FIGURE 1

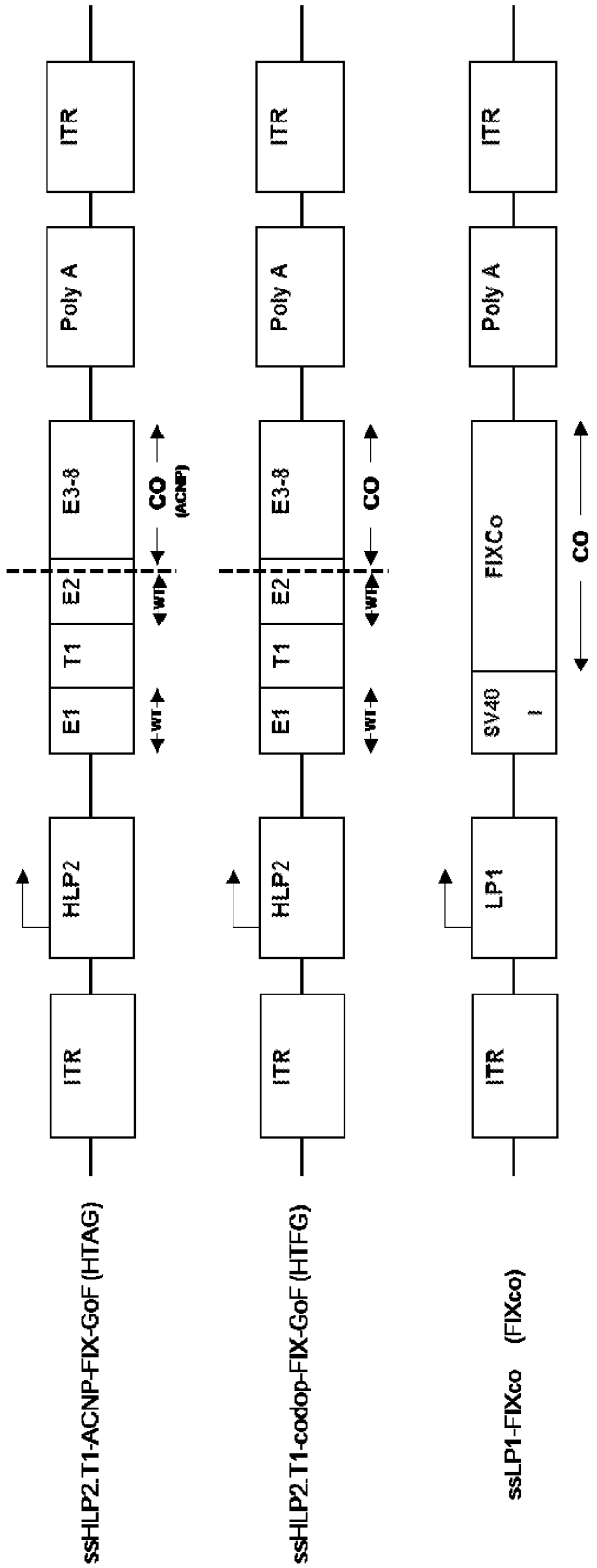

ITR
HLP2
E1
T1
E2
E3-8
Poly A
ITR
CO (ACNP)
WT
ssHLP2.T1-ACNP-FIX-GoF (HTAG)
ITR
HLP2
E1
T1
E2
E3-8
Poly A
ITR
CO
WT
ssHLP2.T1-codop-FIX-GoF (HTFG)
ITR
LP1
SV40 i
FIXCo
Poly A
ITR
CO
ssLP1-FIXco (FIXco)

FIGURE 2

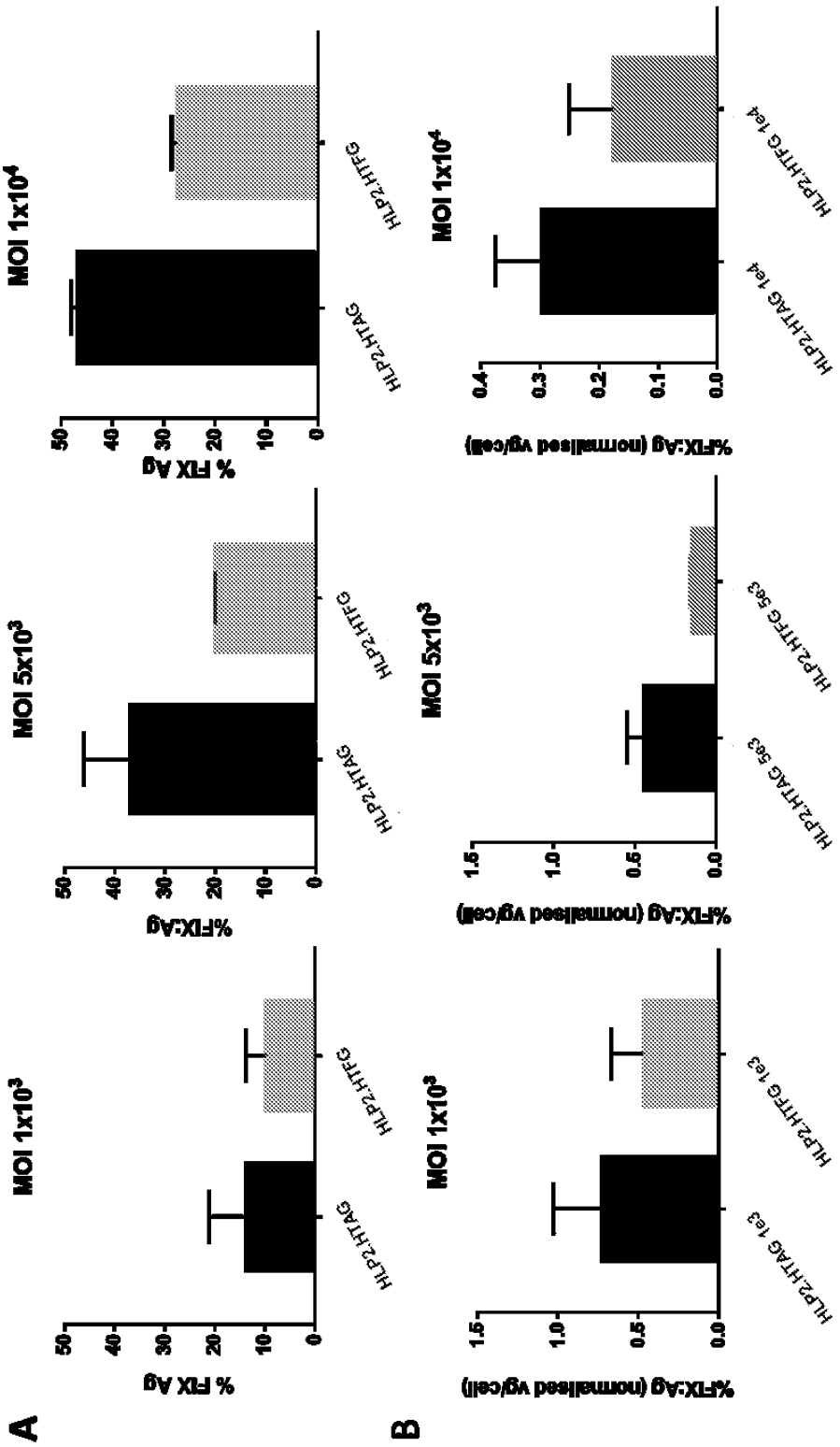

A
B
MOI 1x10^4
MOI 5x10^3
MOI 1x10^3
% FIX Ag
%FIX:Ag
%FIX:Ag (normalised vg/cell)
HLP2.HTAG
HLP2.HTFG
HLP2.HTAG 1e4
HLP2.HTFG 1e4
HLP2.HTAG 5e3
HLP2.HTFG 5e3
HLP2.HTAG 1e3
HLP2.HTFG 1e3

FIGURE 3

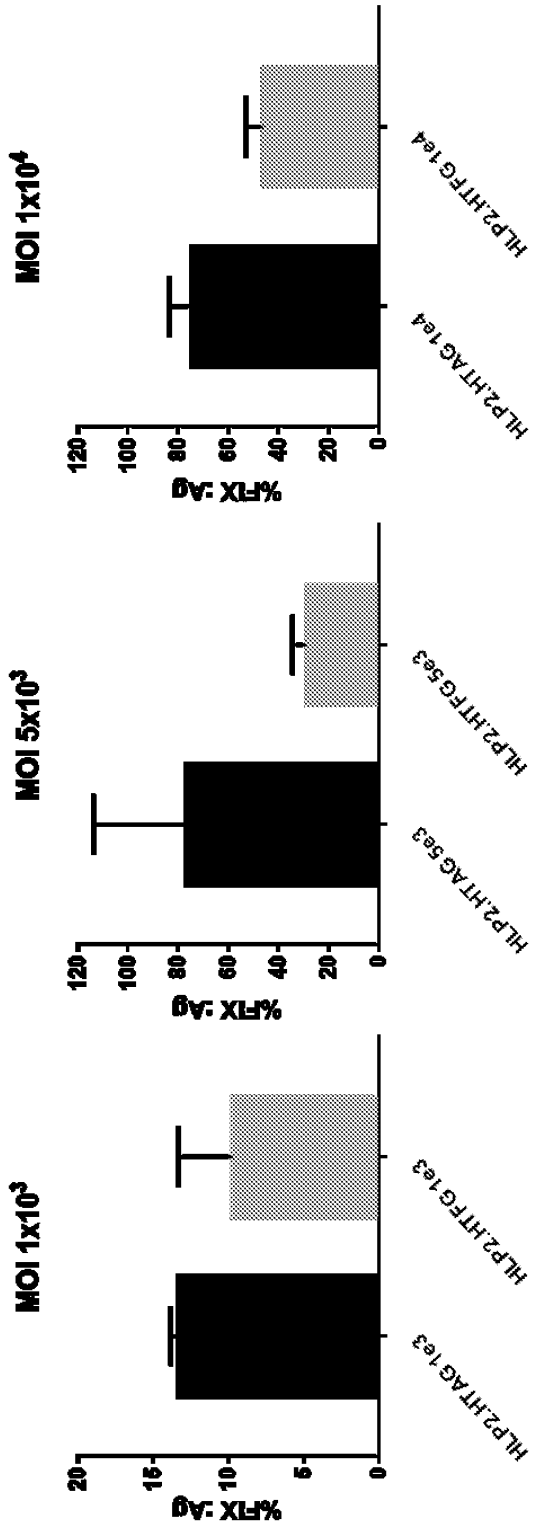

MOI 1x10⁴
MOI 5x10³
MOI 1x10³
%FIX :Ag
0
20
40
60
80
100
120
0
5
10
15
20
HLP2.HTAG1e4
HLP2.HTFG1e4
HLP2.HTAG5e3
HLP2.HTFG5e3
HLP2.HTAG1e3
HLP2.HTFG1e3

FIGURE 4

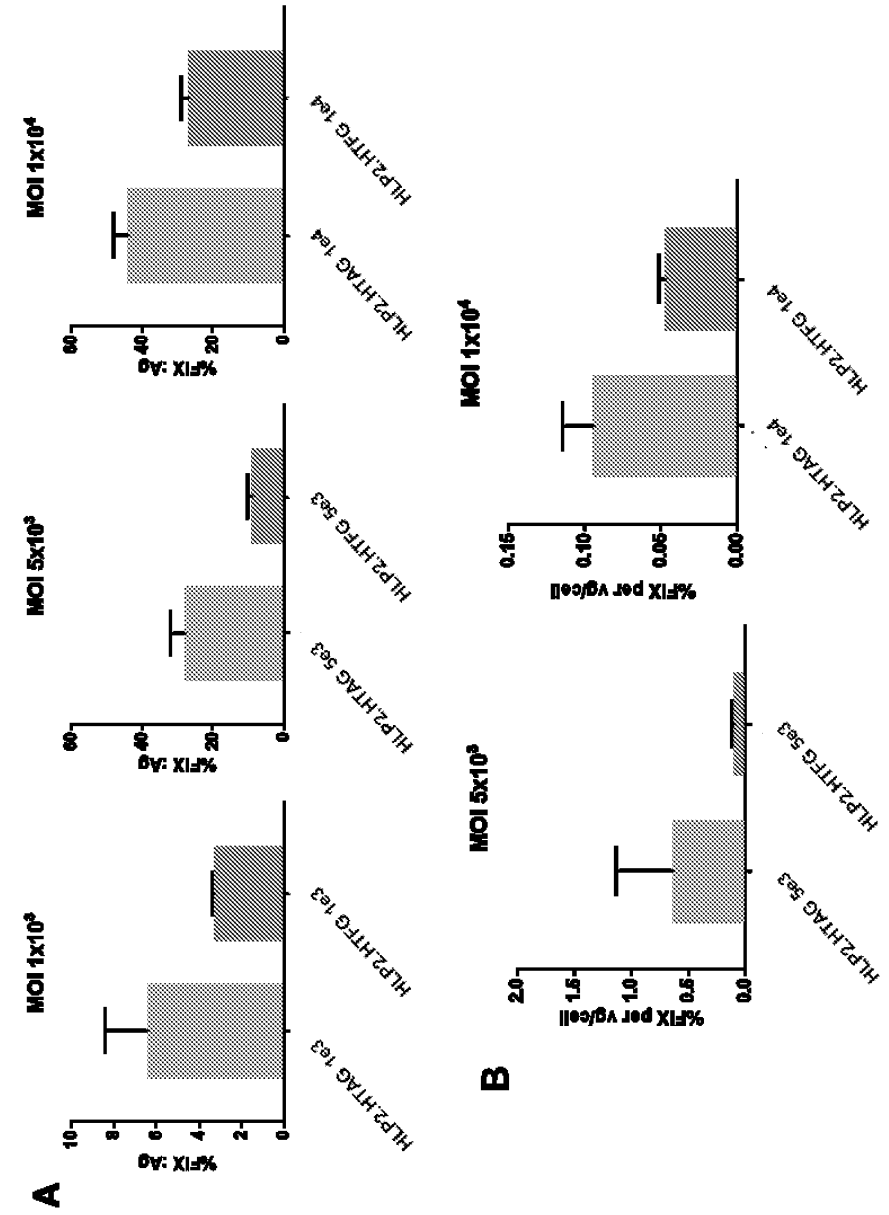

A
MOI 1x10^3
%FIX :AG
0
2
4
6
8
10
HLP2.HTAG 1e3
HLP2.HTFG 1e3
MOI 5x10^3
%FIX :AG
0
20
40
60
HLP2.HTAG 5e3
HLP2.HTFG 5e3
MOI 1x10^4
%FIX :AG
0
20
40
60
HLP2.HTAG 1e4
HLP2.HTFG 1e4
B
MOI 5x10^3
%FIX per VG/cell
0.0
0.5
1.0
1.5
2.0
HLP2.HTAG 5e3
HLP2.HTFG 5e3
MOI 1x10^4
%FIX per VG/cell
0.00
0.05
0.10
0.15
HLP2.HTAG 1e4
HLP2.HTFG 1e4

FIGURE 5

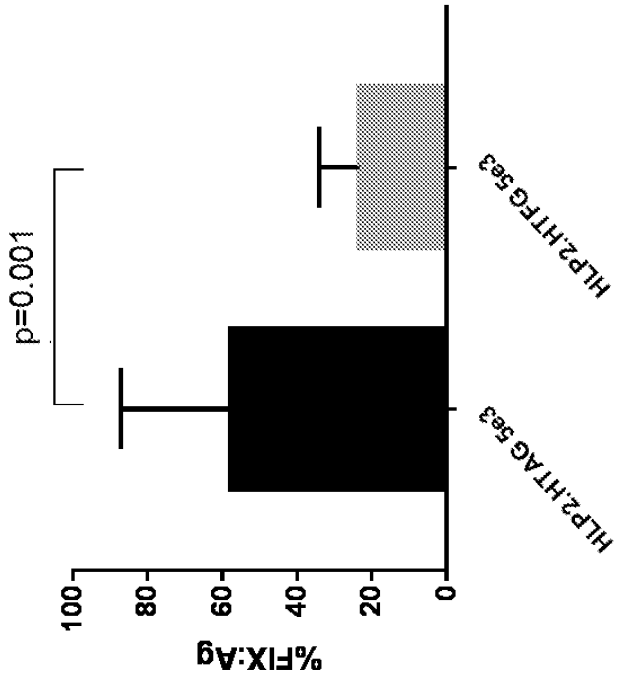


FIGURE 6

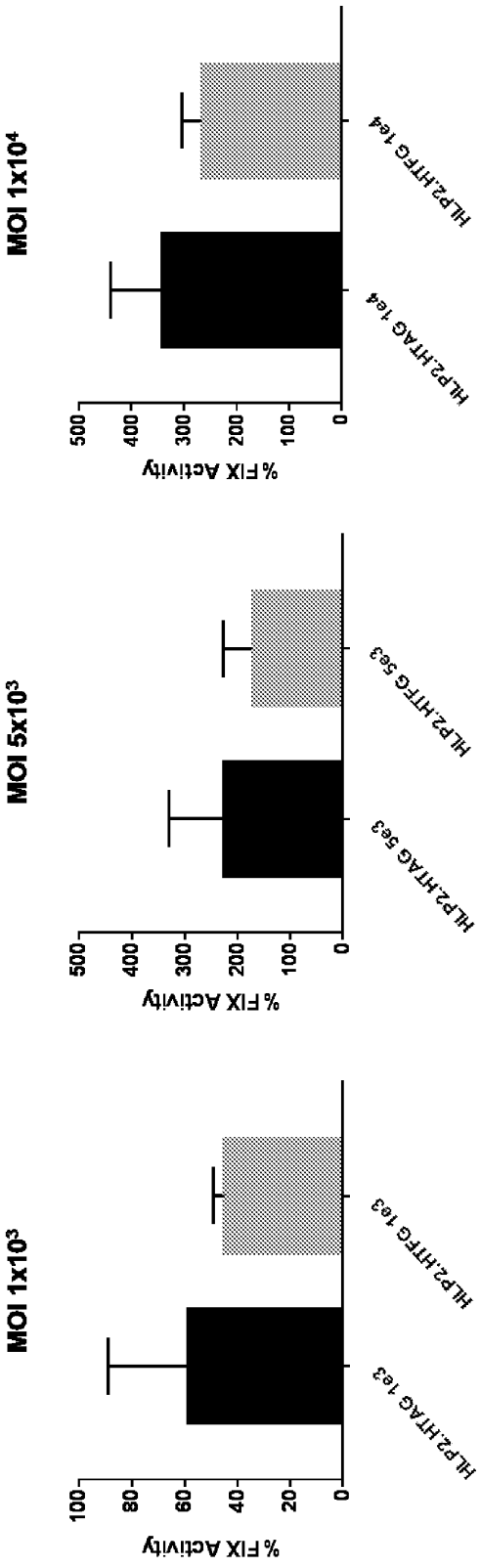

MOI 1x10⁴
MOI 5x10³
MOI 1x10³
% FIX Activity
0
100
200
300
400
500
20
40
60
80
HLP2.HTAG 164
HLP2.HTFG 164
HLP2.HTAG 563
HLP2.HTFG 563
HLP2.HTAG 163
HLP2.HTFG 163

FIGURE 7

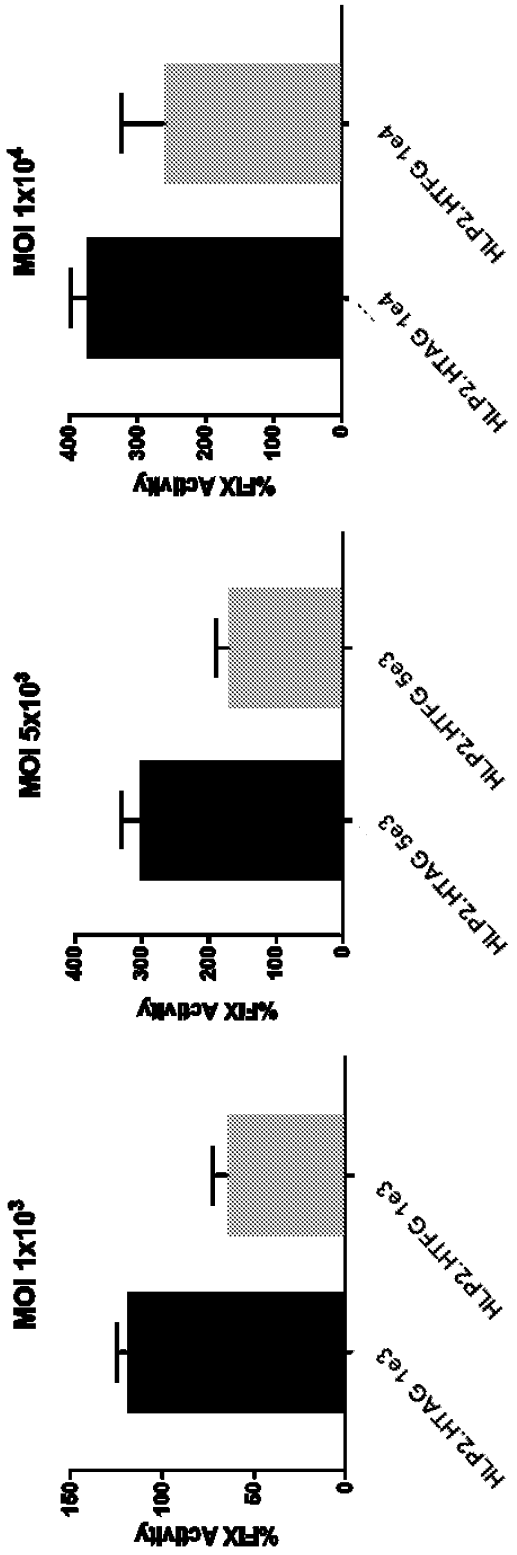

MOI 1x10^4
%FIX Activity
400
300
200
100
0
HLP2.HTAG 1e4
HLP2.HTFG 1e4
MOI 5x10^3
%FIX Activity
400
300
200
100
0
HLP2.HTAG 5e3
HLP2.HTFG 5e3
MOI 1x10^3
%FIX Activity
150
100
50
0
HLP2.HTAG 1e3
HLP2.HTFG 1e3

FIGURE 8

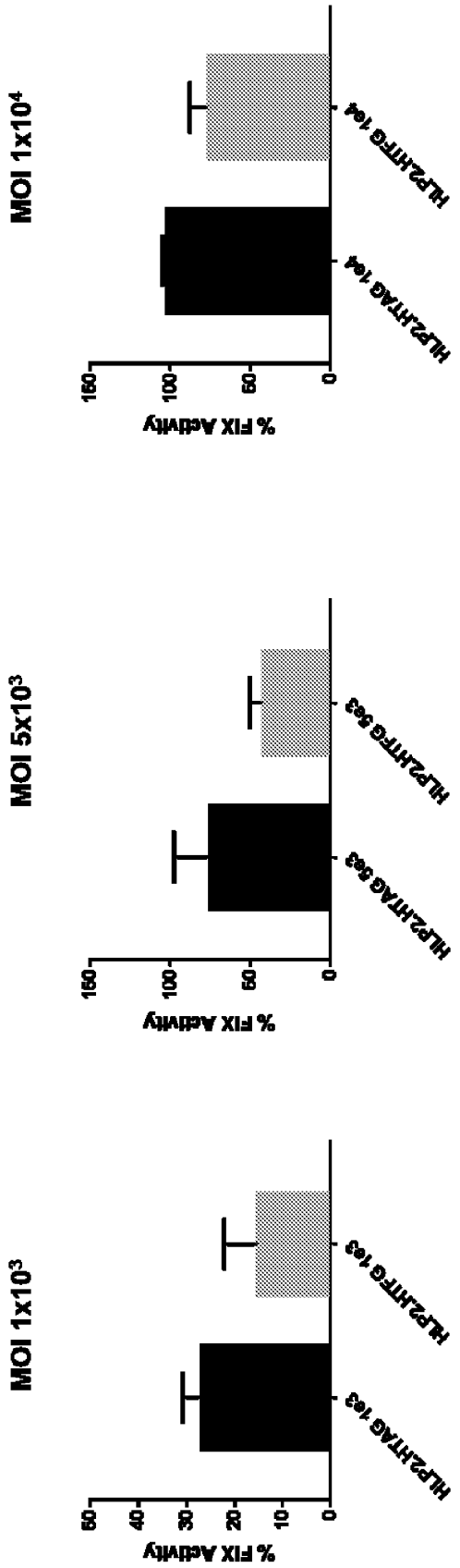

MOI 1x10^4
% FIX Activity
150
100
50
0
HLP2.HTAG 1e4
HLP2.HTFG 1e4
MOI 5x10^3
% FIX Activity
150
100
50
0
HLP2.HTAG 5e3
HLP2.HTFG 5e3
MOI 1x10^3
% FIX Activity
50
40
30
20
10
0
HLP2.HTAG 1e3
HLP2.HTFG 1e3

FIGURE 9

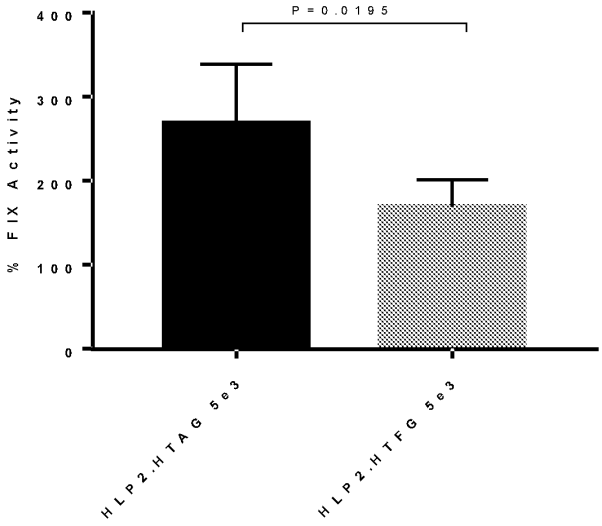

P = 0.0195
400
300
200
100
0
% FIX Activity
HLP2.HTAG 5e3
HLP2.HTFG 5e3

FIGURE 10

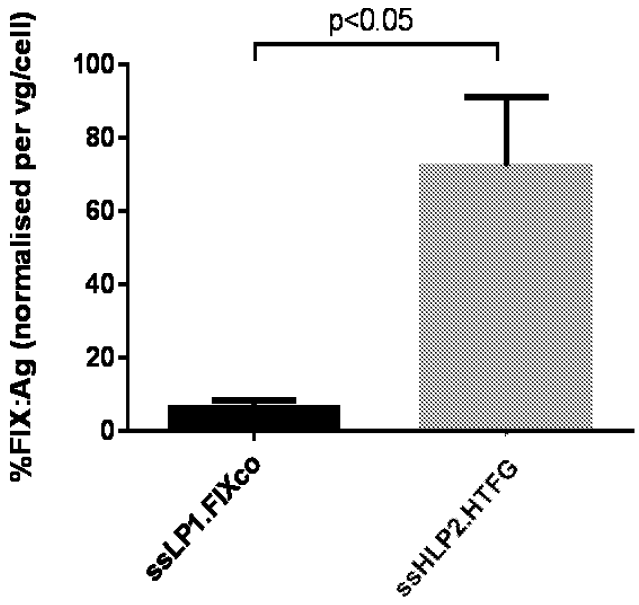

p<0.05
%FIX:Ag (normalised per vg/cell)
100
80
60
40
20
0
ssLP1.FIXco
ssHLP2.HTFG

FIGURE 11

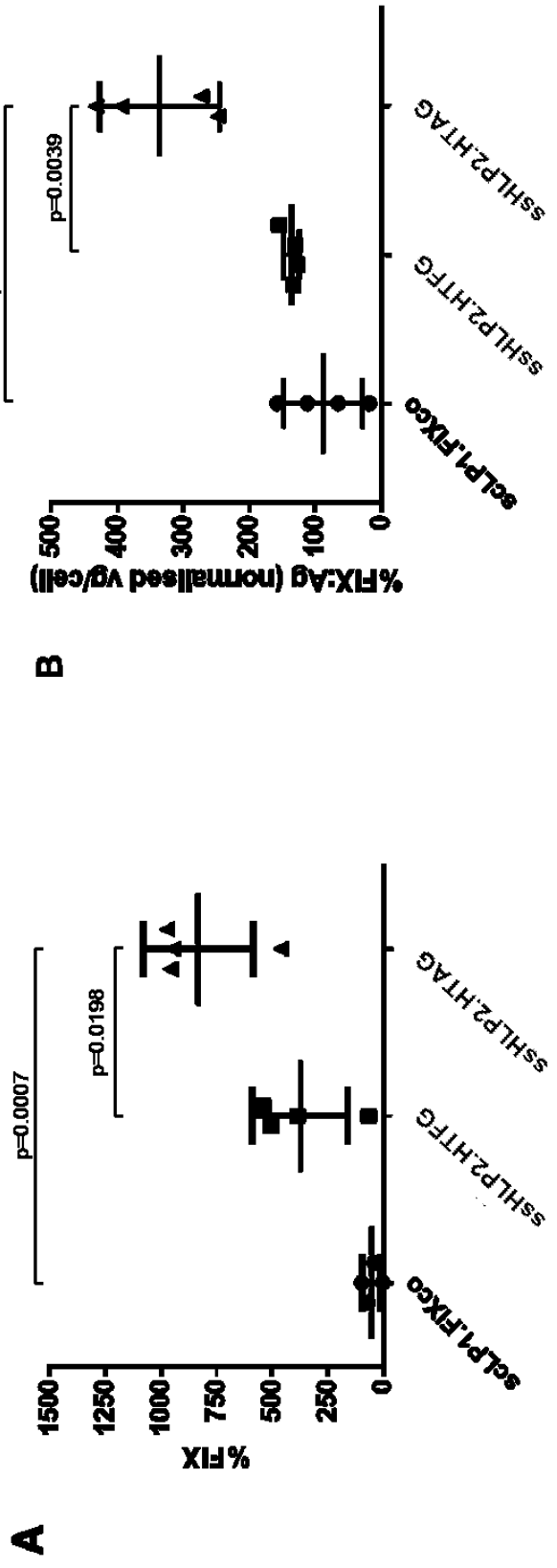

A
%FIX
1500
1250
1000
750
500
250
0
p=0.0007
p=0.0198
scLP1.FIXco
ssHLP2.HTFG
ssHLP2.HTAG
B
%FIX:Ag (normalised vg/cell)
500
400
300
200
100
0
p=0.0009
p=0.0039
scLP1.FIXco
ssHLP2.HTFG
ssHLP2.HTAG

FIGURE 12

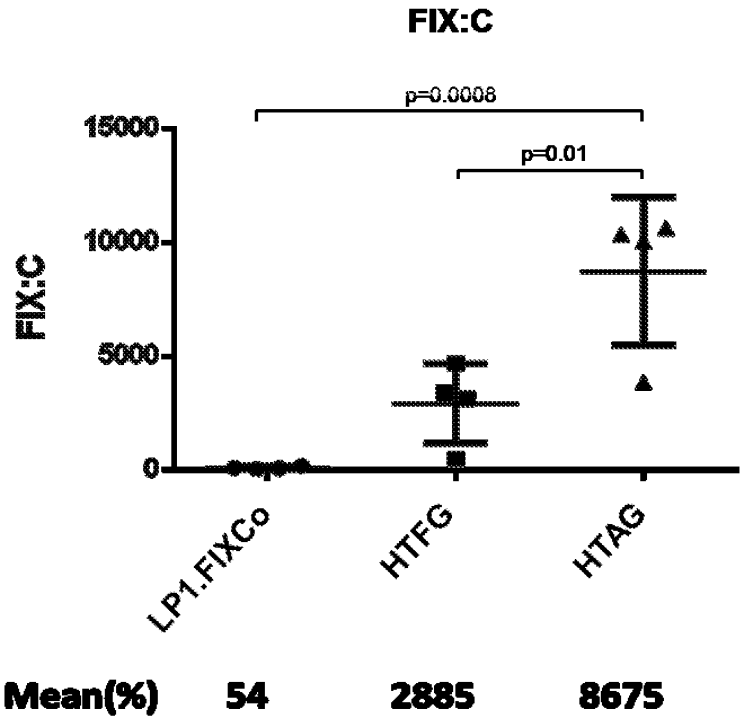

FIX:C
p=0.0008
p=0.01
15000
10000
5000
0
FIX:C
LP1.FIXCo
HTFG
HTAG
Mean(%) 54 2885 8675

FIGURE 13

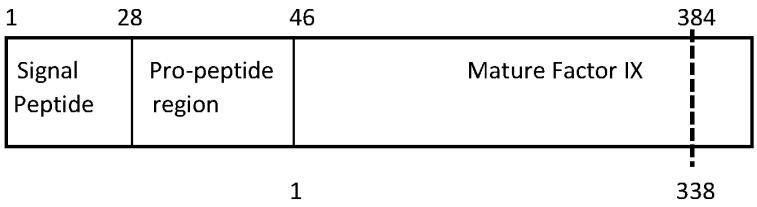

1
28
46
384
Signal Peptide
Pro-peptide region
Mature Factor IX
1
338

FIGURE 14

SEQ ID NO. 1 - Codon optimised portion of TI-FIX-ACNP-GoF coding sequence:

GAGGAGAAGTGCAGCTTTGAGGAGGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAA
GCAGTATGTGGATGGGGACCAGTGTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCA
ACAGCTATGAGTGCTGGTGCCCCTTTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAA
GAATGGCAGATGTGAGCAGTTCTGCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTA
CAGGCTGGCTGAGAACCAGAAGAGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCA
GACCAGCAAGCTGACCAGGGCTGAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAAC
CATCCTGGACAACATCACCCAGAGCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGAGGATGC
CAAGCCTGGCCAGTTCCCCTGGCAAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGT
GAATGAGAAGTGGATTGTGACTGCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGG
AGCACAACATTGAGGAGACTGAGCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACT
ACAATGCTGCCATCAACAAGTACAACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAG
CTATGTGACCCCCATCTGCATTGCTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGT
CTGGCTGGGGCAGGGTGTTCCACAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGG
ACAGGGCCACCTGCCTGCTCAGCACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGG
GGGCAGGGACAGCTGCCAGGGGGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGA
CTGGCATCATCAGCTGGGGGGAGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGAT
ATGTGAACTGGATCAAGGAGAAGACCAAGCTGACCTGA

SEQ ID NO. 2 - Wild type portion of TI-FIX-ACNP-GoF coding sequence, including intron:

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAGGCCTCATCACCATCTGCCTTTTAGGATATCTACTCAG
TGCTGAATGTACAGGTTTGTTTCCTTTTTTAAAATACATTGAGTATGCTTGCCTTTTAGATATAGAAATATCTGA
TGCTGTCTTCTTCACTAAATTTTGATTACATGATTTGACAGCAATATTGAAGAGTCTAACAGCCAGCACGCAGG
TTGGTAAGTACTGTGGGAACATCACAGATTTTGGCTCCATGCCCTAAAGAGAAATTGGCTTTCAGATTATTTGG
ATTAAAAACAAAGACTTTCTTAAGAGATGTAAAATTTTCATGATGTTTTCTTTTTTGCTAAAACTAAAGAATTAT
TCTTTTACATTTCAGTTTTTCTTGATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAATTCA
GGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAATGTATG

SEQ ID NO. 3 - truncated FIX intron 1A:

GTTTGTTTCCTTTTTTAAAATACATTGAGTATGCTTGCCTTTTAGATATAGAAATATCTGATGCTGTCTTCTTCAC
TAAATTTTGATTACATGATTTGACAGCAATATTGAAGAGTCTAACAGCCAGCACGCAGGTTGGTAAGTACTGT
GGGAACATCACAGATTTTGGCTCCATGCCCTAAAGAGAAATTGGCTTTCAGATTATTTGGATTAAAAACAAAG
ACTTTCTTAAGAGATGTAAAATTTTCATGATGTTTTCTTTTTTGCTAAAACTAAAGAATTATTCTTTTACATTTCA
G

SEQ ID NO. 4 - Coding sequence of TI-FIX-ACNP-GoF:

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAGGCCTCATCACCATCTGCCTTTTAGGATATCTACTCAG
TGCTGAATGTACAGTTTTTCTTGATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAATTCA
GGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAATGTATGGAGGAGAAGTGCAGCTTTGAGGA
GGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAAGCAGTATGTGGATGGGGACCAGT
GTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCAACAGCTATGAGTGCTGGTGCCCCT
TTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAAGAATGGCAGATGTGAGCAGTTCT
GCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTACAGGCTGGCTGAGAACCAGAAG
AGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCAGACCAGCAAGCTGACCAGGGCT

GAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAACCATCCTGGACAACATCACCCAGA
GCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGAGGATGCCAAGCCTGGCCAGTTCCCCTGGC
AAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGTGAATGAGAAGTGGATTGTGACT
GCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGGAGCACAACATTGAGGAGACTGA
GCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACTACAATGCTGCCATCAACAAGTAC
AACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAGCTATGTGACCCCCATCTGCATTG
CTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGTCTGGCTGGGGCAGGGTGTTCCA
CAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGGACAGGGCCACCTGCCTGCTCAG
CACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGGGGGCAGGGACAGCTGCCAGGG
GGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGACTGGCATCATCAGCTGGGGGG
AGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGATATGTGAACTGGATCAAGGAGA
AGACCAAGCTGACCTGA

SEQ ID NO. 5 - Coding sequence of TI-FIX-ACNP-GoF Factor IX sequence, including intron:

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAGGCCTCATCACCATCTGCCTTTTAGGATATCTACTCAG
TGCTGAATGTACAGGTTTGTTTCCTTTTTTAAAATACATTGAGTATGCTTGCCTTTTAGATATAGAAATATCTGA
TGCTGTCTTCTTCACTAAATTTTGATTACATGATTTGACAGCAATATTGAAGAGTCTAACAGCCAGCACGCAGG
TTGGTAAGTACTGTGGGAACATCACAGATTTTGGCTCCATGCCCTAAAGAGAAATTGGCTTTCAGATTATTTGG
ATTAAAAACAAAGACTTTCTTAAGAGATGTAAAATTTTCATGATGTTTTCTTTTTTGCTAAAACTAAAGAATTAT
TCTTTTACATTTCAGTTTTTCTTGATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAATTCA
GGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAATGTATGGAGGAGAAGTGCAGCTTTGAGGA
GGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAAGCAGTATGTGGATGGGGACCAGT
GTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCAACAGCTATGAGTGCTGGTGCCCCT
TTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAAGAATGGCAGATGTGAGCAGTTCT
GCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTACAGGCTGGCTGAGAACCAGAAG
AGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCAGACCAGCAAGCTGACCAGGGCT
GAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAACCATCCTGGACAACATCACCCAGA
GCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGAGGATGCCAAGCCTGGCCAGTTCCCCTGGC
AAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGTGAATGAGAAGTGGATTGTGACT
GCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGGAGCACAACATTGAGGAGACTGA
GCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACTACAATGCTGCCATCAACAAGTAC
AACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAGCTATGTGACCCCCATCTGCATTG
CTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGTCTGGCTGGGGCAGGGTGTTCCA
CAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGGACAGGGCCACCTGCCTGCTCAG
CACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGGGGGCAGGGACAGCTGCCAGGG
GGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGACTGGCATCATCAGCTGGGGGG
AGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGATATGTGAACTGGATCAAGGAGA
AGACCAAGCTGACCTGA

SEQ ID NO. 6 - HLP2 transcription regulatory element sequence:

CCCTAAAATGGGCAAACATTGCAAGCAGCAAACAGCAAACACACAGCCCTCCCTGCCTGCTGACCTTGGAGCT
GGGGCAGAGGTCAGACACCTCTCTGGGCCCATGCCACCTCCAACTGGACACAGGACGCTGTGGTTTCTGAGC
CAGGGGGCGACTCAGATCCCAGCCAGTGGACTTAGCCCCTGTTTGCTCCTCCGATAACTGGGGTGACCTTGGT
TAATATTCACCAGCAGCCTCCCCCGTTGCCCCTCTGGATCCACTGCTTAAATACGGACGAGGACAGGGCCCTGT
CTCCTCAGCTTCAGGCACCACCACTGACCTGGGACAGTGAAT

SEQ ID NO. 7 - LP1 transcription regulatory element sequence:

CCCTAAAATG GGCAAACATT GCAAGCAGCA AACAGCAAAC ACACAGCCCT CCCTGCCTGC TGACCTTGGA
GCTGGGGCAG AGGTCAGAGA CCTCTCTGGG CCCATGCCAC CTCCAACATC CACTCGACCC CTTGGAATTT
CGGTGGAGAG GAGCAGAGGT TGTCCTGGCG TGGTTTAGGT AGTGTGAGAG GGGAATGACT
CCTTTCGGTA AGTGCAGTGG AAGCTGTACA CTGCCCAGGC AAAGCGTCCG GGCAGCGTAG
GCGGGCGACT CAGATCCCAG CCAGTGGACT TAGCCCCTGT TTGCTCCTCC GATAACTGGG GTGACCTTGG
TTAATATTCA CCAGCAGCCT CCCCCGTTGC CCCTCTGGAT CCACTGCTTA AATACGGACG AGGACAGGGC
CCTGTCTCCT CAGCTTCAGG CACCACCACT GACCTGGGAC AGTGAAT

SEQ ID NO. 8 – "Mature" Factor IX amino acid sequence encoded by SEQ ID NO. 4:

YNSG KLEEFVQGNL ERECMEEKCS FEEAREVFEN TERTTEFWKQ YVDGDQCESN PCLNGGSCKD
DINSYECWCP FGFEGKNCEL DVTCNIKNGR CEQFCKNSAD NKVVCSCTEG YRLAENQKSC EPAVPFPCGR
VSVSQTSKLT RAEAVFPDVD YVNSTEAETI LDNITQSTQS FNDFTRVVGG EDAKPGQFPW QVVLNGKVDA
FCGGSIVNEK WIVTAAHCVE TGVKITVVAG EHNIEETEHT EQKRNVIRII PHHNYNAAIN KYNHDIALLE
LDEPLVLNSY VTPICIADKE YTNIFLKFGS GYVSGWGRVF HKGRSALVLQ YLRVPLVDRA TCLLSTKFTI
YNNMFCAGFH EGGRDSCQGD SGGPHVTEVE GTSFLTGIIS WGEECAMKGK YGIYTKVSRY VNWIKEKTKL T

SEQ ID NO. 9 - Wild type Factor IX (Malmo B variant) coding sequence:

ATGCAGCGCGT GAACATGATC ATGGCAGAAT CACCAGGCCT CATCACCATC TGCCTTTTAG GATATCTACT
CAGTGCTGAA TGTACAGTTT TTCTTGATCA TGAAAACGCC AACAAAATTC TGAATCGGCC AAAGAGGTAT
AATTCAGGTA AATTGGAAGA GTTTGTTCAA GGGAACCTTG AGAGAGAATG TATGGAAGAA
AAGTGTAGTT TTGAAGAAGC ACGAGAAGTT TTTGAAAACA CTGAAAGAAC AACTGAATTT TGGAAGCAGT
ATGTTGATGG AGATCAGTGT GAGTCCAATC CATGTTTAAA TGGCGGCAGT TGCAAGGATG ACATTAATTC
CTATGAATGT TGGTGTCCCT TTGGATTTGA AGGAAAGAAC TGTGAATTAG ATGTAACATG TAACATTAAG
AATGGCAGAT GCGAGCAGTT TTGTAAAAAT AGTGCTGATA ACAAGGTGGT TTGCTCCTGT ACTGAGGGAT
ATCGACTTGC AGAAAACCAG AAGTCCTGTG AACCAGCAGT GCCATTTCCA TGTGGAAGAG TTTCTGTTTC
ACAAACTTCT AAGCTCACCC GTGCTGAGGC TGTTTTTCCT GATGTGGACT ATGTAAATTC TACTGAAGCT
GAAACCATTT TGGATAACAT CACTCAAAGC ACCCAATCAT TTAATGACTT CACTCGGGTT GTTGGTGGAG
AAGATGCCAA ACCAGGTCAA TTCCCTTGGC AGGTTGTTTT GAATGGTAAA GTTGATGCAT TCTGTGGAGG
CTCTATCGTT AATGAAAAAT GGATTGTAAC TGCTGCCCAC TGTGTTGAAA CTGGTGTTAA AATTACAGTT
GTCGCAGGTG AACATAATAT TGAGGAGACA GAACATACAG AGCAAAAGCG AAATGTGATT CGAATTATTC
CTCACCACAA CTACAATGCA GCTATTAATA AGTACAACCA TGACATTGCC CTTCTGGAAC TGGACGAACC
CTTAGTGCTA AACAGCTACG TTACACCTAT TTGCATTGCT GACAAGGAAT ACACGAACAT CTTCCTCAAA
TTTGGATCTG GCTATGTAAG TGGCTGGGGA AGAGTCTTCC ACAAAGGGAG ATCAGCTTTA GTTCTTCAGT
ACCTTAGAGT TCCACTTGTT GACCGAGCCA CATGTCTTCG ATCTACAAAG TTCACCATCT ATAACAACAT
GTTCTGTGCT GGCTTCCATG AAGGAGGTAG AGATTCATGT CAAGGAGATA GTGGGGGACC CCATGTTACT
GAAGTGGAAG GGACCAGTTT CTTAACTGGA ATTATTAGCT GGGGTGAAGA GTGTGCAATG
AAAGGCAAAT ATGGAATATA TACCAAGGTA TCCCGGTATG TCAACTGGAT TAAGGAAAAA ACAAAGCTCA
CTTAA

SEQ ID NO. 10 - Mut C capsid polypeptide sequence:

MAADGYLPDWLEDNLSEGIREWWALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD
KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ
AKKRVLEPLGLVEEGAKTAPGKKRPVDQSPQEPDSSSGVGKSGKQPARKRLNFGQTGDSE
SVPDPQPLGEPPAAPTSLGSNTMASGGGAPMADNNEGADGVGNSSGNWHCDSQWLGDRVI
TTSTRTWALPTYNNHLYKQISSQSGASNDNHYFGYSTPWGYFDFNRFHCHFSPRDWQRLI
NNNWGFRPKKLSFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGSAHQG

CLPPFPADVFMVPQYGYLTLNNGSQAVGRSSFYCLEYFPSQMLRTGNNFQFSYTFEDVPF
HSSYAHSQSLDRLMNPLIDQYLYYLNRTQGTTSGTTNQSRLLFSQAGPQSMSLQARNWLP
GPCYRQQRLSKTANDNNNSNFPWTAASKYHLNGRDSLVNPGPAMASHKDDEEKFFPMHGN
LIFGKEGTTASNAELDNVMITDEEEIRTTNPVATEQYGTVANNLQSSNTAPTTRTVNDQG
ALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHPPPQIMIKNTPVPANPPT
TFSPAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNYNKSVNVDFTVDTNGV
YSEPRPIGTRYLTRNL

SEQ ID NO. 11 - FIXco coding sequence with TTG GoF codon:

ATGCAGAGGGTGAACATGATCATGGCTGAGAGCCCTGGCCTGATCACCATCTGCCTGCTGGGCTACCTGCTGT
CTGCTGAGTGCACTGTGTTCCTGGACCATGAGAATGCCAACAAGATCCTGAACAGGCCCAAGAGATACAACTC
TGGCAAGCTGGAGGAGTTTGTGCAGGGCAACCTGGAGAGGGAGTGCATGGAGGAGAAGTGCAGCTTTGAG
GAGGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAAGCAGTATGTGGATGGGGACCA
GTGTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCAACAGCTATGAGTGCTGGTGCCC
CTTTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAAGAATGGCAGATGTGAGCAGTT
CTGCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTACAGGCTGGCTGAGAACCAGAA
GAGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCAGACCAGCAAGCTGACCAGGGC
TGAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAACCATCCTGGACAACATCACCCAG
AGCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGGAGGATGCCAAGCCTGGCCAGTTCCCCTGG
CAAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGTGAATGAGAAGTGGATTGTGACT
GCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGGAGCACAACATTGAGGAGACTGA
GCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACTACAATGCTGCCATCAACAAGTAC
AACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAGCTATGTGACCCCCATCTGCATTG
CTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGTCTGGCTGGGGCAGGGTGTTCCA
CAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGGACAGGGCCACCTGCCTGTTGAG
CACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGGGGGCAGGGACAGCTGCCAGGG
GGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGACTGGCATCATCAGCTGGGGGG
AGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGATATGTGAACTGGATCAAGGAGA
AGACCAAGCTGACCTGA

SEQ ID NO. 12 - FIXco coding sequence:

ATGCAGAGGGTGAACATGATCATGGCTGAGAGCCCTGGCCTGATCACCATCTGCCTGCTGGGCTACCTGCTGT
CTGCTGAGTGCACTGTGTTCCTGGACCATGAGAATGCCAACAAGATCCTGAACAGGCCCAAGAGATACAACTC
TGGCAAGCTGGAGGAGTTTGTGCAGGGCAACCTGGAGAGGGAGTGCATGGAGGAGAAGTGCAGCTTTGAG
GAGGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAAGCAGTATGTGGATGGGGACCA
GTGTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCAACAGCTATGAGTGCTGGTGCCC
CTTTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAAGAATGGCAGATGTGAGCAGTT
CTGCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTACAGGCTGGCTGAGAACCAGAA
GAGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCAGACCAGCAAGCTGACCAGGGC
TGAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAACCATCCTGGACAACATCACCCAG
AGCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGGAGGATGCCAAGCCTGGCCAGTTCCCCTGG
CAAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGTGAATGAGAAGTGGATTGTGACT
GCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGGAGCACAACATTGAGGAGACTGA
GCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACTACAATGCTGCCATCAACAAGTAC
AACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAGCTATGTGACCCCCATCTGCATTG
CTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGTCTGGCTGGGGCAGGGTGTTCCA
CAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGGACAGGGCCACCTGCCTGAGGA
GCACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGGGGGCAGGGACAGCTGCCAGG
GGGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGACTGGCATCATCAGCTGGGGG
GAGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGATATGTGAACTGGATCAAGGAG
AAGACCAAGCTGACCTGA

SEQ ID NO. 13 - Enhancer element from HLP2:

CCCTAAAATGGGCAAACATTGCAAGCAGCAAACAGCAAACACACAGCCCTCCCTGCCTGCTGACCTTGGAGCT
GGGGCAGAGGTCAGACACCTCTCTGGGCCCATGCCACCTCCAAC

SEQ ID NO. 14 - Promoter element from HLP2:

GGGCGACTCAGATCCCAGCCAGTGGACTTAGCCCCTGTTTGCTCCTCCGATAACTGGGGTGACCTTGGTTAAT
ATTCACCAGCAGCCTCCCCCGTTGCCCCTCTGGATCCACTGCTTAAATACGGACGAGGACAGGGCCCTGTCTCC
TCAGCTTCAGGCACCACCACTGACCTGGGACAGTGAAT

SEQ ID NO. 15 - Wild type portion of TI-FIX-ACNP-GoF coding sequence, excluding the intron:

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAGGCCTCATCACCATCTGCCTTTTAGGATATCTACTCAG
TGCTGAATGTACAGTTTTTCTTGATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAATTCA
GGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAATGTATG

SEQ ID NO. 16 - "Immature" Factor IX amino acid sequence encoded by SEQ ID NO. 4:

MQRVNMIMAE SPGLITICLL GYLLSAECTV FLDHENANKI LNRPKRYNSG KLEEFVQGNL ERECMEEKCS
FEEAREVFEN TERTTEFWKQ YVDGDQCESN PCLNGGSCKD DINSYECWCP FGFEGKNCEL DVTCNIKNGR
CEQFCKNSAD NKVVCSCTEG YRLAENQKSC EPAVPFPCGR VSVSQTSKLT RAEAVFPDVD YVNSTEAETI
LDNITQSTQS FNDFTRVVGG EDAKPGQFPW QVVLNGKVDA FCGGSIVNEK WIVTAAHCVE TGVKITVVAG
EHNIEETEHT EQKRNVIRII PHHNYNAAIN KYNHDIALLE LDEPLVLNSY VTPICIADKE YTNIFLKFGS
GYVSGWGRVF HKGRSALVLQ YLRVPLVDRA TCLLSTKFTI YNNMFCAGFH EGGRDSCQGD SGGPHVTEVE
GTSFLTGIIS WGEECAMKGK YGIYTKVSRY VNWIKEKTKL T

SEQ ID NO. 17 - AAV5 capsid polypeptide sequence:

MSFVDHPPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNGLDRGEPVNRADEV
AREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQAKKRVLEPFGLVEEGAKTAPT
GKRIDDHFPKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADG
VGNASGDWHCDSTWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHS
HWSPRDWQRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTE
GCLPAFPPQVFTLPQYGYATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPS
QNLFKLANPLVDQYLYRFVSTNNTGGVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFA
TTNRMELEGASYQVPPQPNGMTNNLQGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNR
VAYNVGGQMATNNQSSTTAPATGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLK
HPPPMMLIKNTPVPGNITSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVD
FAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 18 – Coding sequence of TI-codop-FIX-GoF Factor IX sequence, including intron:

ATGCAGCGCGTGAACATGATCATGGCAGAATCACCAGGCCTCATCACCATCTGCCTTTTAGGATATCTACTCAG
TGCTGAATGTACAGGTTTGTTTCCTTTTTTAAAATACATTGAGTATGCTTGCCTTTTAGATATAGAAATATCTGA
TGCTGTCTTCTTCACTAAATTTTGATTACATGATTTGACAGCAATATTGAAGAGTCTAACAGCCAGCACGCAGG
TTGGTAAGTACTGTGGGAACATCACAGATTTTGGCTCCATGCCCTAAAGAGAAATTGGCTTTCAGATTATTTGG
ATTAAAAACAAAGACTTTCTTAAGAGATGTAAAATTTTCATGATGTTTTCTTTTTTGCTAAAACTAAAGAATTAT
TCTTTTACATTTCAGTTTTTCTTGATCATGAAAACGCCAACAAAATTCTGAATCGGCCAAAGAGGTATAATTCA
GGTAAATTGGAAGAGTTTGTTCAAGGGAACCTTGAGAGAGAATGTATGGAGGAG AAGTGTTCTT
TCGAGGAGGC GAGAGAGGTT TTCGAGAATA CTGAGCGAAC AACCGAATTC TGGAAACAAT
ATGTGGATGG CGACCAATGT GAATCTAATC CCTGCCTCAA CGGTGGCTCA TGCAAAGACG ATATCAACAG
CTACGAGTGT TGGTGCCCCT TTGGTTTCGA GGGAAAGAAT TGCGAGCTTG ATGTAACCTG TAACATTAAG

AATGGGCGCT GCGAACAGTT TTGCAAGAAC AGCGCCGACA ATAAGGTCGT CTGCAGTTGT ACCGAAGGCT
ATAGGCTTGC AGAGAATCAG AAGAGTTGCG AGCCTGCTGT GCCGTTCCCA TGTGGCAGAG TCAGTGTGTC
CCAAACTAGC AAGCTGACAA GAGCAGAAGC CGTTTTCCCC GATGTGGACT ACGTGAATTC CACTGAAGCC
GAAACGATCC TGGACAATAT CACACAGAGC ACTCAGTCTT TCAACGACTT CACACGGGTT GTGGGAGGAG
AGGACGCCAA ACCCGGCCAG TTTCCTTGGC AAGTCGTTCT TAACGGCAAG GTCGACGCCT TTTGTGGAGG
GAGTATTGTG AACGAGAAAT GGATTGTCAC CGCTGCTCAT TGTGTTGAAA CTGGGGTGAA AATCACTGTT
GTCGCAGGAG AGCACAATAT CGAAGAGACA GAACACACCG AGCAGAAACG CAACGTTATT
CGGATCATTC CACATCACAA CTACAATGCT GCCATCAACA AGTACAACCA CGACATTGCG CTGCTGGAGT
TGGATGAACC TCTCGTGCTC AACTCCTATG TGACCCCAAT CTGCATAGCA GATAAGGAGT ATACCAACAT
CTTCCTGAAG TTTGGGTCAG GTTATGTGTC AGGCTGGGGA CGAGTGTTTC ATAAAGGGAG ATCAGCACTG
GTGTTGCAGT ATCTGCGCGT ACCACTGGTG GATCGGGCTA CTTGCCTGCT A AGCACAAAA TTCACCATCT
ACAACAACAT GTTTTGTGCC GGTTTTCACG AAGGCGGCAG GGACAGCTGT CAGGGAGATT
CCGGAGGGCC TCATGTCACA GAGGTCGAGG GCACCTCCTT TCTCACTGGG ATTATAAGCT GGGGAGAAGA
ATGCGCCATG AAAGGGAAGT ACGGCATATA CACGAAAGTG TCTAGATACG TGAATTGGAT
TAAGGAAAAG ACCAAACTGA CGTGA

SEQ ID NO. 19 - Wild type Factor IX (Malmo B variant) coding sequence corresponding to mature FIX polypeptide:

TAT AATTCAGGTA AATTGGAAGA GTTTGTTCAA GGGAACCTTG AGAGAGAATG TATGGAAGAA
AAGTGTAGTT TTGAAGAAGC ACGAGAAGTT TTTGAAAACA CTGAAAGAAC AACTGAATTT TGGAAGCAGT
ATGTTGATGG AGATCAGTGT GAGTCCAATC CATGTTTAAA TGGCGGCAGT TGCAAGGATG ACATTAATTC
CTATGAATGT TGGTGTCCCT TTGGATTTGA AGGAAAGAAC TGTGAATTAG ATGTAACATG TAACATTAAG
AATGGCAGAT GCGAGCAGTT TTGTAAAAAT AGTGCTGATA ACAAGGTGGT TTGCTCCTGT ACTGAGGGAT
ATCGACTTGC AGAAAACCAG AAGTCCTGTG AACCAGCAGT GCCATTTCCA TGTGGAAGAG TTTCTGTTTC
ACAAACTTCT AAGCTCACCC GTGCTGAGGC TGTTTTTCCT GATGTGGACT ATGTAAATTC TACTGAAGCT
GAAACCATTT TGGATAACAT CACTCAAAGC ACCCAATCAT TTAATGACTT CACTCGGGTT GTTGGTGGAG
AAGATGCCAA ACCAGGTCAA TTCCCTTGGC AGGTTGTTTT GAATGGTAAA GTTGATGCAT TCTGTGGAGG
CTCTATCGTT AATGAAAAAT GGATTGTAAC TGCTGCCCAC TGTGTTGAAA CTGGTGTTAA AATTACAGTT
GTCGCAGGTG AACATAATAT TGAGGAGACA GAACATACAG AGCAAAAGCG AAATGTGATT CGAATTATTC
CTCACCACAA CTACAATGCA GCTATTAATA AGTACAACCA TGACATTGCC CTTCTGGAAC TGGACGAACC
CTTAGTGCTA AACAGCTACG TTACACCTAT TTGCATTGCT GACAAGGAAT ACACGAACAT CTTCCTCAAA
TTTGGATCTG GCTATGTAAG TGGCTGGGGA AGAGTCTTCC ACAAAGGGAG ATCAGCTTTA GTTCTTCAGT
ACCTTAGAGT TCCACTTGTT GACCGAGCCA CATGTCTTCG ATCTACAAAG TTCACCATCT ATAACAACAT
GTTCTGTGCT GGCTTCCATG AAGGAGGTAG AGATTCATGT CAAGGAGATA GTGGGGGACC CCATGTTACT
GAAGTGGAAG GGACCAGTTT CTTAACTGGA ATTATTAGCT GGGGTGAAGA GTGTGCAATG
AAAGGCAAAT ATGGAATATA TACCAAGGTA TCCCGGTATG TCAACTGGAT TAAGGAAAAA ACAAAGCTCA
CTTAA

SEQ ID NO. 20 – AAV2-5 hybrid VP1u variant 1

MAADGYLPDWLEEVGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNGLDRGEPVNRADEVARE
HDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHFP
KRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCD
STWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLINN
YWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGYA
TLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGG
VQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQ

GSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQEIV
PGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYSTGQ
VTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 21 – AAV2-5 hybrid VP1u variant 2

MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYNYLGPGNGLDRGEPVNRADEVAR
EHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHF
PKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHC
DSTWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLIN
NYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGY
ATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTG
GVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNL
QGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQE
IVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYST
GQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 22 – AAV2-5 hybrid VP1u variant 3

MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRG`LVLPGYKYLGPFNGLDK`GEPVNRADEVAR
EHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHF
PKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHC
DSTWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLIN
NYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGY
ATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTG
GVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNL
QGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQE
IVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYST
GQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 23 – AAV2-5 hybrid VP1u variant 4

MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLDKGEPVNEADAAALE
HDKAYDRQLDSGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHF
PKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHC
DSTWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLIN
NYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGY
ATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTG
GVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNL
QGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQE
IVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYST
GQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 24 – AAV2-5 hybrid VP1u variant 5

MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLDKGEPVNEADAAALE
HDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQAKKRVLEPFGLVEEGAKTAPTGKRIDDHF
PKRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHC
DSTWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLIN
NYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGY
ATLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTG

GVQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNL
QGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQE
IVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYST
GQVTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

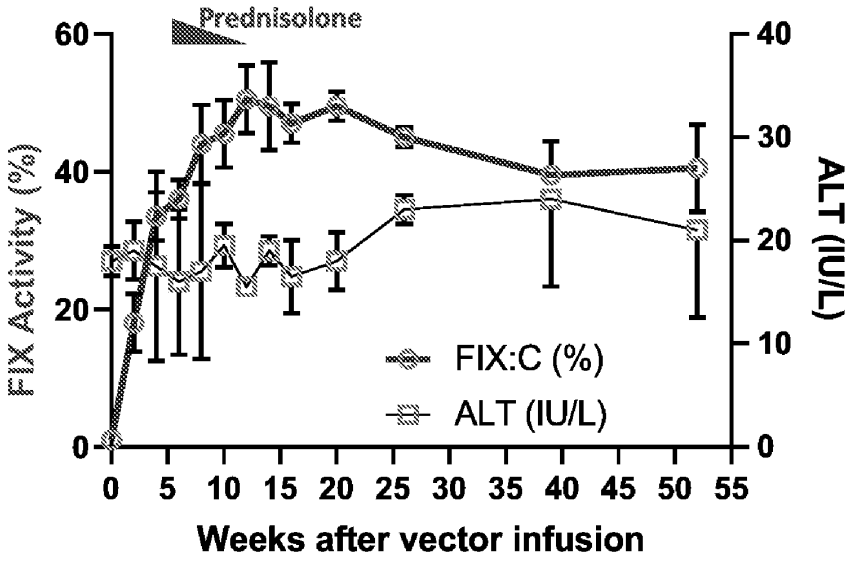
SEQ ID NO. 25 – AAV2-5 hybrid VP1u variant 6

MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLDKGEPVNEADAAALE
HDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQAKKRVLEPLGLVEEPVKTAPTGKRIDDHFP
KRKKARTEEDSKPSTSSDAEAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCD
STWMGDRVVTKSTRTWVLPSYNNHQYREIKSGSVDGSNANAYFGYSTPWGYFDFNRFHSHWSPRDWQRLINN
YWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGNGTEGCLPAFPPQVFTLPQYGYA
TLNRDNTENPTERSSFFCLEYFPSKMLRTGNNFEFTYNFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTGG
VQFNKNLAGRYANTYKNWFPGPMGRTQGWNLGSGVNRASVSAFATTNRMELEGASYQVPPQPNGMTNNLQ
GSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQSSTTAPATGTYNLQEIV
PGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKHPPPMMLIKNTPVPGNITSFSDVPVSSFITQYSTGQ
VTVEMEWELKKENSKRWNPEIQYTNNYNDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL

SEQ ID NO. 26 – FIXco coding sequence with CTG GoF codon

ATGCAGAGGGTGAACATGATCATGGCTGAGAGCCCTGGCCTGATCACCATCTGCCTGCTGGGCTACCTGCTGT
CTGCTGAGTGCACTGTGTTCCTGGACCATGAGAATGCCAACAAGATCCTGAACAGGCCCAAGAGATACAACTC
TGGCAAGCTGGAGGAGTTTGTGCAGGGCAACCTGGAGAGGGAGTGCATGGAGGAGAAGTGCAGCTTTGAG
GAGGCCAGGGAGGTGTTTGAGAACACTGAGAGGACCACTGAGTTCTGGAAGCAGTATGTGGATGGGGACCA
GTGTGAGAGCAACCCCTGCCTGAATGGGGGCAGCTGCAAGGATGACATCAACAGCTATGAGTGCTGGTGCCC
CTTTGGCTTTGAGGGCAAGAACTGTGAGCTGGATGTGACCTGCAACATCAAGAATGGCAGATGTGAGCAGTT
CTGCAAGAACTCTGCTGACAACAAGGTGGTGTGCAGCTGCACTGAGGGCTACAGGCTGGCTGAGAACCAGAA
GAGCTGTGAGCCTGCTGTGCCATTCCCATGTGGCAGAGTGTCTGTGAGCCAGACCAGCAAGCTGACCAGGGC
TGAGGCTGTGTTCCCTGATGTGGACTATGTGAACAGCACTGAGGCTGAAACCATCCTGGACAACATCACCCAG
AGCACCCAGAGCTTCAATGACTTCACCAGGGTGGTGGGGGGGGGAGGATGCCAAGCCTGGCCAGTTCCCCTGG
CAAGTGGTGCTGAATGGCAAGGTGGATGCCTTCTGTGGGGGCAGCATTGTGAATGAGAAGTGGATTGTGACT
GCTGCCCACTGTGTGGAGACTGGGGTGAAGATCACTGTGGTGGCTGGGGAGCACAACATTGAGGAGACTGA
GCACACTGAGCAGAAGAGGAATGTGATCAGGATCATCCCCCACCACAACTACAATGCTGCCATCAACAAGTAC
AACCATGACATTGCCCTGCTGGAGCTGGATGAGCCCCTGGTGCTGAACAGCTATGTGACCCCCATCTGCATTG
CTGACAAGGAGTACACCAACATCTTCCTGAAGTTTGGCTCTGGCTATGTGTCTGGCTGGGGCAGGGTGTTCCA
CAAGGGCAGGTCTGCCCTGGTGCTGCAGTACCTGAGGGTGCCCCTGGTGGACAGGGCCACCTGCCTGCTGAG
CACCAAGTTCACCATCTACAACAACATGTTCTGTGCTGGCTTCCATGAGGGGGGCAGGGACAGCTGCCAGGG
GGACTCTGGGGGCCCCCATGTGACTGAGGTGGAGGGCACCAGCTTCCTGACTGGCATCATCAGCTGGGGGG
AGGAGTGTGCCATGAAGGGCAAGTATGGCATCTACACCAAAGTCTCCAGATATGTGAACTGGATCAAGGAGA
AGACCAAGCTGACCTGA

FIGURE 15


Prednisolone
FIX Activity (%)
ALT (IU/L)
FIX:C (%)
ALT (IU/L)
Weeks after vector infusion
0
20
40
60
0
10
20
30
40
0 5 10 15 20 25 30 35 40 45 50 55