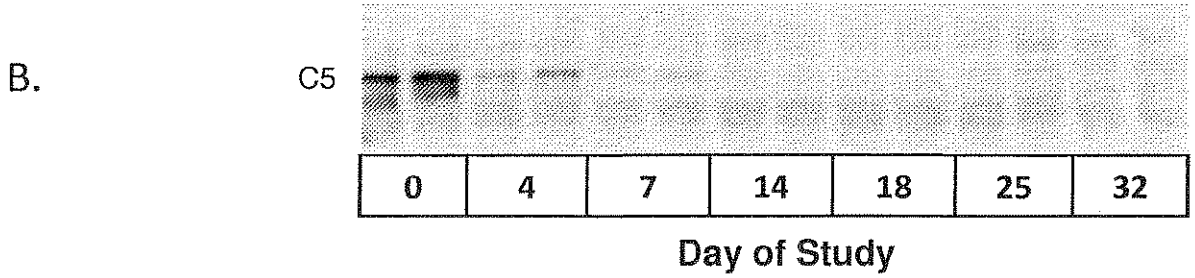

B.
C5
0
4
7
14
18
25
32
Day of Study

Figure 11

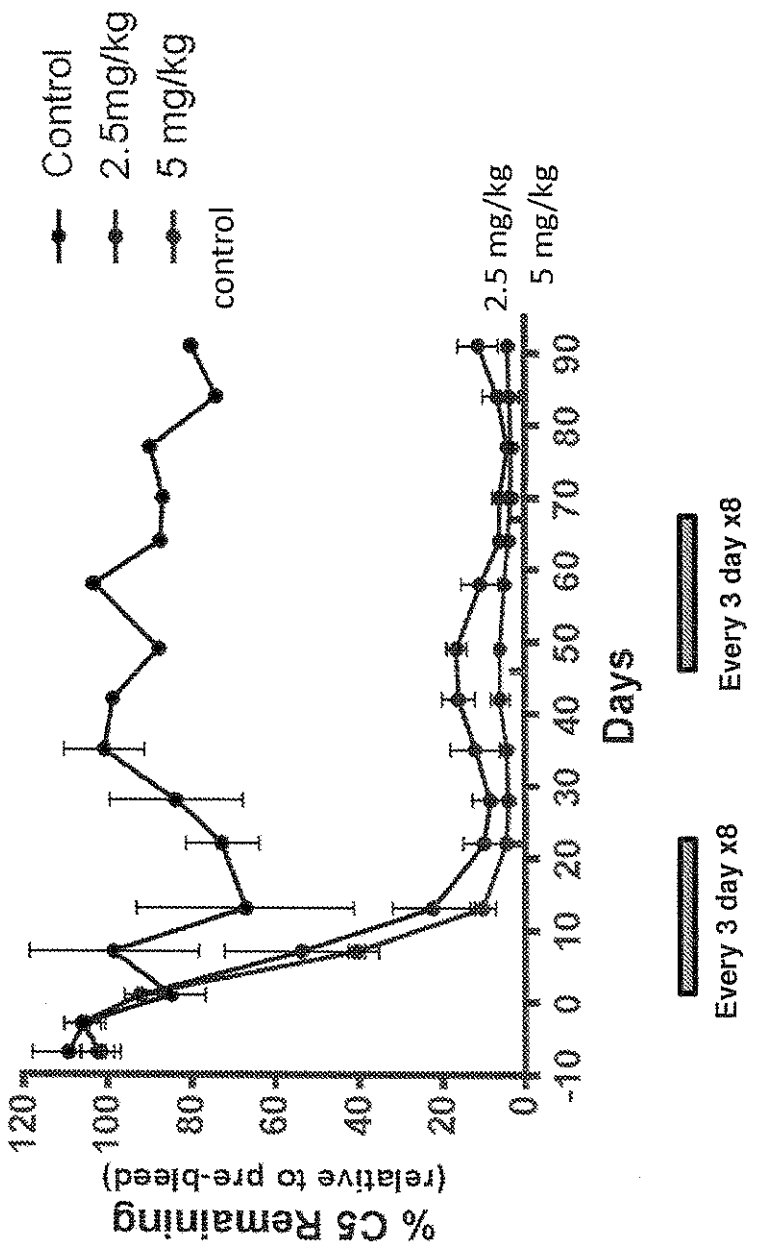

Control
2.5mg/kg
5 mg/kg
control
2.5 mg/kg
5 mg/kg
% C5 Remaining
(relative to pre-bleed)
120
100
80
60
40
20
0
-10
0
10
20
30
40
50
60
70
80
90
Days
Every 3 day x8
Every 3 day x8

Figure 12

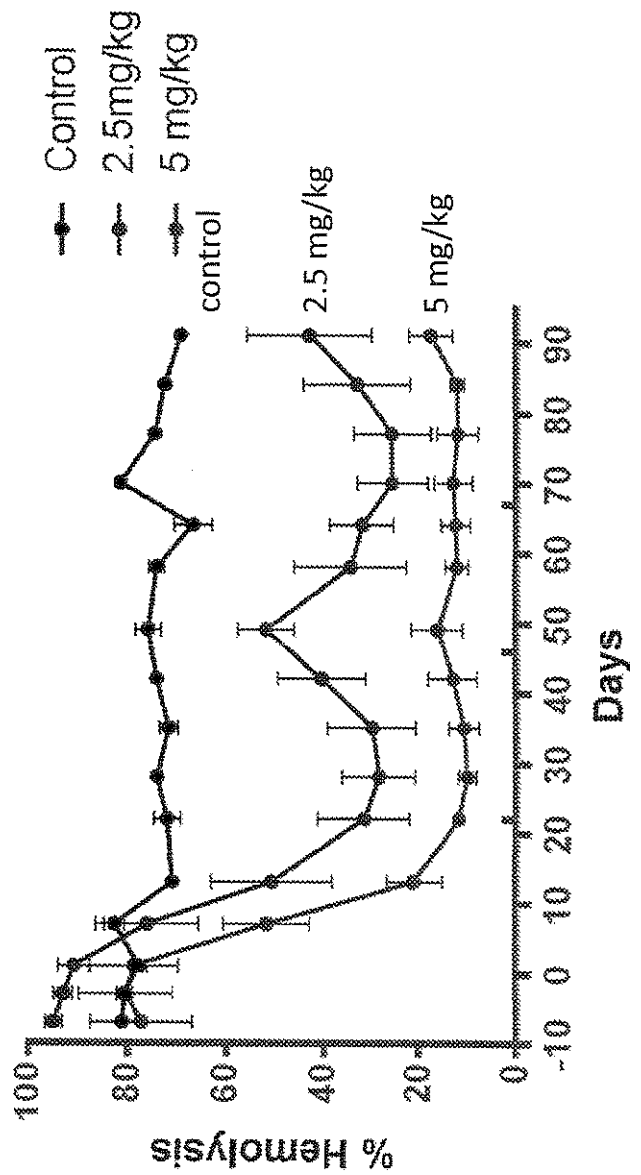

Control
2.5mg/kg
5 mg/kg
control
2.5 mg/kg
5 mg/kg
% Hemolysis
Days
100
80
60
40
20
0
-10
0
10
20
30
40
50
60
70
80
90

Figure 13

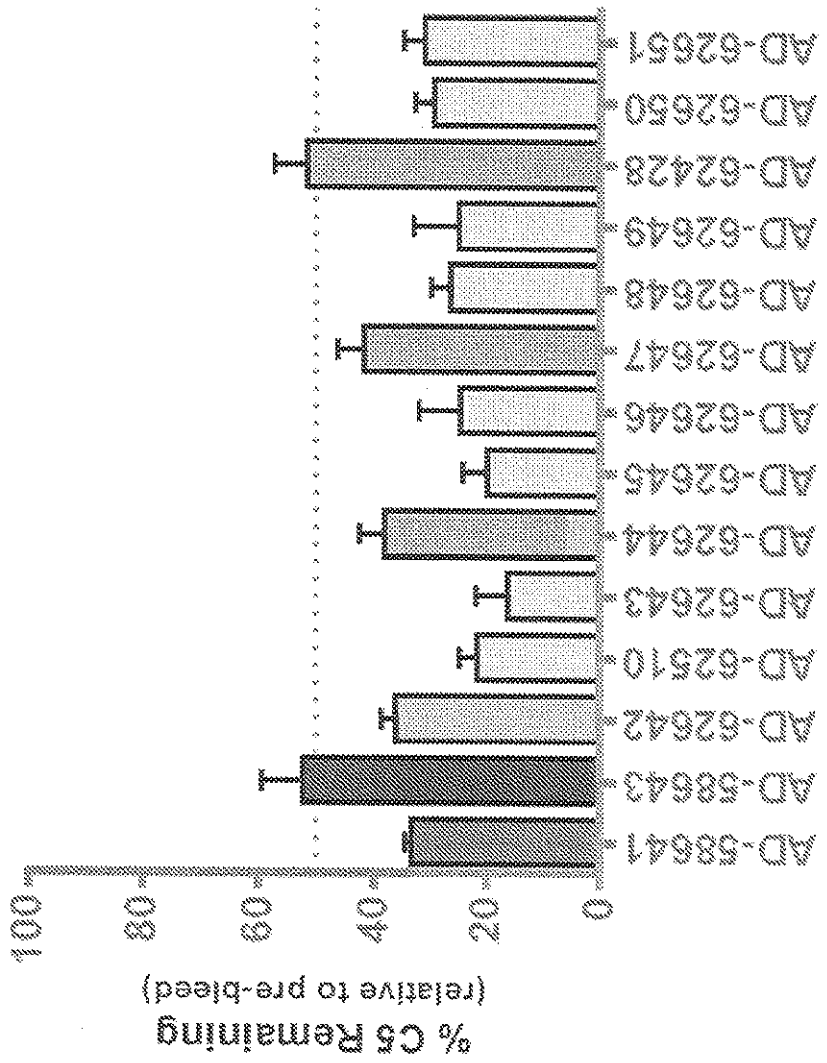

% C5 Remaining
(relative to pre-bleed)
100
80
60
40
20
0
AD-58641
AD-58643
AD-62642
AD-62510
AD-62643
AD-62644
AD-62645
AD-62646
AD-62647
AD-62648
AD-62649
AD-62428
AD-62650
AD-62651

Figure 14

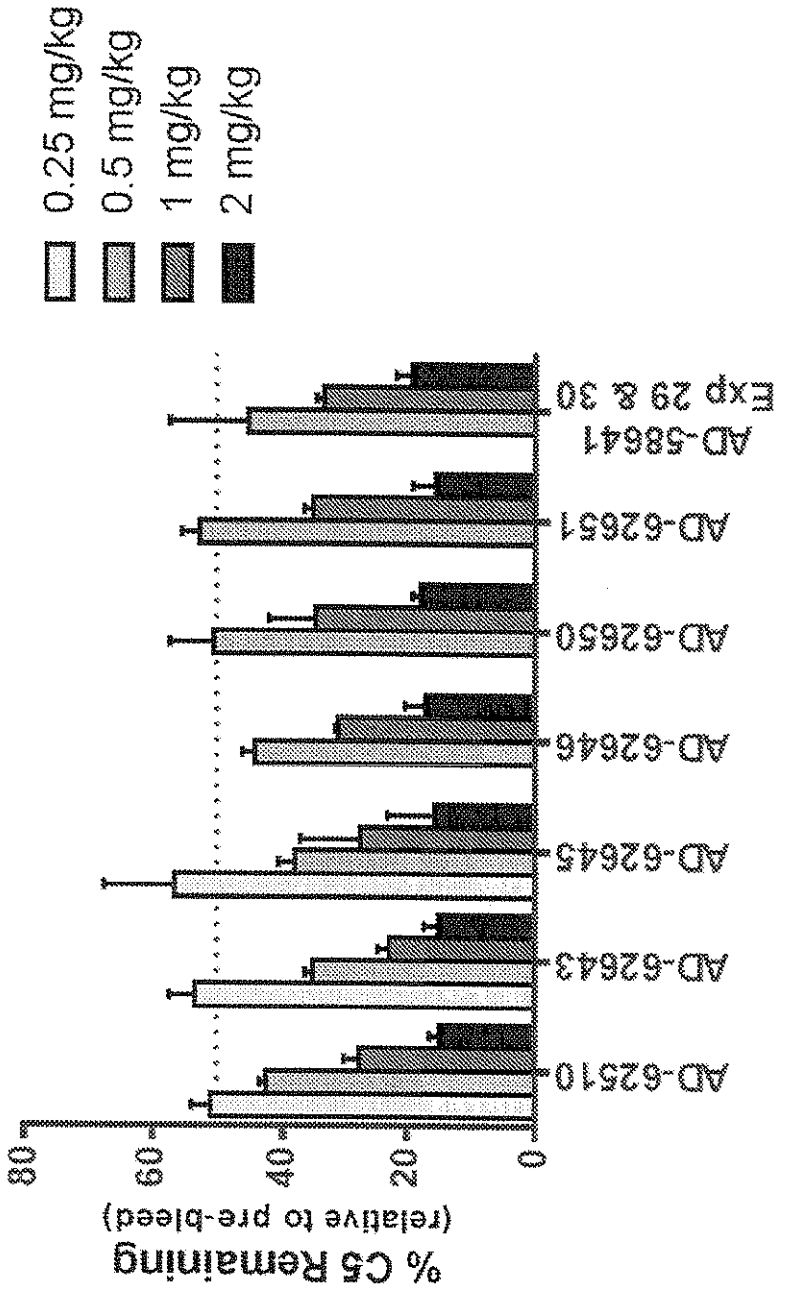

0.25 mg/kg
0.5 mg/kg
1 mg/kg
2 mg/kg
% C5 Remaining
(relative to pre-bleed)
0
20
40
60
80
AD-62510
AD-62643
AD-62645
AD-62646
AD-62650
AD-62651
AD-58641
Exp 29 & 30

Figure 15

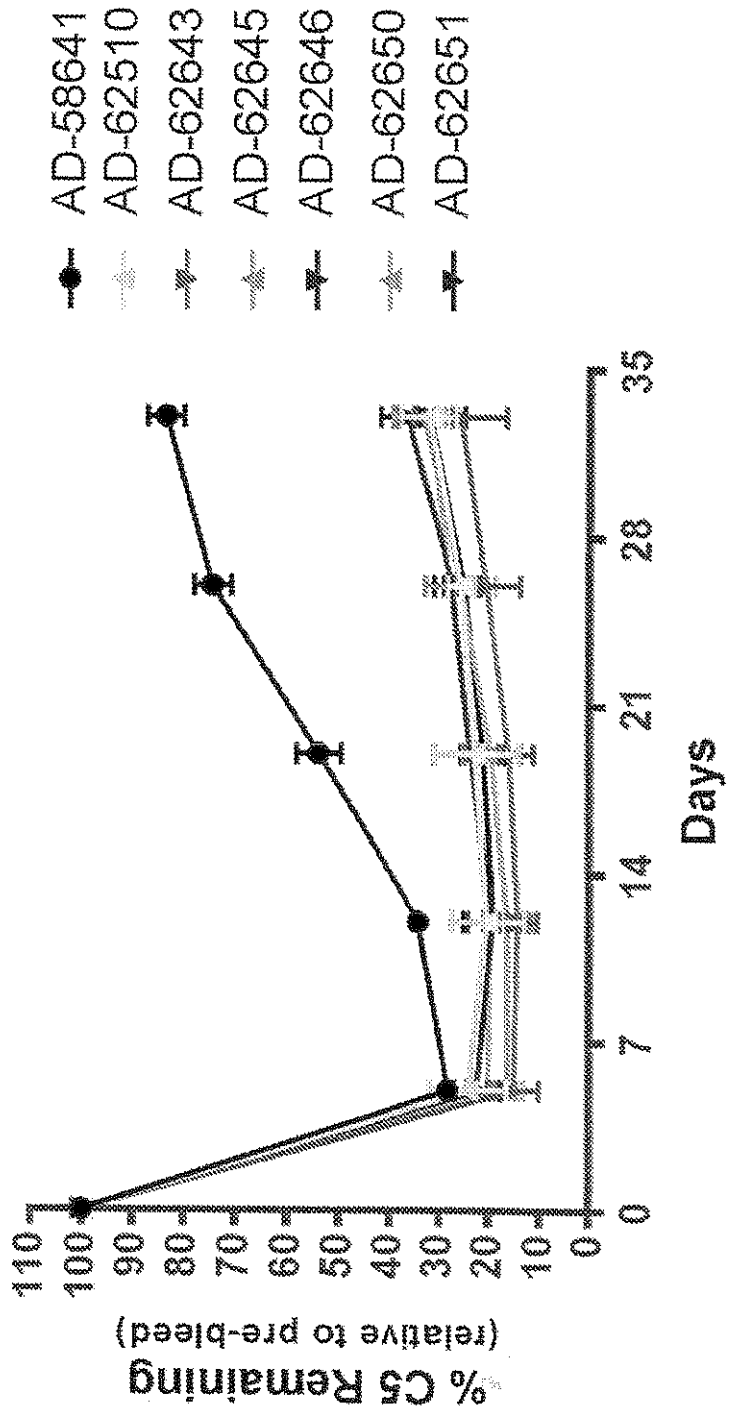

AD-58641
AD-62510
AD-62643
AD-62645
AD-62646
AD-62650
AD-62651
% C5 Remaining
(relative to pre-bleed)
110
100
90
80
70
60
50
40
30
20
10
0
0
7
14
21
28
35
Days

Figure 16

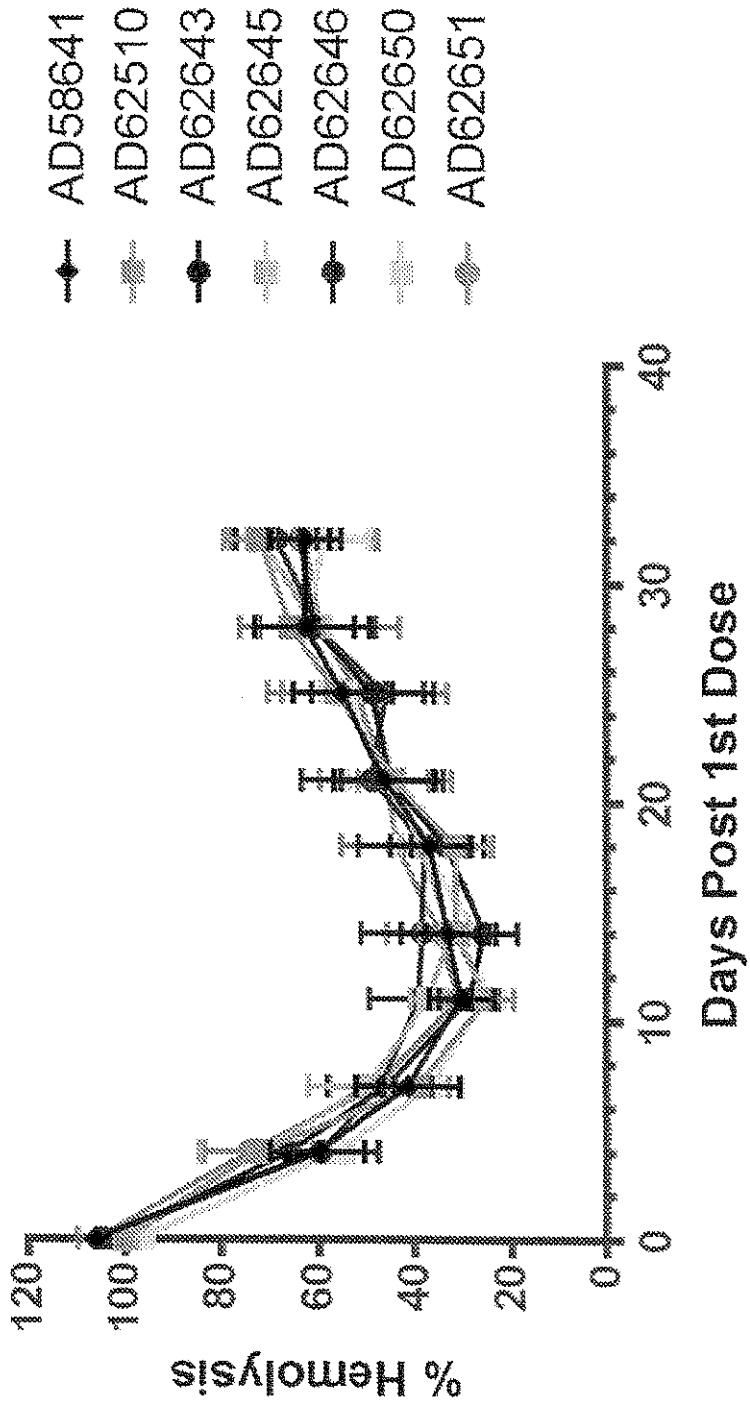

AD58641
AD62510
AD62643
AD62645
AD62646
AD62650
AD62651
% Hemolysis
120
100
80
60
40
20
0
0
10
20
30
40
Days Post 1st Dose

Figure 17

SEQ ID NO:1
>gi|38016946|ref|NM_001735.2| Homo sapiens complement component 5 (C5),
mRNATATATCCGTGGTTTCCTGCTACCTCCAACCATGGGCCTTTTGGGAATACTTTGTTTTTTAATCTTCCTGGGGAAAACCTGGGGACAGGAGC
AAACATATGTCATTTCAGCACCAAAAATATTCCGTGTTGGAGCATCTGAAAATATTGTGATTCAAGTTTATGGATACACTGAAGCATTTGATGCA
ACAATCTCTATTAAAAGTTATCCTGATAAAAAATTTAGTTACTCCTCAGGCCATGTTCATTTATCCTCAGAGAATAAATTCCAAAACTCTGCAAT
CTTAACAATACAACCAAAACAATTGCCTGGAGGACAAAACCCAGTTTCTTATGTGTATTTGGAAGTTGTATCAAAGCATTTTTCAAAATCAAAAA
GAATGCCAATAACCTATGACAATGGATTTCTCTTCATTCATACAGACAAACCTGTTTATACTCCAGACCAGTCAGTAAAAGTTAGAGTTTATTCG
TTGAATGACGACTTGAAGCCAGCCAAAAGAGAAACTGTCTTAACTTTCATAGATCCTGAAGGATCAGAAGTTGACATGGTAGAAGAAATTGATCA
TATTGGAATTATCTCTTTTCCTGACTTCAAGATTCCGTCTAATCCTAGATATGGTATGTGGACGATCAAGGCTAAATATAAAGAGGACTTTTCAA
CAACTGGAACCGCATATTTTGAAGTTAAAGAATATGTCTTGCCACATTTTTCTGTCTCAATCGAGCCAGAATATAATTTCATTGGTTACAAGAAC
TTTAAGAATTTTGAAATTACTATAAAAGCAAGATATTTTTATAATAAAGTAGTCACTGAGGCTGACGTTTATATCACATTTGGAATAAGAGAAGA
CTTAAAAGATGATCAAAAAGAAATGATGCAAACAGCAATGCAAAACACAATGTTGATAAATGGAATTGCTCAAGTCACATTTGATTCTGAAACAG
CAGTCAAAGAACTGTCATACTACAGTTTAGAAGATTTAAACAACAAGTACCTTTATATTGCTGTAACAGTCATAGAGTCTACAGGTGGATTTTCT
GAAGAGGCAGAAATACCTGGCATCAAATATGTCCTCTCTCCCTACAAACTGAATTTGGTTGCTACTCCTCTTTTCCTGAAGCCTGGGATTCCATA
TCCCATCAAGGTGCAGGTTAAAGATTCGCTTGACCAGTTGGTAGGAGGAGTCCCAGTAACACTGAATGCACAAACAATTGATGTAAACCAAGAGA
CATCTGACTTGGATCCAAGCAAAAGTGTAACACGTGTTGATGATGGAGTAGCTTCCTTTGTGCTTAATCTCCCATCTGGAGTGACGGTGCTGGAG
TTTAATGTCAAAACTGATGCTCCAGATCTTCCAGAAGAAAATCAGGCCAGGGAAGGTTACCGAGCAATAGCATACTCATCTCTCAGCCAAAGTTA
CCTTTATATTGATTGGACTGATAACCATAAGGCTTTGCTAGTGGGAGAACATCTGAATATTATTGTTACCCCCAAAAGCCCATATATTGACAAAA
TAACTCACTATAATTACTTGATTTTATCCAAGGGCAAAATTATCCACTTTGGCACGAGGGAGAAATTTTCAGATGCATCTTATCAAAGTATAAAC
ATTCCAGTAACACAGAACATGGTTCCTTCATCCCGACTTCTGGTCTATTACATCGTCACAGGAGAACAGACAGCAGAATTAGTGTCTGATTCAGT
CTGGTTAAATATTGAAGAAAAATGTGGCAACCAGCTCCAGGTTCATCTGTCTCCTGATGCAGATGCATATTCTCCAGGCCAAACTGTGTCTCTTA
ATATGGCAACTGGAATGGATTCCTGGGTGGCATTAGCAGCAGTGGACAGTGCTGTGTATGGAGTCCAAAGAGGAGCCAAAAAGCCCTTGGAAAGA
GTATTTCAATTCTTAGAGAAGAGTGATCTGGGCTGTGGGGCAGGTGGTGGCCTCAACAATGCCAATGTGTTCCACCTAGCTGGACTTACCTTCCT
CACTAATGCAAATGCAGATGACTCCCAAGAAAATGATGAACCTTGTAAAGAAATTCTCAGGCCAAGAAGAACGCTGCAAAAGAAGATAGAAGAAA
TAGCTGCTAAATATAAACATTCAGTAGTGAAGAAATGTTGTTACGATGGAGCCTGCGTTAATAATGATGAAACCTGTGAGCAGCGAGCTGCACGG
ATTAGTTTAGGGCCAAGATGCATCAAAGCTTTCACTGAATGTTGTGTCGTCGCAAGCCAGCTCCGTGCTAATATCTCTCATAAAGACATGCAATT
GGGAAGGCTACACATGAAGACCCTGTTACCAGTAAGCAAGCCAGAAATTCGGAGTTATTTTCCAGAAAGCTGGTTGTGGGAAGTTCATCTTGTTC
CCAGAAGAAAACAGTTGCAGTTTGCCCTACCTGATTCTCTAACCACCTGGGAAATTCAAGGCGTTGGCATTTCAAACACTGGTATATGTGTTGCT
GATACTGTCAAGGCAAAGGTGTTCAAAGATGTCTTCCTGGAAATGAATATACCATATTCTGTTGTACGAGGAGAACAGATCCAATTGAAAGGAAC
TGTTTACAACTATAGGACTTCTGGGATGCAGTTCTGTGTTAAAATGTCTGCTGTGGAGGGAATCTGCACTTCGGAAAGCCCAGTCATTGATCATC
AGGGCACAAAGTCCTCCAAATGTGTGCGCCAGAAAGTAGAGGGCTCCTCCAGTCACTTGGTGACATTCACTGTGCTTCCTCTGGAAATTGGCCTT
CACAACATCAATTTTTCACTGGAGACTTGGTTTGGAAAAGAAATCTTAGTAAAAACATTACGAGTGGTGCCAGAAGGTGTCAAAAGGGAAAGCTA
TTCTGGTGTTACTTTGGATCCTAGGGGTATTTATGGTACCATTAGCAGACGAAAGGAGTTCCCATACAGGATACCCTTAGATTTGGTCCCCAAAA
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CTCCCCAAAGGGAGTGCAGAGGCGGAGCTGATGAGCGTTGTCCCAGTATTCTATGTTTTTCACTACCTGGAAACAGGAAATCATTGGAACATTTT
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CAGGACACAATCAATGCCATTGAGGGCCTGACGGAATATTCACTCCTGGTTAAACAACTCCGCTTGAGTATGGACATCGATGTTTCTTACAAGCA
TAAAGGTGCCTTACATAATTATAAAATGACAGACAAGAATTTCCTTGGGAGGCCAGTAGAGGTGCTTCTCAATGATGACCTCATTGTCAGTACAG
GATTTGGCAGTGGCTTGGCTACAGTACATGTAACAACTGTAGTTCACAAAACCAGTACCTCTGAGGAAGTTTGCAGCTTTTATTTGAAAATCGAT
ACTCAGGATATTGAAGCATCCCACTACAGAGGCTACGGAAACTCTGATTACAAACGCATAGTAGCATGTGCCAGCTACAAGCCCAGCAGGGAAGA
ATCATCATCTGGATCCTCTCATGCGGTGATGGACATCTCCTTGCCTACTGGAATCAGTGCAAATGAAGAAGACTTAAAAGCCCTTGTGGAAGGGG
TGGATCAACTATTCACTGATTACCAAATCAAAGATGGACATGTTATTCTGCAACTGAATTCGATTCCCTCCAGTGATTTCCTTTGTGTACGATTC
CGGATATTTGAACTCTTTGAAGTTGGGTTTCTCAGTCCTGCCACTTTCACAGTGTACGAATACCACAGACCAGATAAACAGTGTACCATGTTTTA
TAGCACTTCCAATATCAAAATTCAGAAAGTCTGTGAAGGAGCCGCGTGCAAGTGTGTAGAAGCTGATTGTGGGCAAATGCAGGAAGAATTGGATC
TGACAATCTCTGCAGAGACAAGAAAACAAACAGCATGTAAACCAGAGATTGCATATGCTTATAAAGTTAGCATCACATCCATCACTGTAGAAAAT
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ACACCTCCTCAAACCTACCACTCAGGAATGTTTGCTGGGGCCGAAAGAACAGTCCATTGAAAGGGAGTATTACAAAAACATGGCCTTTGCTTGAA
AGAAAATACCAAGGAACAGGAAACTGATCATTAAAGCCTGAGTTTGCTTTCAAAAAAAAAAAAAAAAAA

Figure 18A

SEQ ID NO:2

>gi|297270262|ref|XM_001095750.2| PREDICTED: Macaca mulatta complement component 5 (C5), mRNA

CATGATTTCCTGCTACCTCCAACCATGGGCCTTTTGGGAATACTTTGTTTTTTAATCTTCCTGGGAAAAACTTGGGGACAGGAGCAAACATATGTCATT
TCAGCACCAAAAATATTCCGTGTTGGAGCATCTGAAAACATTGTGATTCAAGTTTATGGATACACTGAAGCATTTGATGCAACAATCTCTATTAAAAG
TTATCCTGATAAAAAATTTAGTTACTCCTCAGGCCATGTTCATTTATCCTCAGAGAATAAATTCCAAAACTCGGCAGTCTTAACAATACAACCAAAACA
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ATTCCGTCTAATCCTAGATATGGTATGTGGATGATCCAGGCTAAATATAAAGAGGACTTTTCAACAACTGGAACTGCATTTTTTGAAGTTAAAGAATA
TGTCTTGCCACATTTTTCTGTCTCAGTAGAACCAGAAAGTAATTTCATTGGTTATAAGAACTTTAAGAATTTTGAAATTACTATAAAAGCAAGATATTT
TTATAATAAAGTAGTCACTGAGGCTGATGTTTATATCACATTTGGAATAAGAGAAGACTTAAAAGATGATCAAAAAGAAATGATGCAAACAGCAATG
CAAAACACAATGTTGATAAATGGAATTGCTCAAGTCACATTTGATTCTGAAACAGCAGTCAAAGAACTGTCATACTACAGTTTAGAAGATTTAAACAA
CAAGTACCTTTATATTGCTGTAACAGTCATAGAGTCTACAGGTGGATTTTCTGAAGAGGCAGAAATACCTGGCATCAAATATGTCCTCTCTCCCTACA
AACTGAATTTGGTTGCTACTCCTCTTTTCCTGAAGCCTGGGATTCCATATTCCATCAAGGTGCAGGTTAAAGATGCGCTTGACCAGTTGGTAGGAGGG
GTCCCAGTAACACTGAATGCACAAACAATTGATGTCAACCAAGAGACATCTGACTTGGAGCCAAGGAAAAGTGTAACACGTGTTGATGATGGAGTA
GCTTCGTTTGTGGTTAATCTCCCATCTGGAGTGACGGTGCTGGAGTTTAATGTCAAAACTGATGCTCCAGATCTTCCAGACGAAAATCAGGCCAGGG
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AATATTATTGTTACCCCCAAAAGCCCATATATTGACAAAATAACTCACTATAATTACTTGATTTTATCCAAGGGCAAAATTATCCACTTTGGCACAAGG
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ACATATTCTCCAGGCCAAACTGTGTCTCTTAATATGGTAACTGGGATGGATTCCTGGGTGGCATTAACAGCAGTGGACAGCGCTGTGTATGGAGTCC
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TGTTCCACCTAGCTGGACTTACCTTCCTCACTAATGCAAATGCAGATGACTCCCAAGAAAATGATGAACCTTGTAAAGAAATTATCAGGCCAAGAAGA
ATGCTACAAGAGAAGATAGAAGAAATAGCTGCTAAATATAAACATTTAGTAGTGAAGAAATGTTGTTACGATGGAGTCCGTATTAATCATGATGAA
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ACTCTCATAAAGACTTGCAATTGGGAAGGCTACACATGAAGACCCTGTTACCAGTAAGCAAGCCAGAAATTCGGAGTTATTTTCCAGAAAGCTGGTT
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CCAGTTGAAAGGAACTGTTTACAACTATAGGACTTCTGGGATGCAGTTCTGTGTTAAAATGTCTGCTGTGGAGGGAATCTGCACTTCAGAAAGCCCA
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AATTGGCCTTCAGAACATCAATTTCTCACTGGAGACTTCGTTTGGAAAAGAAATCTTAGTAAAATCGTTACGAGTGGTGCCAGAAGGTGTCAAAAGG
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AGCTGCATACAGTTTGCACTTATGGACTCCTGTTGTTGAAGTTTGTTTTTTTTTCTCGTTTTTTTGTCTTTAAACATTCACAGCTGGTCTTATTTGTAAAG
CTCACTTTACTTAGAATTAGTGGCACTTGCTTTTATTAGAGAATGATTTTAAACGCTGTAACTTTCTGAAATAACATGGCCTTGGAGGGCATGAAGAC
AGATACTCCTCCAAGGTTATTGGACACCGGAAACAATAAATTAGAACACCTCCTCAAACCTACCACTTAGGAATGTTTGCTGGAGCCGAAAGAACAG
TCCATTGAAATGGAGTATTACAAAAACATGGCCTTTGCTTGAAAGAAAATACCAGGGGACAGGAAACTGATCATTAAAGCCTGAGTTTGCTTTCAAA
CTGTGCTAAAAA

Figure 18B

SEQ ID NO:3>gi|291575171|ref|NM_010406.2| Mus musculus hemolytic complement (Hc),
mRNATTTAAAAGGAAAGTGGTTACAGGGAGGCCATGCCCATGGGTTTATGCCGCTACCAGCCATGGGTCTTTGGGGAATACTTTGTCTTTTAATTTT
CCTGGACAAAACTTGGGGACAGGAACAAACCTACGTCATTTCAGCACCCAAAATCCTCCGGGTCGGCTCGTCTGAAAATGTGGTAATTCAAGTCCAT
GGCTACACTGAAGCATTTGATGCAACTCTTTCTCTAAAAAGCTATCCTGACAAAAAAGTCACCTTCTCTTCAGGCTATGTTAATTTGTCCCCGGAAAAC
AAATTCCAAAACGCGGCACTGTTGACACTACAGCCCAATCAAGTTCCTAGAGAAGAAAGCCCAGTCTCTCACGTGTATCTGGAAGTTGTGTCAAAAC
ACTTTTCAAAATCAAAGAAAATACCAATTACCTATAACAATGGAATTCTCTTCATCCATACAGACAAACCTGTTTACACGCCGGACCAGTCAGTAAAG
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AGCAGTTAAAGAGCTGTCCTACAACAGTCTAGAAGACTTAAACAACAAGTACCTTTATATTGCAGTAACAGTCACAGAATCTTCAGGTGGATTTTCAG
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TCAAGGCACAGGTTAAAGATTCACTCGAGCAGGCGGTAGGAGGGGTCCCAGTAACTCTGATGGCACAAACAGTCGATGTGAATCAAGAGACATCTG
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CAGAACTGATGACCCAGAACTTCCCGAAGAAAATCAAGCCAGCAAAGAGTACGAAGCAGTTGCGTACTCGTCTCTCAGCCAAAGTTACATTTACATC
GCTTGGACTGAAAACTACAAGCCCATGCTTGTGGGAGAATACCTGAATATTATGGTTACCCCCAAGAGCCCATATATCGACAAAATAACTCACTATAA
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CATTTGGGAAAGACATCTTAGTAAAGACATTACGGGTAGTGCCAGAAGGAGTCAAGAGGGAAAGCTATGCCGGCGTGATTCTGGACCCTAAGGGA
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GACTGCTTGTAGGGGAGTTCTTGTCCACGGTTCTGAGTAAGGAAGGCATCAACATCCTAACCCACCTCCCCAAGGGCAGTGCAGAGGCAGAGCTCAT
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ATTGTGTCGGCCCTGAGGAAGGAAGCTTTTGTTAAAGGTGATCCGCCCATTTACCGTTACTGGAGAGATACCCTCAAACGTCCAGACAGCTCTGTGCC
CAGCAGCGGCACAGCAGGTATGGTTGAAACCACAGCCTATGCTTTGCTCGCCAGCCTGAAACTGAAGGATATGAATTACGCCAACCCCATCATCAAG
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AAACGAGGAAGATTTACGGGCTCTTGTGGAAGGAGTGGATCAACTACTAACTGATTACCAGATCAAAGATGGCCATGTCATTCTGCAACTGAATTCG
ATCCCCTCCAGAGATTTCCTCTGTGTCCGGTTCCGGATATTTGAACTTTTCCAAGTTGGGTTTCTGAATCCTGCTACCTTCACGGTGTACGAGTATCACA
GACCAGATAAGCAGTGCACCATGATTTATAGCATTTCTGACACCAGGCTTCAGAAAGTCTGTGAAGGAGCAGCTTGCACATGTGTGGAAGCTGACTG
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TCTGGCTTGGAAACCTAGCCTAGAATCAGATACACTTTCTTTAGAGTAAAGCACAAGCTGATGAGTTACGACTTTGTGAAATGGATAGCCTTGAGGG
GAGGCGAAAACAGGTCCCCCAAGGCTATCAGATGTCAGTGCCAATAGACTGAAACAAGTCTGTAAAGTTAGCAGTCAGGGGTGTTGGTTGGGGCCG
GAAGAAGAGACCCACTGAAACTGTAGCCCCTTATCAAAACATATCCTTGCTTGAAAGAAAAATACCAAGGACAGAAAATGCCATAAAATCTTGACTT
TGCACTC

Figure 18C

SEQ ID NO:4>gi|392346248|ref|XM_345342.4| PREDICTED: Rattus norvegicus complement component 5 (C5), mRNA

ATGGATAGCACAGAGACCGACAGATGTCCTACAGCCCGCCATCATCTTTCCGGAAACATTAACTCAGTGCTTGCTGCCCTTGTAGGTGGGTTT
TCGGAAGAGGCAGAAATTCCTGGCATCAAATACGTCCTCTCTCCCTATACACTGAATTTGGTCGCTACCCCTCTTTTCCTGAAGCCTGGGATTCCATTT
TCCATCAAGGTACAGGTTAAGGATTCACTCGAGCAGTTGGTAGGAGGGGTCCCAGTAACTCTGATGGCACAAACAGTCAATGTGAATCAAGAGACA
TCTGACTTGGAACCAAAGAGGAGCATCACACACTCTGCTGATGGAGTGGCTTCATTTGTGGTGAACCTCCCATCAGAAGTGACATCACTGAAGTTTG
AGGTCAAAACTGATGCCCCGGAACTTCCCGAAGAAAATCAAGCCAGCAAAGAATATGAAGCAGTTACATACTCATCCCTCAGCCAGAGTTACATTTA
CATTGGCTGGACTGAAAACTACAAGCCCATGCTTGTGGGAGAATATCTGAATATTATCGTCACCCCCAAGAGTCCATATATTGACAAAATAACTCACT
ATAATTACTTGATTTTATCCAAAGGCAAAATTGTACAGTATGGCACAAAGGAGAAACTTCTCTATTCATCTTATCAAAATATAAACATCCCAGTGACAC
AGGACATGGTTCCTTCAGCGCGGCTCCTGGTCTATTACATAGTCACGGGGGAGCAGACAGCAGAATTGGTGGCTGACGCAGTCTGGATAAACATTG
AGGAGAAGTGTGGCAACCAGCTCCAGGTCCATCTGTCTCCAGATAAAGACGTGTATTCTCCAGGCCAAACTGTGTCCCTTGACATGGTGACTGAAGC
AGACTCATGGGTGGCACTATCTGCGGTGGACAGCGCTGTGTATGGAGTCCGGGGAAAAGCCAAAAGGGCCATGCAAAGAGTGTTCCAAGCTTTTGA
TGACAAGAGTGACCTGGGCTGTGGGGCAGGTGGTGGCCGTGACAATGTAGATGTATTCCATCTAGCTGGGCTCACCTTCCTCACCAATGCAAACGCA
GATGACTCCCAATACCACGATGACTCTTGTAAGGAAATTCTCAGGCCAAAGAGAGACCTGCAGCTCCTGCATCAGAAAGTGGAAGAACAAGCTGCT
AAATACAAACACCGTGTGCCCAAGAAATGCTGTTATGATGGAGCCCGAGAAAACAAATACGAAACCTGTGAGCAGCGAGTTGCCCGGGTGACCATA
GGCCCACACTGCATCAGGGCCTTCAACGAGTGTTGTACTATTGCGGATAAGATCCGAAAAGAAAGCCACCACAAAGGCATGCTGTTGGGAAGGATC
CAAATAAAGGCCCTGTTACCAGTGATGAAGGCAGAAATCCGAAGCTACTTTCCAGAGAGCTGGCTATGGGAAGTTCATCGTGTTCCCAAAAGAAACC
AGCTGCAGGTTGCACTGCCTGACTCACTGACGACCTGGGAAATTCAAGGCATCGGCATCTCAGACAATGGTATATGTGTTGCTGACACACTCAAGGC
AAAGGTGTTCAAAGATGTCTTCCTGGAGATGAACATACCATATTCTGTTGTACGAGGGGAGCAGATCCAATTGAAGGGAACCGTTTACAATTATAGG
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GGGAGTTTATGGTATTGTTAACAGACGAAAGGAATTCCCATACAGGATACCATTAGATTTGGTCCCCAAAACCAACGTCAAAAGGATTTTGAGTGTA
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CCTGCAGAAAAAAATAAAAGAAGGGCTGGTGAGCGTCATGTCCTACAGAAACGCTGACTATTCCTACAGCATGTGGAAGGGAGCAAGCTCTAGTGC
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GCCAGTGGAGGTACCCCTCAATGATGACCTCATCGTCACCACAGGCTATAGCAGTGGCTTGGCTACAGTATATGTAAAAACTGTGGTTCACAAAACT
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CAAACACAATTTCAGTTTCAAGTATATATACCCTCTAGATTCCTCCACCTGGATTGAATATTGGCCCACAGACACAACGTGTCCATCCTGCCAAGCGTT
TGTAGCTAATTTGGACGAGTTCGCTGAAGACATCTTTCTAAATGGCTGTGAAAATGCCTGAGGAAGTTCTGCTGCGTGGCCTTCCCGGGTACTCCTGT
TGGTGGCTCCTAGGAGCCAGGATCGCTTGGAAACTTAGCCTAGAATCGGATACATTTTCTTTATAGTAAAGCGTAAGTTGAAGAGTTACTTTGTGAA
ACAAAATAGCCTTGTGGAGAGCCGAAGGCAGGTCCCCCAAGGCTATTGGACATCAGCACCAATAAGCTGGAACAAGTCTGTAACGTTAGCAGCCAG
GGGTGTTTGTTGGGGCCGGAAGAAGAGACTCACTGAAATTGTAGCCCCTTAGGAAAACATGGTCTTGCTTGAAAAAAAAAATACCAAGGACAGAAA
ATGCCATAAAAGCTTGACTTTGCACTCAACTGTA

Figure 18D

SEQ ID NO:5 Reverse Complement of SEQ ID NO:1

TTTTTTTTTTTTTTTTTTGAAAGCAAACTCAGGCTTTAATGATCAGTTTCCTGTTCCTTGGTATTTTCTTTCAAGCAAAGGCCATGTTTTTGTAATACTCCC
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ACATGCTGTTTGTTTTCTTGTCTCTGCAGAGATTGTCAGATCCAATTCTTCCTGCATTTGCCCACAATCAGCTTCTACACACTTGCACGCGGCTCCTTCA
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AAACCCAACTTCAAAGAGTTCAAATATCCGGAATCGTACACAAAGGAAATCACTGGAGGGAATCGAATTCAGTTGCAGAATAACATGTCCATCTTTG
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GCATGAGAGGATCCAGATGATGATTCTTCCCTGCTGGGCTTGTAGCTGGCACATGCTACTATGCGTTTGTAATCAGAGTTTCCGTAGCCTCTGTAGTG
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TAAGGCACCTTTATGCTTGTAAGAAACATCGATGTCCATACTCAAGCGGAGTTGTTTAACCAGGAGTGAATATTCCGTCAGGCCCTCAATGGCATTGA
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GGTGAGTAAAGCATAGGCAGTTGTTTCTACCATACGTGCCGTACCAGTGTTAGGTACAGAGCTGTCTTTATGCTGAAGATTGTCTTTCCAAAAACGAT
AAATGGGTGGATTACCTTTAACCAAAGCTTCTCTCTTCAAAGCTGAAACAATTGAACGAAACTGTGGGTGAGTTTTATCTCCCAGGGAAAGAGCATA
CGCAGAAATGGCCAATGTAAAGGTGCTCTGGGCTGGCAGTGTATTTTCAAGCAGAAAGTTGTCAGCTTTAATTAGAGCTGTGTCGATTTTCACCAGG
GGGCATATATCGAAAGCCTTTCTAATTCCAATCACAGTAAAGGCTGTAAGATATAAGCTGTTCTCTCGGGCTTCAACAGGCAAGGTACCCTGTAATTT
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TCTACGTATTTATTTACTTGTCCAAGTACTCTTAAAGCAAAAGCTGTTAACCAAGTGCTAGCACTTCCACCCTTCCACACACTGTAAGAGTAGTCAGCA
TTTCTGTAGGACATAATGCTCAACATCCCTTCTTTTAATTTTTTCTTCAGTTTCTGCTTTTCAATTAATGGGTCAGAATGAAAAATGTTCCAATGATTTCC
TGTTTCCAGGTAGTGAAAAACATAGAATACTGGGACAACGCTCATCAGCTCCGCCTCTGCACTCCCTTTGGGGAGGTGGGTTAGGATATTGATGCCT
TCCTGACTTAGAACTGCAGACAAGATCTCACCTACAAGCAGTCCTTTTACACTCAAAATCCTTTTGATTTCTGTTTTGGGGACCAAATCTAAGGGTATC
CTGTATGGGAACTCCTTTCGTCTGCTAATGGTACCATAAATACCCCTAGGATCCAAAGTAACACCAGAATAGCTTTCCCTTTTGACACCTTCTGGCACC
ACTCGTAATGTTTTTACTAAGATTTCTTTTCCAAACCAAGTCTCCAGTGAAAAATTGATGTTGTGAAGGCCAATTTCCAGAGGAAGCACAGTGAATGT
CACCAAGTGACTGGAGGAGCCCTCTACTTTCTGGCGCACACATTTGGAGGACTTTGTGCCCTGATGATCAATGACTGGGCTTTCCGAAGTGCAGATTC
CCTCCACAGCAGACATTTTAACACAGAACTGCATCCCAGAAGTCCTATAGTTGTAAACAGTTCCTTTCAATTGGATCTGTTCTCCTCGTACAACAGAAT
ATGGTATATTCATTTCCAGGAAGACATCTTTGAACACCTTTGCCTTGACAGTATCAGCAACACATATACCAGTGTTTGAAATGCCAACGCCTTGAATTT
CCCAGGTGGTTAGAGAATCAGGTAGGGCAAACTGCAACTGTTTTCTTCTGGGAACAAGATGAACTTCCCACAACCAGCTTTCTGGAAAATAACTCCG
AATTTCTGGCTTGCTTACTGGTAACAGGGTCTTCATGTGTAGCCTTCCCAATTGCATGTCTTTATGAGAGATATTAGCACGGAGCTGGCTTGCGACGA
CACAACATTCAGTGAAAGCTTTGATGCATCTTGGCCCTAAACTAATCCGTGCAGCTCGCTGCTCACAGGTTTCATCATTATTAACGCAGGCTCCATCGT
AACAACATTTCTTCACTACTGAATGTTTATATTTAGCAGCTATTTCTTCTATCTTCTTTTGCAGCGTTCTTCTTGGCCTGAGAATTTCTTTACAAGGTTCA
TCATTTTCTTGGGAGTCATCTGCATTTGCATTAGTGAGGAAGGTAAGTCCAGCTAGGTGGAACACATTGGCATTGTTGAGGCCACCACCTGCCCCACA
GCCCAGATCACTCTTCTCTAAGAATTGAAATACTCTTTCCAAGGGCTTTTTGGCTCCTCTTTGGACTCCATACACAGCACTGTCCACTGCTGCTAATGCC
ACCCAGGAATCCATTCCAGTTGCCATATTAAGAGACACAGTTTGGCCTGGAGAATATGCATCTGCATCAGGAGACAGATGAACCTGGAGCTGGTTGC
CACATTTTTCTTCAATATTTAACCAGACTGAATCAGACACTAATTCTGCTGTCTGTTCTCCTGTGACGATGTAATAGACCAGAAGTCGGGATGAAGGA
ACCATGTTCTGTGTTACTGGAATGTTTATACTTTGATAAGATGCATCTGAAAATTTCTCCCTCGTGCCAAAGTGGATAATTTTGCCCTTGGATAAAATC
AAGTAATTATAGTGAGTTATTTTGTCAATATATGGGCTTTTGGGGGTAACAATAATATTCAGATGTTCTCCCACTAGCAAAGCCTTATGGTTATCAGTC
CAATCAATATAAAGGTAACTTTGGCTGAGAGATGAGTATGCTATTGCTCGGTAACCTTCCCTGGCCTGATTTTCTTCTGGAAGATCTGGAGCATCAGT
TTTGACATTAAACTCCAGCACCGTCACTCCAGATGGGAGATTAAGCACAAAGGAAGCTACTCCATCATCAACACGTGTTACACTTTTGCTTGGATCCA
AGTCAGATGTCTCTTGGTTTACATCAATTGTTTGTGCATTCAGTGTTACTGGGACTCCTCCTACCAACTGGTCAAGCGAATCTTTAACCTGCACCTTGAT
GGGATATGGAATCCCAGGCTTCAGGAAAAGAGGAGTAGCAACCAAATTCAGTTTGTAGGGAGAGAGGACATATTTGATGCCAGGTATTTCTGCCTC
TTCAGAAAATCCACCTGTAGACTCTATGACTGTTACAGCAATATAAAGGTACTTGTTGTTTAAATCTTCTAAACTGTAGTATGACAGTTCTTTGACTGC
TGTTTCAGAATCAAATGTGACTTGAGCAATTCCATTTATCAACATTGTGTTTTGCATTGCTGTTTGCATCATTTCTTTTTGATCATCTTTTAAGTCTTCTC
TTATTCCAAATGTGATATAAACGTCAGCCTCAGTGACTACTTTATTATAAAAATATCTTGCTTTTATAGTAATTTCAAAATTCTTAAAGTTCTTGTAACC
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TGTCAACTTCTGATCCTTCAGGATCTATGAAAGTTAAGACAGTTTCTCTTTTGGCTGGCTTCAAGTCGTCATTCAACGAATAAACTCTAACTTTTACTGA
CTGGTCTGGAGTATAAACAGGTTTGTCTGTATGAATGAAGAGAAATCCATTGTCATAGGTTATTGGCATTCTTTTTGATTTTGAAAAATGCTTTGATAC
AACTTCCAAATACACATAAGAAACTGGGTTTTGTCCTCCAGGCAATTGTTTTGGTTGTATTGTTAAGATTGCAGAGTTTTGGAATTTATTCTCTGAGGA
TAAATGAACATGGCCTGAGGAGTAACTAAATTTTTTATCAGGATAACTTTTAATAGAGATTGTTGCATCAAATGCTTCAGTGTATCCATAAACTTGAA
TCACAATATTTTCAGATGCTCCAACACGGAATATTTTTGGTGCTGAAATGACATATGTTTGCTCCTGTCCCCAGGTTTTCCCCAGGAAGATTAAAAAAC
AAAGTATTCCCAAAAGGCCCATGGTTGGAGGTAGCAGGAAACCACGGATATA

Figure 18E

SEQ ID NO:6 Reverse Complement of SEQ ID NO:2

TTTTTAGCACAGTTTGAAAGCAAACTCAGGCTTTAATGATCAGTTTCCTGTCCCCTGGTATTTTCTTTCAAGCAAAGGCCATGTTTTTGTAATACTCCAT
TTCAATGGACTGTTCTTTCGGCTCCAGCAAACATTCCTAAGTGGTAGGTTTGAGGAGGTGTTCTAATTTATTGTTTCCGGTGTCCAATAACCTTGGAGG
AGTATCTGTCTTCATGCCCTCCAAGGCCATGTTATTTCAGAAAGTTACAGCGTTTAAAATCATTCTCTAATAAAAGCAAGTGCCACTAATTCTAAGTAA
AGTGAGCTTTACAAATAAGACCAGCTGTGAATGTTTAAAGACAAAAAAACGAGAAAAAAAAACAAACTTCAACAACAGGAGTCCATAAGTGCAAAC
TGTATGCAGCTGAACTTCAGGAATTTTAGCATCCATTTAAAAAGATGTCTTCAGCAAATTCATCTAAATTAGCTAAAAATGCTTGACACGATGAACAT
GTTGTGTCTCTAGGCCAGTATTCAATCCAGGTCAAGGAATCTAAAGGGTAGATGTACCTGAAAGTGAAATTGTATTTTATCTGGAGAGCTTCTTTCCC
CATAATTAAGTACTGTCTTCCTTTCACCAGCTCAGCGTTAGTGCAGGTTACCTTTTTAATGAAGGTGATTTCAGAGTCTTTTTCAGCAACAGCTTCCCCA
GTTTTGTAGATATCCAGAAGGGTTGCCTTGTACTTGACAAAAACATTTTCTGTAGTGATGGATGTGATGATAACTTTATAAGCATATGCAATCTCTGG
GTTACATGCTGTTTGTTTTCTAGTCTCTGCAGAGATTGTCAGATCCAATTCTTTCTGCATTTGCCCACAATCAGCTTCTATACACTTGCACGTGGCTCCTT
CACAGACTTTCTGAATTTTGATATTGGAAGTGCTATAAAACATGGTACACTGTTTATCTGGTCTGTGGTATTCATACACTGTGAAAGTGGCAGGACTA
AGAAACCCAACTTCAAAGAGTTCAAAAATCCGGAATCGTACACAAAGGAAATCACTGGAGGGGATCGAATTCAGTTGCAGAATAACATGTCCATCTT
TTATTTGGTAATCAGTGAATAGCTGATCCACCCCTTCCACAAGAGCTTTTAAGTCTTCTTCATTTGCATTGATTCCAGTAGGCAAGGAGATGTCCATCA
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TGGGATGCTTCAATATCCTGAGTATCAATTTTCAAATAAAAGCTGCAAACTTCCTCAGAGGTACTGGTTTTGTGAACTACAGTTGTTACATGTACCGTA
GCCAAGCCACTGCCAAATCCTGTACTGACAACGAGGTCATCATTGAGAAGCACCTCTACTGGCCTCCCAAGGAAATTCTTGTCTGTCATTTTATAATTA
TGTAAGGGACCTTTATGCTTGTAAGCAACATCGATGTCCATATTCAAGCGGAGCTGTTTAACCAGGAGTGAATATTCTGTCAGGCCCTCGATGGCATT
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GATAAATGGGTGGATTACCTTTAACCAAAGCTTCTCTCTTCAAAGCTGAAACAATTGAACAAAACTGTGGGTGAGTTTTATCTCCCAGGGAAAGAGC
ATAGGCAGAAATGGCCAATGTAAAGGTGCTCTGGGCTGGCAGTGTATTTTCAAGCAGAAAGGTGTCAGCTTTAATTAGAGCTGTGTTGATTTTCTGT
AATTTTATTGGTTGATACTGTGAATTTTCCTTGAAGGATCCATTATCTAACTGATAATTCTCAACCAGCCACAATAAAGAATTACATATTGAATTTTGGT
TCTGCTCTACATATTTATGTACTTGTCCAAGTACTCTTAAAGCAAAAGCTGTTAACCAAGTGCTAGCACTGCCACCCTTCCACACGCTGTAAGAATAGT
CAGCATTTCTGTAGGACATAATGCTCACCATCCCTTCTTTTAATTTTTTCTCCAGGTTCCGCTTTTCAATTAATGGGTCGGAATGAAAAATGTTCCAATG
ATTTCCTGTTTCCAGGTAGTGAAAAACATAGAATACTGGGACAACGCTCATCAGCTCCGCCTCTGCACTCCCTTTGGGGAGGTGGGTTAGGATATTGA
TGCCTTCCCGACTTAGAACTGCAGACAAGATCTCACCTACAAGCAGTCCTTTTACACTCAAAATCCTTTTGATTTCTGTTTTGGGGACCAAATCTAATG
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CACCTTCTGGCACCACTCGTAACGATTTTACTAAGATTTCTTTTCCAAACGAAGTCTCCAGTGAGAAATTGATGTTCTGAAGGCCAATTTCCAGAGGA
AGCACAGTAAAGGTCACCAAGTGATTAGAGGAGCCCTCTACTTTCTGTCGCACACATTTGGAGGACTTTGTGCCCTGATGATCAATGACTGGGCTTTC
TGAAGTGCAGATTCCCTCCACAGCAGACATTTTAACACAGAACTGCATCCCAGAAGTCCTATAGTTGTAAACAGTTCCTTTCAACTGGACCTGTTCTCC
TCGTACAACAGAATATGGTATATTCATTTCCAGGAAGACATCTTTGAACACCTTTGCCTTAATAGTATCAGCAACACATATACCACTGTTTGAAATGCC
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GAAAATAACTCCGAATTTCTGGCTTGCTTACTGGTAACAGGGTCTTCATGTGTAGCCTTCCCAATTGCAAGTCTTTATGAGAGTTATTAGCACGGAGC
TGGCTTGCGACGACACAACATTCAGTGAAAGCTTTGACGCATCTCGGCCCTACACTAATCCGTGCAGCTCGCTGCTCACAGGTTTCATCATGATTAAT
ACGGACTCCATCGTAACAACATTTCTTCACTACTAAATGTTTATATTTAGCAGCTATTTCTTCTATCTTCTCTTGTAGCATTCTTCTTGGCCTGATAATTT
CTTTACAAGGTTCATCATTTTCTTGGGAGTCATCTGCATTTGCATTAGTGAGGAAGGTAAGTCCAGCTAGGTGGAACACATTGGCATTGTTGAGGCCA
CCACCTGCCCCACAGCCCAGATCACTCTTCTCTAAGAATTGAAATACTCTTTCCAAGGGCTTTTTGGCTCTTCTTTGGACTCCATACACAGCGCTGTCCA
CTGCTGTTAATGCCACCCAGGAATCCATCCCAGTTACCATATTAAGAGACACAGTTTGGCCTGGAGAATATGTATCTGCATCAGGAGACAGATGAAC
CTGGAGCTGGTTGCCACATTTTTCTTCAATATTTAACCAGACTGAATCAGACACTAATTCTGCTGTCTGCTCTCCTGTGACGATGTAATAGACCAGGAG
TCGGGATGAAGGAACCATGTTCTGCGTTACTGGAATGTTTATACTTTGATAAGATGCATCTGAAAGTTTCTCCCTTGTGCCAAAGTGGATAATTTTGC
CCTTGGATAAAATCAAGTAATTATAGTGAGTTATTTTGTCAATATATGGGCTTTTGGGGGTAACAATAATATTCAAATATTCTCCCACTAGCAAAGCCT
TGTGGTTATCAGTCCAATCGATATAAAGGTAACTTTGGCTGAGAGATGAGTATGCTATTGCTCGGTAACCTTCCCTGGCCTGATTTTCGTCTGGAAGA
TCTGGAGCATCAGTTTTGACATTAAACTCCAGCACCGTCACTCCAGATGGGAGATTAACCACAAACGAAGCTACTCCATCATCAACACGTGTTACACT
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GGTATTTCTGCCTCTTCAGAAAATCCACCTGTAGACTCTATGACTGTTACAGCAATATAAAGGTACTTGTTGTTTAAATCTTCTAAACTGTAGTATGAC
AGTTCTTTGACTGCTGTTTCAGAATCAAATGTGACTTGAGCAATTCCATTTATCAACATTGTGTTTTGCATTGCTGTTTGCATCATTTCTTTTTGATCATC
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AGTTCTTATAACCAATGAAATTACTTTCTGGTTCTACTGAGACAGAAAAATGTGGCAAGACATATTCTTTAACTTCAAAAAATGCAGTTCCAGTTGTTG
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TAACCTTTACTGATTGGTCTGGAGTATAAACAGGTTTGTCTGTATGAATGAAGAGAAATCCATTGTCATAGGTTATTGGAATTTTTTTTGATTTTGAAA
AATGCTTTGATACAACTTCCAAATACACATAAGAAACTTGGTTTTGTCCTCCAGGTAATTGTTTTGGTTGTATTGTTAAGACTGCCGAGTTTTGGAATT
TATTCTCTGAGGATAAATGAACATGGCCTGAGGAGTAACTAAATTTTTTATCAGGATAACTTTTAATAGAGATTGTTGCATCAAATGCTTCAGTGTAT
CCATAAACTTGAATCACAATGTTTTCAGATGCTCCAACACGGAATATTTTTGGTGCTGAAATGACATATGTTTGCTCCTGTCCCCAAGTTTTTCCCAGG
AAGATTAAAAAACAAAGTATTCCCAAAAGGCCCATGGTTGGAGGTAGCAGGAAATCATG

Figure 18F

SEQ ID NO:7 Reverse Complement of SEQ ID NO:3

GAGTGCAAAGTCAAGATTTTATGGCATTTTCTGTCCTTGGTATTTTTCTTTCAAGCAAGGATATGTTTTGATAAGGGGCTACAGTTTCAGTGGGTCTCT
TCTTCCGGCCCCAACCAACACCCCTGACTGCTAACTTTACAGACTTGTTTCAGTCTATTGGCACTGACATCTGATAGCCTTGGGGGACCTGTTTTCGCC
TCCCCTCAAGGCTATCCATTTCACAAAGTCGTAACTCATCAGCTTGTGCTTTACTCTAAAGAAAGTGTATCTGATTCTAGGCTAGGTTTCCAAGCCAGA
GGAGGAGCAATCCCCCCGCCGCAGGAGGAATCTTCGTGCAGCAGAACTTTTCATTCACAGCTGTTTAAAAAGAGGTCTTCAGCAAAGTTATTCAAAT
TCTCTACAAATGCTTGACAGGATGGACACGTTGTGTCTGTGGGCCAATATTCAATCCAGGTGGAGGAATCTAGAGGGTATATATACTTGAAACTGAA
ATTGTGTTTGATCTGCAGAACCTCTTTGCCCATGATTAAATACTGCTTCCCTTTCACCAGGTTGGCATTGGTACAGCTCATCTTTTTAATGAAGGTGACC
TCCGAATTCTCATCAGCAGCTTCCCCTGTTTTGTAAGTGACCAGAAGAGTCGCAGTGTACTTGACAAAAACATTTTCTTCAGTGGCTGATGTGATCCTG
ACTTTATAAGCATATGCAGTCTCTGGTTTACAGGCTTTCTCTTTTCTGGAGTCTGCAGAGATGGCTAGGTCTACTTCTGCCTGCAGTTGCGCACAGTCA
GCTTCCACACATGTGCAAGCTGCTCCTTCACAGACTTTCTGAAGCCTGGTGTCAGAAATGCTATAAATCATGGTGCACTGCTTATCTGGTCTGTGATAC
TCGTACACCGTGAAGGTAGCAGGATTCAGAAACCCAACTTGGAAAAGTTCAAATATCCGGAACCGGACACAGAGGAAATCTCTGGAGGGGATCGA
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GATTCCAGTCGGCAGTGATATATCCATTACTGCATGGGAGGACCCGGATGTTGACTCCTCCTTGCTGGGCTTGTAGCTGGCACATGCTATTATGCGCT
TGAATCCAGAGTCACTGAGCCTGAAGTGGCTGGATGCTTCAATATCTTGGGTATCAATTTTCAAGTAAAAGCTGCAAAATTCCTCAGAGACACTAATT
TTGTGAACCACAGTTTTTACATATACTGTGGCCAAGCCACTGCTGTAGCCTGTGCTGACAACAAGGTCATCATTGAGAGATACCTCCACTGGCCTCCC
CAGGAAATGCTTCTCTGTCACCTTATACTTGTGGAAGTCACCTTCGTGTTTGTAGGCGACATTGATGTCCATATCCAAATGAATTTGTTTTAACAGGAG
TGAATATTCTGTCAGGCCCTCGATGGCATTAATCGTATCCTGGGTGGAATAAAAGCCGCCTCCATACCTCTGCTCTTCAGATAGCCACTTGATGATGG
GGTTGGCGTAATTCATATCCTTCAGTTTCAGGCTGGCGAGCAAAGCATAGGCTGTGGTTTCAACCATACCTGCTGTGCCGCTGCTGGGCACAGAGCT
GTCTGGACGTTTGAGGGTATCTCTCCAGTAACGGTAAATGGGCGGATCACCTTTAACAAAAGCTTCCTTCCTCAGGGCCGACACAATTAGACGAAAC
CTCGGGTGGGTTCTGTCTCCTAGGGAAAGAGCATAGGCTACAATGGCCAGTGTGAAGGTGCTCTTGGATGGCAGGGTGTTTTCAAGCAGGAAGGAG
TCGGCTTTATCTAGCGCTGTGTGGATTTTCATGGTGGGGCATATGTCAACTGCCTTTCTAATTCCAATCACAGAAAAGGCTGTAAGATACAAAGTTTT
CTCTTGGGCTTCAGCAGGCAAAGTACCCTGTAATTTTATTGGTAGATATTGGGAATTTTCCTTGAAAGAGCCGTTTTCCAGCTGACACTTCTCAACCAG
CCATAGCAAAGAGTTACAAATTGAGTTTTCATCCTGTTTTACATACTTGGCCACCTGTCCAAGCACTCTCAGAGCAAAAGCTGTCAGCCAGGTACTAG
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CACTGCCCTTGGGGAGGTGGGTTAGGATGTTGATGCCTTCCTTACTCAGAACCGTGGACAAGAACTCCCCTACAAGCAGTCCTTTGACACTCAAAATC
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GGTGTGAAGGCTAGCAGCTGAGCTTCCTGAAGTGCAGATCCCCTCCACAGCAGACATTTTAACACAGAACTTTGTCCCTGAGGTCATATAGTTGTAA
ACAGTTCCTTTCAATTGGATCTGTTCTCCTCGCACAACAGAATATGGTATGTTCATCTCCAGGAAGACTTCTTTGAACACCTTTGCCTTGAGTGTATCA
GCAACACATATACCATTGTCTGAAATGCCAATGCCTTGAATTTCCCAAGTCGTTAGTGAGTCAGGCAGCGTGACCTGCAGCTGTTTTCTTTTGGGAAC
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TCGCTCCTCACAGGTTTCGTAGAAGTTCACTCGGGCTCCGTCATAGCAGCATTTCTTTGGCACACTATGTTTGTACTTAGCAGCTTGTTCTTCTATTTTC
TGCCTTAGGAGATGCAGGTTTCTCTTTGACCTGAGAATTTCTTTACAAGAGTCATCACGATAATGGGAGTCATCTGCGTTTGCGTTGGTGAGGAAGGT
GAGCCCAGCTAGATGGAATACATCTGCATTGTCATGGCCACCACCTGCCCCACAGCCCAGGTCACTCTTTTCATCCAAAGCTTGAAAGACTCTTTGCAT
GGCCCTTTTGGCGTTTCCCTGGACTTTATACACAGCTCTGTCCACTGCTGATAGTGCTACCCATGAGTCTGCTTCAGTCACCATGTCAAGGGACACAGT
TTGGCCTGGAGAATACACATATTCATCTGGAGACAGATGGACCTGGAGCTGGTTGCCACACTTCTCCTCAATATTTATCCAGACTGCGTCAGCCACTA
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AGGAGAAAAGTTTCTCTCTTGTGCCGTACTGTACAATTTTGCCTTTGGATAAAATCAAGTAATTATAGTGAGTTATTTTGTCGATATATGGGCTCTTGG
GGGTAACCATAATATTCAGGTATTCTCCCACAAGCATGGGCTTGTAGTTTTCAGTCCAAGCGATGTAAATGTAACTTTGGCTGAGAGACGAGTACGC
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AGTTACTGGGACCCCTCCTACCGCCTGCTCGAGTGAATCTTTAACCTGTGCCTTGATGGAAAATGGAATCCCGGGCTTCACGAAAAGAGGAGTAGCG
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ATAAAGGTACTTGTTGTTTAAGTCTTCTAGACTGTTGTAGGACAGCTCTTTAACTGCTGTTTCAGAATCAAAAGAGATCTGAGCAACTCCGTCAACCA
ACTTTGCGGCTTGTGTGGCTTTGTGCATCATCTGCTTCTCCTCATCTTTTATGTCCTCTCTCAATCCAAAAAAGGCATACACTTCAGCATCAGGTACCAC
TTTATTATAAAAATATCTTGCTTTCACAGTGATTTCAAAGTTCTTAAAGTTTTTATAGCCAATGAAGGTTCTTTCTAGTTCTATTGAAACAGAGAATCGT
GGCAAGACATATTCTTTAATTTCAAAGTATGCAGTTCCAGTTGTTGTAAAATCCTTCTTATAGTTAGCTTTAATTGTCCAAACACCATACTTGGGATTA
GATGGAATCTTGAAGTCAGGAAAAGAGATAATTCCGGTGTAATCATTTTCTTCTACAATGTCAACTTCTGATCCTTCGGGGTCTATGAAAGTTAAGAC
AGTCTCCCGTTTGGCTGGCTTCAAGTCGTCACCCAGAGAATAGACTCTGATCTTTACTGACTGGTCCGGCGTGTAAACAGGTTTGTCTGTATGGATGA
AGAGAATTCCATTGTTATAGGTAATTGGTATTTTCTTTGATTTTGAAAAGTGTTTTGACACAACTTCCAGATACACGTGAGAGACTGGGCTTTCTTCTC
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GTCAGGATAGCTTTTTAGAGAAAGAGTTGCATCAAATGCTTCAGTGTAGCCATGGACTTGAATTACCACATTTTCAGACGAGCCGACCCGGAGGATT
TTGGGTGCTGAAATGACGTAGGTTTGTTCCTGTCCCCAAGTTTTGTCCAGGAAAATTAAAAGACAAAGTATTCCCCAAAGACCCATGGCTGGTAGCG
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Figure 18G

SEQ ID NO:8 Reverse Complement of SEQ ID NO:4

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CTTCGGCTCTCCACAAGGCTATTTTGTTTCACAAAGTAACTCTTCAACTTACGCTTTACTATAAAGAAAATGTATCCGATTCTAGGCTAAGTTTCCAAGC
GATCCTGGCTCCTAGGAGCCACCAACAGGAGTACCCGGGAAGGCCACGCAGCAGAACTTCCTCAGGCATTTTCACAGCCATTTAGAAAGATGTCTTC
AGCGAACTCGTCCAAATTAGCTACAAACGCTTGGCAGGATGGACACGTTGTGTCTGTGGGCCAATATTCAATCCAGGTGGAGGAATCTAGAGGGTA
TATATACTTGAAACTGAAATTGTGTTTGATCTGCAGAGCCTCTTTGCCCATGATTAAATATTGCTTTCCTTTCACCAGGTTGGCGTTGGTACAGCTTATC
TTTTTAATGAAGGTGATCTCAGAGTCCTTCTCAGCAGCGGCTTCCCCTGTTTTGTAAATATCCAGAAGCGTCGCAGTGTACTTGACAAAAATGTTTTCT
TCCGTGGCCGACGTGATCCTGACCTTATAAGCATATGCAATCTCTGGTTTACATGCTGTTTCTTTCCTGGTGTCTGCAGAGATGGCCAGGTCCAGTTCT
GCCTGCAGTTGCCCACAATCAGCTTCAACGCATTTGCATGCCGCTCCTTCACAGACTCTCTGAAGGTTGGTGTCAGAAGTGCTGTAAATCATGGTACA
CTGCTTATCTGGTCTGTGATACTCGTACACCGTGAACGTAGCAGGATTCAGAAACCCAACTTGGAAAAGTTCAAATATCCGGAACCGAACACAAAGG
AAATCTCTGGAGGGAATCGAATTCAATTGCAGAATAACATGACTGTCTTTGATCTGGTAATCAGTTAGGAGTTGATCTACTCCTTCCACAAGAGCTCG
TAAATCTTCTTGGTTTGCTCCGATTCCGGTCGGCAGCAGTATATCCATTACTGCATGGGAGGACCCAGATGCTGACTCCTCCTTGCTGGGCTTGTAGCT
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AATTCCTCAGCGACACTAGTTTTGTGAACCACAGTTTTTACATATACTGTAGCCAAGCCACTGCTATAGCCTGTGGTGACGATGAGGTCATCATTGAG
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CAGATAGCCACTTGATGATCGGGTTGACATAACTCGTCTCCTTCAGGTTCAGGCTGGTGAGCAAAGCATAGGCCGTGGTTTCTACCATACCTGCTGTG
CCGCTGTTGGGTGCTGAGCTGTCTGGACGTTGGAGAGTGTCTCTCCAGAAACGGTAAATGGGCGGGTCTCCTTTAACCAAAGCTTCCCTCTTCAGGG
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GTCCTTTCAAGTAGGAAGGAGTCAGCTTTAGCCAGCGCTGTGTAGATTTTCTCCGTGGGGCATATGCCAATAGCCTTTCTAATTCCAATCACAGAAAA
GGCTGTAAGATATAAAGTGTTCTCTTGGGCTTCAGCAGGCAAAGTACCCTGTAATTTTATTGGTAGATATTGGGAATTTTCCTTGAAAGATCCGTTTTC
CAGCTGACACTTCTCAATCAGCCATAACAAGGAGTTACAGATCGAGTATTGGTCTTGTTTCACATACTTGTTCACCTGTCCAAGCACTCTCAGAGCAAA
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AGTCCTTTTACACTCAAAATCCTTTTGACGTTGGTTTTGGGGACCAAATCTAATGGTATCCTGTATGGGAATTCCTTTCGTCTGTTAACAATACCATAA
ACTCCCCTGGGGTCCAGAGTCACACCAGCATAGCTTTCCCTTTTGATCCCTTCTGGCACTACCCGTAATGTCTTCACTAAGATTTCTTTCCCAAATGAAG
TCTCTAGTGAGAAGTTTATGGAGTGAAGGCCAATTTCCAGAGGAAGCAGGCTGAAGGTCACCAAGTGACTGGAGGAGCCCTCTATTCTCTGGCGCA
CACATCTGGAGGACCTAGAGGTCTGAGGGCTAGCAGCCGAGCTTCCTGGAGTGCAGATTCCCTCCACGGCAGACATTTTAACACAGAACATTGTCCC
AGAGGTCCTATAATTGTAAACGGTTCCCTTCAATTGGATCTGCTCCCCTCGTACAACAGAATATGGTATGTTCATCTCCAGGAAGACATCTTTGAACAC
CTTTGCCTTGAGTGTGTCAGCAACACATATACCATTGTCTGAGATGCCGATGCCTTGAATTTCCCAGGTCGTCAGTGAGTCAGGCAGTGCAACCTGCA
GCTGGTTTCTTTTGGGAACACGATGAACTTCCCATAGCCAGCTCTCTGGAAAGTAGCTTCGGATTTCTGCCTTCATCACTGGTAACAGGGCCTTTATTT
GGATCCTTCCCAACAGCATGCCTTTGTGGTGGCTTTCTTTTCGGATCTTATCCGCAATAGTACAACACTCGTTGAAGGCCCTGATGCAGTGTGGGCCTA
TGGTCACCCGGGCAACTCGCTGCTCACAGGTTTCGTATTTGTTTTCTCGGGCTCCATCATAACAGCATTTCTTGGGCACACGGTGTTTGTATTTAGCAG
CTTGTTCTTCCACTTTCTGATGCAGGAGCTGCAGGTCTCTCTTTGGCCTGAGAATTTCCTTACAAGAGTCATCGTGGTATTGGGAGTCATCTGCGTTTG
CATTGGTGAGGAAGGTGAGCCCAGCTAGATGGAATACATCTACATTGTCACGGCCACCACCTGCCCCACAGCCCAGGTCACTCTTGTCATCAAAAGC
TTGGAACACTCTTTGCATGGCCCTTTTGGCTTTTCCCCGGACTCCATACACAGCGCTGTCCACCGCAGATAGTGCCACCCATGAGTCTGCTTCAGTCAC
CATGTCAAGGGACACAGTTTGGCCTGGAGAATACACGTCTTTATCTGGAGACAGATGGACCTGGAGCTGGTTGCCACACTTCTCCTCAATGTTTATCC
AGACTGCGTCAGCCACCAATTCTGCTGTCTGCTCCCCCGTGACTATGTAATAGACCAGGAGCCGCGCTGAAGGAACCATGTCCTGTGTCACTGGGAT
GTTTATATTTTGATAAGATGAATAGAGAAGTTTCTCCTTTGTGCCATACTGTACAATTTTGCCTTTGGATAAAATCAAGTAATTATAGTGAGTTATTTT
GTCAATATATGGACTCTTGGGGGTGACGATAATATTCAGATATTCTCCCACAAGCATGGGCTTGTAGTTTTCAGTCCAGCCAATGTAAATGTAACTCT
GGCTGAGGGATGAGTATGTAACTGCTTCATATTCTTTGCTGGCTTGATTTTCTTCGGGAAGTTCCGGGGCATCAGTTTTGACCTCAAACTTCAGTGAT
GTCACTTCTGATGGGAGGTTCACCACAAATGAAGCCACTCCATCAGCAGAGTGTGTGATGCTCCTCTTTGGTTCCAAGTCAGATGTCTCTTGATTCAC
ATTGACTGTTTGTGCCATCAGAGTTACTGGGACCCCTCCTACCAACTGCTCGAGTGAATCCTTAACCTGTACCTTGATGGAAAATGGAATCCCAGGCT
TCAGGAAAAGAGGGGTAGCGACCAAATTCAGTGTATAGGGAGAGAGGACGTATTTGATGCCAGGAATTTCTGCCTCTTCCGAAAACCCACCTACAA
GGGCAGCAAGCACTGAGTTAATGTTTCCGGAAAGATGATGGCGGGCTGTAGGACATCTGTCGGTCTCTGTGCTATCCAT

Figure 18H