FIGS. 1A-1C

FIG. 1A

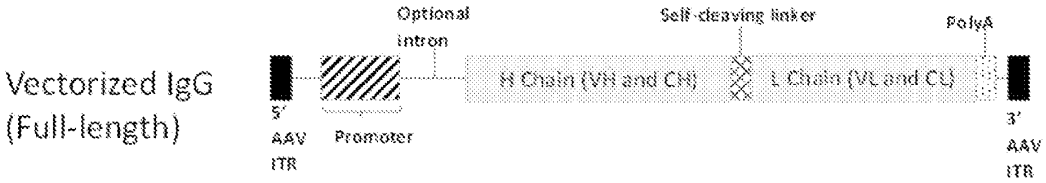

FIG. 1B

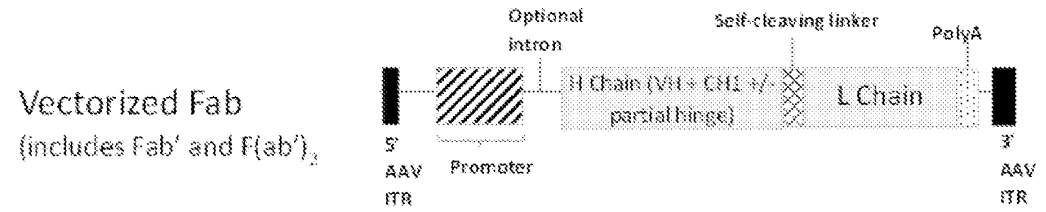

FIG. 1C

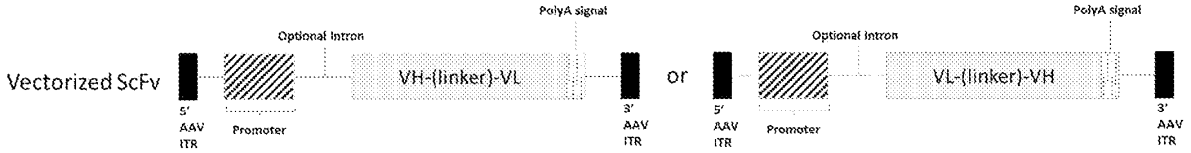

FIG. 2A C5-D-MAB IgG1 Fab Construct

Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-D-mab Heavy Chain (SEQ ID NO: 168):
QVQLVESGGG LVQPGRSLRL SCAASGFTVH SSYYMAWVRQ APGKGLEWVG AIFTGSGAEY KAEWAKGRVT
ISKDTSKNQV VLTMTNMDPV DTATYYCASD AGYDYPTHAM HYWGQGTLVT VSSASTKGPS VFPLAPSSKS
TSGGTAALGC LVKDYFPEPV TVSWNSGALT SGVHTFPAVL QSSGLYSLSS VVTVPSSSLG TQTYICNVNH
KPSNTKVDKK V***EPKSCDKTH***
Linker: RKRR +/- GSG + (EGRGSLLTCGDVEENPGP or APVKQTLNFDLLKLAGDVESNPGP)
(SEQ ID NOs: 109, 117,115, 116; full-length sequences disclosed as SEQ ID NOS 24 and 26, respectively)
Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-D-mab Light Chain (SEQ ID NO: 169)
DIQMTQSPSS LSASVGDRVT ITCRASQGIS SSLAWYQQKP GKAPKLLIYG ASETESGVPS RFSGSGSGTD
FTLTISSLQP EDFATYYCQN TKVGSSYGNT FGGGTKVEIK RTVAAPSVFI FPPSDEQLKS GTASVVCLLN
NFYPREAKVQ WKVDNALQSG NSQESVTEQD SKDSTYSLSS TLTLSKADYE KHKVYACEVT HQGLSSPVTK
SFNRGEC

Predicted CDRs are underscored

FIG. 2B C5-A-MAB IgG1 Fab Construct

Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-A-mab Heavy Chain (SEQ ID NO: 170):
QVQLVQSGAE VKKPGASVKV SCKASGYIFS NYWIQWVRQA PGQGLEWMGE ILPGSGSTEY ***TEN***FKDRVTM TRDTSTSTVY MELSSLRS*ED TAVYY*CARYF FGSSPNWYFD VWG**QGT**LVTV SSASTKGPSV FPLAPSSKST SGGTAALGCL VKDYFPEPVT V***SWN***SGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSSLGT QTYICNVNHK PSNTKVDKRV EPKSCV*EPKS CD +/- KTHT*
Linker: RKRR +/- GSG + (EGRGSLLTCGDVEENPGP or APVKQTLNFDLLKLAGDVESNPGP)
(SEQ ID NOs: 109, 117,115, 116; full-length sequences disclosed as SEQ ID NOS 24 and 26, respectively)
Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-A-mab Light Chain (SEQ ID NO: 172)
DIQMTQSPSS LSASVGDRVT ITCGA***SEN***IY GALNWYQQKP GKAPKLLIYG ATNLADGVPS RFSGSGSGTD FTLTISSLQP *EDFATYY*CQN VLNTPLTFG**Q GT**KVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQ***SGN***SQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG LSSPVTK***SFN*** RGEC

Heavy Chain Legend:
CDRs are underscored (predicted for C5-A-mab)
EDTAVYY = Y-sulfation site
QGT= Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site
EPKSCDKTHT = Hinge region

Light Chain Legend:
CDRs are underscored (predicted for C5-A-mab)
EDFATYY = Y-sulfation site
QGT = Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site

FIG. 2C C5-A-MAB IgG2 Fab Construct

Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-A-mab Heavy Chain (SEQ ID NO: 171):
QVQLVQSGAE VKKPGASVKV SCKASGYIFS NYWIQWVRQA PGQGLEWMGE ILPGSGSTEY ***TEN***FKDRVTM TRDTSTSTVY MELSSLRSED TAVYYCARYF FGSSPNWYFD VWG**QGT**LVTV SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT V***SWN***SGALTS GVHTFPAVLQ SSGLYSLSSV VTVP***SSN***FGT QTY***TCN***VDHK PSNTKVDKTV
Linker: RKRR +/- GSG + (EGRGSLLTCGDVEENPGP or APVKQTLNFDLLKLAGDVESNPGP)
(SEQ ID NOs: 109, 117,115, 116; full-length sequences disclosed as SEQ ID NOS 24 and 26, respectively)
Leader (SEQ ID NO: 55):
MYRMQLLLLIALSLALVTNS
C5-A-mab Light Chain (SEQ ID NO: 172)
DIQMTQSPSS LSASVGDRVT ITCGA***SEN***IY GALNWYQQKP GKAPKLLIYG ATNLADGVPS RFSGSGSGTD FTLTISSLQP *EDFATYY*CQN VLNTPLTFG**Q GT**KVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQ***SGN***SQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG LSSPVTK***SFN*** RGEC

Heavy Chain Legend:
CDRs are underscored (predicted for C5-A-mab)
EDTAVYY= Y-sulfation site
QGT = Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site

Light Chain Legend:
CDRs are underscored (predicted for C5-A-mab)
EDFATYY= Y-sulfation site
QGT = Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site

FIG. 2D C5-C-MAB IgG1 FAB CONSTRUCT:

Leader (SEQ ID NO: 55)
MYRMQLLLLIALSLALVTNS
C5-C-mab Heavy Chain (SEQ ID NO: 173)
QVQLVQSGAE VKKPGASVKV SCKASGHIFS NYWIQWVRQA PGQGLEWMGE ILPGSGHTEY TENFKDRVTM TRDTSTSTVY MELSSLRSED TAVYYCARYF FGSSPNWYFD VWGQGTLVTV SSASTKGPSV FPLAPCSRST SESTAALGCL VKDYFPEPVT VSWNSGALTS GVHTFPAVLQ SSGLYSLSSV VTVPSSNFGT QTYTCNVDHK PSNTKVDKTV ERKCCVE +/- CPPCPA+/- PPVAG
Linker: RKRR +/- GSG + (EGRGSLLTCGDVEENPGP or APVKQTLNFDLLKLAGDVESNPGP)
(SEQ ID NOs: 109, 117,115, 116; full-length sequences disclosed as SEQ ID NOS 24 and 26, respectively)
Leader (SEQ ID NO: 55)
MYRMQLLLLIALSLALVTNS
C5-C-mab Light Chain (SEQ ID NO: 174)
DIQMTQSPSS LSASVGDRVT ITCGASENIY GALNWYQQKP GKAPKLLIYG ATNLADGVPS RFSGSGSGTD FTLTISSLQP EDFATYYCQN VLNTPLTFGQ GTKVEIKRTV AAPSVFIFPP SDEQLKSGTA SVVCLLNNFY PREAKVQWKV DNALQSGNSQ ESVTEQDSKD STYSLSSTLT LSKADYEKHK VYACEVTHQG LSSPVTKSFN RGEC

Heavy Chain Legend:
ERKSCVECPPCPAPPVAG = Hinge region (SEQ ID NO: 163)

Predicted CDRs are underscored

FIG. 2E C5-B-MAB IgG1 FAB CONSTRUCT:

Leader (SEQ ID NO: 55)
MYRMQLLLLIALSLALVTNS
C5-B-mab Heavy Chain (SEQ ID NO: 175)
EVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG IGPFFG***TAN***Y AQKFQGRVTI TADESTSTAY MELSSLRS*ED TAVYY*CARDT PYFDYWG**QGT** LVTVSSASTK GPSVFPLAPS SKSTSGGTAA LGCLVKDYFP EPVTV***SWN***SG ALTSGVHTFP AVLQSSGLYS LSSVVTVPSS SLGTQTYICN VNHKPSNTKV DKRV*EPKSCD +/- KTHT (or KTHL)+/- CPPCPA +/- PEAAGG*PSVFL
Linker: RKRR +/- GSG + (EGRGSLLTCGDVEENPGP or APVKQTLNFDLLKLAGDVESNPGP)
(SEQ ID NOs: 109, 117,115, 116; full-length sequences disclosed as SEQ ID NOS 24 and 26, respectively)
Leader (SEQ ID NO: 55)
MYRMQLLLLIALSLALVTNS
C5-B-mab Light Chain (SEQ ID NO: 176)
SYELTQPLSV SVALGQTARI TCSG*DSIPNY* YVYWYQQKPG QAPVLVIYDD SNRPSGIPER FSGSN**SGN**TA TLTISRAQAG *DEADYYCQSF DS***SLN**AEVFG GGTKLTVLGQ PKAAPSVTLF PPSSEELQAN KATLVCLISD FYPGAVTVAW KADSSPVKAG VETTTPSKQ**S** **NN**KYAASSYL SLTPEQWKSH RSYSCQVTHE GSTVEKTVAP TECS

Heavy Chain Legend:
CDRs are underscored (predicted for C5-B-mab)
EDTAVYY = Y-sulfation site
QGT= Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site
EPKSCDKTHTCPPCPAPEAAGG = Hinge Region (SEQ ID NO: 161)

Light Chain Legend:
CDRs are underscored (predicted for C5-B-mab)
DSIPNY and *YCQSFD and DEADYY* = Y-sulfation sites
QGT = Glutamine (Q) glycosylation site
(S/T)XN = Non-consensus Asparaginal (N) glycosylation site

FIG. 3

```
                          |         |         |         |         |         |
AAV1            MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
AAV2            MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
AAV3            MAADGYLPDWLEDNLSEGIREWWALKPGVPQPKANQQHQDNRRGLVLPGYKYLGPGNGLD 60
AAV3-3          MAADGYLPDWLEDNLSEGIREWWALKPGVPQPKANQQHQDNRRGLVLPGYKYLGPGNGLD 60
AAV3B           MAADGYLPDWLEDNLSEGIREWWALKPGVPQPKANQQHQDNRRGLVLPGYKYLGPGNGLD 60
AAV4            -MTDGYLPDWLEDNLSEGVREWWALQPGAPKPKANQQHQDNARGLVLPGYKYLGPGNGLD 59
AAV4-4          -MTDGYLPDWLEDNLSEGVREWWALQPGAPKPKANQQHQDNARGLVLPGYKYLGPGNGLD 59
AAV5            MSFVDHPPDWLEE-VGEGLREFLGLEAGPPKPKPNQQHQDQARGLVLPGYNYLGPGNGLD 59
AAV6            MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
AAV7            MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLD 60
AAV8            MAADGYLPDWLEDNLSEGIREWWALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
AAV9            MAADGYLPDWLEDNLSEGIREWWALKPGAPQPKANQQHQDNARGLVLPGYKYLGPGNGLD 60
AAV9e           MAADGYLPDWLEDNLSEGIREWWALKPGAPQPKANQQHQDNARGLVLPGYKYLGPGNGLD 60
rh.10           MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
rh.20           MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
rh.39           MAADGYLPDWLEDNLSEGIREWWALKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
rh.73           MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
rh.74v1         MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLD 60
rh.74v2         MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDNGRGLVLPGYKYLGPFNGLD 60
hu.12           MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHQDDSRGLVLPGYKYLGPFNGLD 60
hu.21           MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
hu.26           MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
hu.37           MAADGYLPDWLEDNLSEGIREWWDLKPGAPKPKANQQKQDDGRGLVLPGYKYLGPFNGLD 60
hu.51           MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
hu.53           MAADGYLPDWLEDTLSEGIRQWWKLKPGPPPPKPAERHKDDSRGLVLPGYKYLGPFNGLD 60
                    .: *****: :.**:*::  *: * * **  ::::*: ********:**** ****
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FIG. 3 (Continued)

```
                    |         |         |         |         |         |
AAV1                KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV2                KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
AAV3                KGEPVNEADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV3-3              KGEPVNEADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV3B               KGEPVNEADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV4                KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQQRLQGDTSFGGNLGRAVFQ 119
AAV4-4              KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQQRLQGDTSFGGNLGRAVFQ 119
AAV5                RGEPVNRADEVAREHDISYNEQLEAGDNPYLKYNHADAEFQEKLADDTSFGGNLGKAVFQ 119
AAV6                KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV7                KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV8                KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
AAV9                KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
AAV9e               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
rh.10               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
rh.20               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
rh.39               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
rh.73               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
rh.74v1             KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
rh.74v2             KGEPVNAADAAALEHDKAYDQQLQAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
hu.12               KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
hu.21               KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
hu.26               KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
hu.37               KGEPVNAADAAALEHDKAYDQQLKAGDNPYLRYNHADAEFQERLQEDTSFGGNLGRAVFQ 120
hu.51               KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120
hu.53               KGEPVNEADAAALEHDKAYDRQLDSGDNPYLKYNHADAEFQERLKEDTSFGGNLGRAVFQ 120

                    |         |         |         |         |         |
AAV1                AKKRVLEPLGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGKTGQQPAKKRLNFGQTGDS 179
AAV2                AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPV-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179
AAV3                AKKRILEPLGLVEEAAKTAPGKKGAVDQSPQ-EPDSSSGVGKSGKQPARKRLNFGQTGDS 179
AAV3-3              AKKRILEPLGLVEEAAKTAPGKKGAVDQSPQ-EPDSSSGVGKSGKQPARKRLNFGQTGDS 179
AAV3B               AKKRILEPLGLVEEAAKTAPGKKRPVDQSPQ-EPDSSSGVGKSGKQPARKRLNFGQTGDS 179
AAV4                AKKRVLEPLGLVEQAGETAPGKKRPLIESPQ-QPDSSTGIGKKGKQPAKKKLVFEDETGA 178
AAV4-4              AKKRVLEPLGLVEQAGETAPGKKRPLIESPQ-QPDSSTGIGKKGKQPAKKKLVFEDETGA 178
AAV5                AKKRVLEPFGLVEEGAKTAPTGKRIDDHFPKRKKARTEEDSKP-----------STSSDA 168
AAV6                AKKRVLEPFGLVEEGAKTAPGKKRPVEQSPQ-EPDSSSGIGKTGQQPAKKRLNFGQTGDS 179
AAV7                AKKRVLEPLGLVEEGAKTAPAKKRPVEPSPQRSPDSSTGIGKKGQQPARKRLNFGQTGDS 180
AAV8                AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPARKRLNFGQTGDS 180
AAV9                AKKRLLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGAQPAKKRLNFGQTGDT 179
AAV9e               AKKRLLEPLGLVEEAAKTAPGKKRPVEQSPQ-EPDSSAGIGKSGAQPAKKRLNFGQTGDT 179
rh.10               AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS 180
rh.20               AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRSPDSSTGIGKTGQQPAKKRLNFGQTGDS 180
rh.39               AKKRVLEPLGLVEEAAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS 180
rh.73               AKKRVLEPLGLVEEGAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPARKRLNFGQTGDS 180
rh.74v1             AKKRVLEPLGLVESPVKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS 180
rh.74v2             AKKRVLEPLGLVESPVKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS 180
hu.12               AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPV-EPDSSSGTGKAGHQPARKRLNFGQTGDA 179
hu.21               AKKRILEPLGLVEEPVKTAPGKKRPVEHSPA-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179
hu.26               AKKRILEPLGLVEEPVKTAPGKKRPVEHSPA-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179
hu.37               AKKRVLEPLGLVEEAAKTAPGKKRPVEPSPQRSPDSSTGIGKKGQQPAKKRLNFGQTGDS 180
hu.51               AKKRVLEPLGLVGEPVKTAPGKKRPVEHSPV-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179
hu.53               AKKRVLEPLGLVEEPVKTAPGKKRPVEHSPA-EPDSSSGTGKAGQQPARKRLNFGQTGDA 179
                    ****:***:****.  :***  *      *  .   :   .*               .:
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FIG. 3 (Continued)

```
                          |         |         |         |         |         |
AAV1              ESVP-DPQPLGEPPATPAAVGPTTMASGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 238
AAV2              DSVP-DPQPLGQPPAAPSGLGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDR 238
AAV3              ESVP-DPQPLGEPPAAPTSLGSNTMASGGGAPMADNNEGADGVGNSSGNWHCDSQWLGDR 238
AAV3-3            ESVP-DPQPLGEPPAAPTSLGSNTMASGGGAPMADNNEGADGVGNSSGNWHCDSQWLGDR 238
AAV3B             ESVP-DPQPLGEPPAAPTSLGSNTMASGGGAPMADNNEGADGVGNSSGNWHCDSQWLGDR 238
AAV4              GDGP----PEGSTSGAMS--DDSEMRAAAGGAAVEGGQGADGVGNASGDWHCDSTWSEGH 232
AAV4-4            GDGP----PEGSTSGAMS--DDSEMRAAAGGAAVEGGQGADGVGNASGDWHCDSTWSEGH 232
AAV5              EAGPSGSQQLQIPAQPASSLGADTMSAGGGGPLGDNNQGADGVGNASGDWHCDSTWMGDR 228
AAV6              ESVP-DPQPLGEPPATPAAVGPTTMASGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 238
AAV7              ESVP-DPQPLGEPPAAPSSVGSGTVAAGGGAPMADNNEGADGVGNASGNWHCDSTWLGDR 239
AAV8              ESVP-DPQPLGEPPAAPSGVGPNTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
AAV9              ESVP-DPQPIGEPPAAPSGVGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDR 238
AAV9e             ESVP-DPQPIGEPPAAPSGVGSLTMASGGGAPVADNNEGADGVGSSSGNWHCDSQWLGDR 238
rh.10             ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
rh.20             ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
rh.39             ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
rh.73             ESVP-DPQPLGEPPAAPSSVGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
rh.74v1           ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
rh.74v2           ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
hu.12             DSVP-DPQPLGQPPAAPTSLGSTTMATGSGAPMADNNEGADGVGNSSGNWHCDSQWLGDR 238
hu.21             DSVP-DPRPLGQPPAAPSGLGTNTMASGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDR 238
hu.26             DSVP-DPQPLGQPPAAPSGLGTNTMASGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDR 238
hu.37             ESVP-DPQPIGEPPAGPSGLGSGTMAAGGGAPMADNNEGADGVGSSSGNWHCDSTWLGDR 239
hu.51             DSVP-DPQPLGQPPAAPSGLGTNTMATGSGAPMADNNEGADGVGNSSGNWHCDSTWMGDR 238
hu.53             DSVP-DPQPLRQPPAAPTSLGSTTMATGSGAPMADNNEGADGVGNSSGNWHCDSQWLGDR 238
                     *             :  .   : :..*.   :..:******.:**:***** *  .:

                  |         |         |         |         |         |
AAV1              VITTSTRTWALPTYNNHLYKQISSAST-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 297
AAV2              VITTSTRTWALPTYNNHLYKQISSQ-S-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
AAV3              VITTSTRTWALPTYNNHLYKQISSQ-S-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
AAV3-3            VITTSTRTWALPTYNNHLYKQISSQ-S-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
AAV3B             VITTSTRTWALPTYNNHLYKQISSQ-S-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
AAV4              VTTTSTRTWVLPTYNNHLYKRLGE-----SLQSNTYNGFSTPWGYFDFNRFHCHFSPRDW 287
AAV4-4            VTTTSTRTWVLPTYNNHLYKRLGE-----SLQSNTYNGFSTPWGYFDFNRFHCHFSPRDW 287
AAV5              VVTKSTRTWVLPSYNNHQYREIKSGSVD-GSNANAYFGYSTPWGYFDFNRFHSHWSPRDW 287
AAV6              VITTSTRTWALPTYNNHLYKQISSAST-GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 297
AAV7              VITTSTRTWALPTYNNHLYKQISSETA-GSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 298
AAV8              VITTSTRTWALPTYNNHLYKQISNGTSGGATNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
AAV9              VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDW 298
AAV9e             VITTSTRTWALPTYNNHLYKQISNSTSGGSSNDNAYFGYSTPWGYFDFNRFHCHFSPRDW 298
rh.10             VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
rh.20             VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
rh.39             VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
rh.73             VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
rh.74v1           VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
rh.74v2           VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
hu.12             VITTSTRTWALPTYNNHLYKQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
hu.21             VITTSTRTWALPTYNNHLYKQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
hu.26             VITTSTRTWALPTYNNHLYKQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
hu.37             VITTSTRTWALPTYNNHLYKQISNGTSGGSTNDNTYFGYSTPWGYFDFNRFHCHFSPRDW 299
hu.51             VITTSTRTWALPTYNNHLYKQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
hu.53             VITTSTRTWALPTYNNHLYKQISSQS--GASNDNHYFGYSTPWGYFDFNRFHCHFSPRDW 296
                  * *.*****.**:**** *:.:       . : * * *:**************.*:*****
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FIG. 3 (Continued)

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                          |         |         |         |         |         |
AAV1            QRLINNNWGFRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDSEYQLPYVLGS 357
AAV2            QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
AAV3            QRLINNNWGFRPKKLSFKLFNIQVRGVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
AAV3-3          QRLINNNWGFRPKKLSFKLFNIQVRGVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
AAV3B           QRLINNNWGFRPKKLSFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
AAV4            QRLINNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQIFADSSYELPYVMDA 347
AAV4-4          QRLINNNWGMRPKAMRVKIFNIQVKEVTTSNGETTVANNLTSTVQIFADSSYELPYVMDA 347
AAV5            QRLINNYWGFRPRSLRVKIFNIQVKEVTVQDSTTTIANNLTSTVQVFTDDDYQLPYVVGN 347
AAV6            QRLINNNWGFRPKRLNFKLFNIQVKEVTTNDGVTTIANNLTSTVQVFSDSEYQLPYVLGS 357
AAV7            QRLINNNWGFRPKKLRFKLFNIQVKEVTTNDGVTTIANNLTSTIQVFSDSEYQLPYVLGS 358
AAV8            QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
AAV9            QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS 358
AAV9e           QRLINNNWGFRPKRLNFKLFNIQVKEVTDNNGVKTIANNLTSTVQVFTDSDYQLPYVLGS 358
rh.10           QRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
rh.20           QRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
rh.39           QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
rh.73           QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
rh.74v1         QRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
rh.74v2         QRLINNNWGFRPKRLNFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
hu.12           QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 359
hu.21           QRLINNNWGFRPKRLSFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
hu.26           QRLINNNWGFRPKRLSFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
hu.37           QRLINNNWGFRPKRLSFKLFNIQVKEVTQNEGTKTIANNLTSTIQVFTDSEYQLPYVLGS 359
hu.51           QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
hu.53           QRLINNNWGFRPKRLNFKLFNIQVKEVTQNDGTTTIANNLTSTVQVFTDSEYQLPYVLGS 356
                ****** **:**: : .*:*****: ** .:. .*:*******:*:*:*..*:****:.

                          |         |         |         |         |         |
AAV1            AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV2            AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
AAV3            AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
AAV3-3          AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
AAV3B           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
AAV4            GQEGSLPPFPNDVFMVPQYGYCGLVTGNTSQQQTDRNAFYCLEYFPSQMLRTGNNFEITY 407
AAV4-4          GQEGSLPPFPNDVFMVPQYGYCGLVTGNTSQQQTDRNAFYCLEYFPSQMLRTGNNFEITY 407
AAV5            GTEGCLPAFPPQVFTLPQYGYATLNRDNT-ENPTERSSFFCLEYFPSKMLRTGNNFEFTY 406
AAV6            AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 414
AAV7            AHQGCLPPFPADVFMIPQYGYLTLNNG---SQSVGRSSFYCLEYFPSQMLRTGNNFEFSY 415
AAV8            AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFTY 416
AAV9            AHEGCLPPFPADVFMIPQYGYLTLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
AAV9e           AHEGCLPPFPADVFMIPQYGYLTLNDG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 415
rh.10           AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
rh.20           AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
rh.39           AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
rh.73           AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFSFSY 416
rh.74v1         AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
rh.74v2         AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
hu.12           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRPSFYCLEYFPSQMLRTGNNFTFSY 413
hu.21           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
hu.26           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
hu.37           AHQGCLPPFPADVFMIPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFEFSY 416
hu.51           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFTFSY 413
hu.53           AHQGCLPPFPADVFMVPQYGYLTLNNG---SQAVGRSSFYCLEYFPSQMLRTGNNFQFSY 413
                . :*.** ** :** :*****  *  .   .: . *.:*:*******:******** ::*
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FIG. 3 (Continued)

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                |         |         |         |         |         |
AAV1            TFEEVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQN QSGSAQNKDLLFSRGSPAGMSV 473
AAV2            TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTN-TPSGTTTQSRLQFSQAGASDIRD 472
AAV3            TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQGTTSGTTNQSRLLFSQAGPQSMSL 473
AAV3-3          TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQGTTSGTTNQSRLLFSQAGPQSMSL 473
AAV3B           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQGTTSGTTNQSRLLFSQAGPQSMSL 473
AAV4            SFEKVPFHSMYAHSQSLDRLMNPLIDQYLWGLQSTTTGTTLNAGTATTNFTKLRPTNFSN 467
AAV4-4          SFEKVPFHSMYAHSQSLDRLMNPLIDQYLWGLQSTTTGTTLNAGTATTNFTKLRPTNFSN 467
AAV5            NFEEVPFHSSFAPSQNLFKLANPLVDQYLYRFVSTNNTG-------GVQFNKNLAGRYAN 459
AAV6            TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQN-QSGSAQNKDLLFSRGSPAGMSV 473
AAV7            SFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLARTQSNPGGTAGNRELQFYQGGPSTMAE 475
AAV8            TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQT-TGGTANTQTLGFSQGGPNTMAN 475
AAV9            EFENVPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTINGS--GQNQQTLKFSVAGPSNMAV 473
AAV9e           EFENVPFHSSYAHSQSLDRLMNPLIDQYLYYLSKTINGS--GQNQQTLKFSVAGPSNMAV 473
rh.10           QFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTAGTQQLLFSQAGPNNMSA 475
rh.20           QFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTAGTQQLLFSQAGPNNMSA 475
rh.39           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTQGTQQLLFSQAGPANMSA 475
rh73            TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTAGTQQLLFSQAGPSNMSA 475
rh.74v1         NFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTAGTQQLLFSQAGPNNMSA 475
rh.74v2         NFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTAGTQQLLFSQAGPNNMSA 475
hu.12           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQS-NSGTLQQSRLLFSQAGPTSMSL 472
hu.21           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTN-TPSGTTTMSRLQFSQAGASDIRD 472
hu.26           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTN-TPSGTTTMSRLQFSQAGASDIRD 472
hu.37           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLSRTQS-TGGTQGTQQLLFSQAGPANMSA 475
hu.51           TFEDVPFHSGYAHSQSLDRLMNPLIDQYLYYLSTTN-TPSGTTTQSRLQFSQAGASDIRD 472
hu.53           TFEDVPFHSSYAHSQSLDRLMNPLIDQYLYYLNRTQ-TASGTQ-QSRLLFSQAGPTSMSL 471
                 **.***** :* **.* :* ***:****: :  *             *

                          |         |         |         |         |         |
AAV1            QPKNWLPGPCYRQQRVSKTKTDNNNSNF-----TWTGASKYNLNGRESIINPGTAMASHK 528
AAV2            QSRNWLPGPCYRQQRVSKTSADNNNSEY-----SWTGATKYHLNGRDSLVNPGPAMASHK 527
AAV3            QARNWLPGPCYRQQRLSKTANDNNNSNF-----PWTAASKYHLNGRDSLVNPGPAMASHK 528
AAV3-3          QARNWLPGPCYRQQRLSKTANDNNNSNF-----PWTAASKYHLNGRDSLVNPGPAMASHK 528
AAV3B           QARNWLPGPCYRQQRLSKTANDNNNSNF-----PWTAASKYHLNGRDSLVNPGPAMASHK 528
AAV4            FKKNWLPGPSIKQQGFSKTANQNYKIPATGSDSLIKYETHSTLDGRWSALTPGPPMATAG 527
AAV4-4          FKKNWLPGPSIKQQGFSKTANQNYKIPATGSDSLIKYETHSTLDGRWSALTPGPPMATAG 527
AAV5            TYKNWFPGPMGRTQGWNLGSGVNRASVS-----AFATTNRMELEGASYQVPPQPNGMTNN 514
AAV6            QPKNWLPGPCYRQQRVSKTKTDNNNSNF-----TWTGASKYNLNGRESIINPGTAMASHK 528
AAV7            QAKNWLPGPCFRQQRVSKTLDQNNNSNF-----AWTGATKYHLNGRNSLVNPGVAMATHK 530
AAV8            QAKNWLPGPCYRQQRVSTTTGQNNNSNF-----AWTAGTKYHLNGRNSLANPGIAMATHK 530
AAV9            QGRNYIPGPSYRQQRVSTTVTQNNNSEF-----AWPGASSWALNGRNSLMNPGPAMASHK 528
AAV9e           QGRNYIPGPSYRQQRVSTTVTQNNNSEF-----AWPGASSWALNGRNSLMNPGPAMASHK 528
rh.10           QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
rh.20           QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
rh.39           QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
rh.73           QARNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATNK 530
rh.74v1         QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
rh.74v2         QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
hu.12           QAKNWLPGPCYRQQRLSKQANDNNNSNF-----PWTAATKYHLNGRDSLVNPGPAMASHK 527
hu.21           QSRNWLPGPCYRQQRVSKTAADNNNSDY-----SWTGATKYHLNGRDSLVNPGPAMASHK 527
hu.26           QSRNWLPGPCYRQQRVSKTAADNNNSDY-----SWTGATKYHLNGRDSLVNPGPAMASHK 527
hu.37           QAKNWLPGPCYRQQRVSTTLSQNNNSNF-----AWTGATKYHLNGRDSLVNPGVAMATHK 530
hu.51           QSRNWLPGPCYRQQRVSKTSADNNNSEY-----SWTGATKYHLNGRDSLVNPGPAMASHK 527
hu.53           QAKNWLPGPCYRQQRLSKQANDNNNSNF-----PWTGATKYYLNGRDSLVNPGPAMASHK 526
                  :*::***  : *  .     *               .   *:*      *     :
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FIG. 3 (Continued)

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                          |         |         |         |         |         |
AAV1            DDEDKFFPMSGVMIFGKESAGA---SNTALDNVMITDEEEIKATNPVATERFGTVAVNFQ 585
AAV2            DDEEKFFPQSGVLIFGKQGSEK---TNVDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQ 584
AAV3            DDEEKFFPMHGNLIFGKEGTTA---SNAELDNVMITDEEEIRTTNPVATEQYGTVANNLQ 585
AAV3-3          DDEEKFFPMHGNLIFGKEGTTA---SNAELDNVMITDEEEIRTTNPVATEQYGTVANNLQ 585
AAV3B           DDEEKFFPMHGNLIFGKEGTTA---SNAELDNVMITDEEEIRTTNPVATEQYGTVANNLQ 585
AAV4            PADSKFSN-SQLIFAGPKQNGN---TATVPGTLIFTSEEELAATNATDTDMWGNLPGGDQ 583
AAV4-4          PADSKFSN-SQLIFAGPKQNGN---TATVPGTLIFTSEEELAATNATDTDMWGNLPGGDQ 583
AAV5            LQGSNTYALENTMIFNSQPANPGTTATYLEGNMLITSESETQPVNRVAYNVGGQMATNNQ 574
AAV6            DDKDKFFPMSGVMIFGKESAGA---SNTALDNVMITDEEEIKATNPVATERFGTVAVNLQ 585
AAV7            DDEDRFFPSSGVLIFGKTGATN----KTTLENVLMTNEEEIRPTNPVATEEYGIVSSNLQ 586
AAV8            DDEERFFPSNGILIFGKQNAAR---DNADYSDVMLTSEEEIKTTNPVATEEYGIVADNLQ 587
AAV9            EGEDRFFPLSGSLIFGKQGTGR---DNVDADKVMITNEEEIKTTNPVATESYGQVATNHQ 585
AAV9e           EGEDRFFPLSGSLIFGKQGTGR---DNVDADKVMITNEEEIKTTNPVATESYGQVATNHQ 585
rh.10           DDEERFFPSSGVLMFGKQGAGK---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
rh.20           DDEERFFPSSGVLMFGKQGAGK---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
rh.39           DDEERFFPSSGVLMFGKQGAGR---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
rh.73           DDEDRFFPSSGILMFGKQGAGK---DNVDYSNVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
rh.74v1         DDEERFFPSSGVLMFGKQGAGK---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
rh.74v2         DDEERFFPSSGVLMFGKQGAGK---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
hu.12           DDEEKFFPMHGTLIFGKQGTNA---NDADLEHVMITDEEEIRTTNPVATEQYGNVSNNLQ 584
hu.21           DDEEKYFPQSGVLIFGKQDSGK---TNVDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQ 584
hu.26           DDEEKYFPQSGVLIFGKQDSGK---TNVDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQ 584
hu.37           DDEERFFPSSGVLMFGKQGAGR---DNVDYSSVMLTSEEEIKTTNPVATEQYGVVADNLQ 587
hu.51           DNEEKFFPQSGVLIFGKQGSEK---TNVDIEKVMITDEEEIRTTNPVATEQYGSVSTNLQ 584
hu.53           DDEEKFFPMHGTLIFGKEGTNA---TNAELENVMITDEEEIRTTNPVATEQYGYVSNNLQ 583
                   ..       :: .               :::*.*.*   .* .  :  * :  . *

                  |         |         |         |         |         |
AAV1            SSS#TDPATGDVHAMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKN-PPP 645
AAV2            RGN#RQAATADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 644
AAV3            SSN#TAPTTGTVNHQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 645
AAV3-3          SSN#TAPTTGTVNHQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 645
AAV3B           SSN#TAPTTRTVNDQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 645
AAV4            SNS#NLPTVDRLTALGAVPGMVWQNRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKH-PPP 643
AAV4-4          SNS#NLPTVDRLTALGAVPGMVWQNRDIYYQGPIWAKIPHTDGHFHPSPLIGGFGLKH-PPP 643
AAV5            SST#TAPATGTYNLQEIVPGSVWMERDVYLQGPIWAKIPETGAHFHPSPAMGGFGLKH-PPP 634
AAV6            SSS#TDPATGDVHVMGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 645
AAV7            AAN#TAAQTQVVNNQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 646
AAV8            QQN#TAPQIGTVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
AAV9            SAQ#AQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKH-PPP 645
AAV9e           SDG#AQAQTGWVQNQGILPGMVWQDRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGMKH-PPP 645
AAVrh10         QQN#AAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
AAVrh20         QQN#AAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
rh.39           QTN#TGPIVGNVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
rh.73           RQN#TAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
rh.74v1         QQN#AAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
rh.74v2         QQN#AAPIVGAVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
hu.12           NSN#TGPTTENVNHQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 644
hu.21           SGN#TQAATSDVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 644
hu.26           SGN#TQAATSDVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 644
hu.37           QTN#TGPIVGNVNSQGALPGMVWQNRDVYLQGPIWAKIPHTDGNFHPSPLMGGFGLKH-PPP 647
hu.51           RGN#RQAATADVNTQGVLPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKHHPPP 645
hu.53           NSN#TAASTETVNHQGALPGMVWQDRDVYLQGPIWAKIPHTDGHFHPSPLMGGFGLKH-PPP 644
                          :** ** :**:* *********.*..:***** :****:*:***
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FIG. 3 (Continued)

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                          |         |         |         |         |         |
AAV1            QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENSKRWNPEVQYTSNY 705
AAV2            QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 704
AAV3            QIMIKNTPVPANPPTTFSPAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
AAV3-3          QIMIKNTPVPANPPTTFSPAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
AAV3B           QIMIKNTPVPANPPTTFSPAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
AAV4            QIFIKNTPVPANPATTFSSTPVNSFITQYSTGQVSVQIDWEIQKERSKRWNPEVQFTSNY 703
AAV4-4          QIFIKNTPVPANPATTFSSTPVNSFITQYSTGQVSVQIDWEIQKERSKRWNPEVQFTSNY 703
AAV5            MMLIKNTPVPGNI-TSFSDVPVSSFITQYSTGQVTVEMEWELKKENSKRWNPEIQYTNNY 693
AAV6            QILIKNTPVPANPPAEFSATKFASFITQYSTGQVSVEIEWELQKENSKRWNPEVQYTSNY 705
AAV7            QILIKNTPVPANPPEVFTPAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNF 706
AAV8            QILIKNTPVPADPPTTFNQSKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
AAV9            QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
AAV9e           QILIKNTPVPADPPTAFNKDKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
rh.10           QILIKNTPVPADPPTTFSQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
rh.20           QILIKNTPVPADPPTTFSQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
rh.39           QILIKNTPVPADPPTTFSQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
rh.73           QILIKNTPVPADPPTAFNQAKLNSFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
rh.74v1         QILIKNTPVPADPPTTFTKAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
rh.74v2         QILIKNTPVPADPPTTFNQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
hu.12           QIMIKNTPVPANPPTNFSSAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 704
rh.21           QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 704
hu.26           QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 704
hu.37           QILIKNTPVPADPPTTFSQAKLASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 707
hu.51           QILIKNTPVPANPSTTFSAAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 705
hu.53           QIMIKNTPVPANPPTNFSSAKFASFITQYSTGQVSVEIEWELQKENSKRWNPEIQYTSNY 704
                 ::*******.:    *.   . ***********:*:::**::**.*******:*:*.*:

                          |         |         |
AAV1            AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO: 250)
AAV2            NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 735 (SEQ ID NO: 251)
AAV3            NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 252)
AAV3-3          NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 253)
AAV3B           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 254)
AAV4            GQQNSLLWAPDAAGKYTEPRAIGTRYLTHHL 734 (SEQ ID NO: 255)
AAV4-4          GQQNSLLWAPDAAGKYTEPRAIGTRYLTHHL 734 (SEQ ID NO: 256)
AAV5            NDPQFVDFAPDSTGEYRTTRPIGTRYLTRPL 724 (SEQ ID NO: 257)
AAV6            AKSANVDFTVDNNGLYTEPRPIGTRYLTRPL 736 (SEQ ID NO: 258)
AAV7            EKQTGVDFAVDSQGVYSEPRPIGTRYLTRNL 737 (SEQ ID NO: 259)
AAV8            YKSTSVDFAVNTEGVYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 260)
AAV9            YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 261)
AAV9e           YKSNNVEFAVNTEGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 262)
rh.10           YKSTNVDFAVNTDGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 263)
rh.20           YKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 264)
rh.39           YKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 265)
rh.73           YKSTNVDFAVNTEGVYSEPRPIGTRYLTRNL 739 (SEQ ID NO: 266)
rh.74v1         YKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 267)
rh.74v2         YKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 268)
hu.12           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 735( SEQ ID NO: 269)
hu.21           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 735 (SEQ ID NO: 270)
hu.26           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 735 (SEQ ID NO: 271)
hu.37           YKSTNVDFAVNTEGTYSEPRPIGTRYLTRNL 738 (SEQ ID NO: 272)
hu.51           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 736 (SEQ ID NO: 273)
hu.53           NKSVNVDFTVDTNGVYSEPRPIGTRYLTRNL 737 (SEQ ID NO: 274)
                 .   : :: :  * *   * *******: *
```

FIG. 4

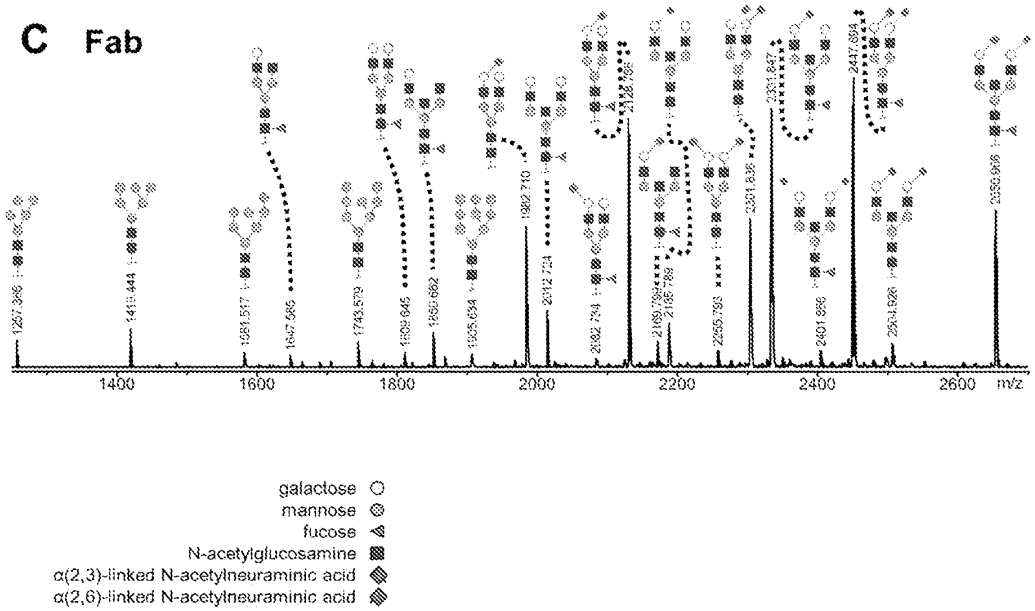

C Fab
1400
1600
1800
2000
2200
2400
2600
m/z
galactose
mannose
fucose
N-acetylglucosamine
α(2,3)-linked N-acetylneuraminic acid
α(2,6)-linked N-acetylneuraminic acid

FIG. 5

```
IgG1   EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK     274
IgG2   E---RKCCVECPPCPAPPV-AGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQ     274
IgG4   E---SKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQ     274
       *    :    ** **** . .*****************************:*****:

IgG1   FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK    334
IgG2   FNWYVDGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEK    334
IgG4   FNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEK    334
       ********************:***:********:****************.**: ***
IgG1   TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT    394
IgG2   TISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDISVEWESNGQPENNYKTT    394
IgG4   TISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT    394
       ****:***************::*:******************:****************

IgG1   PPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK  447 (SEQ ID NO: 192)
IgG2   PPMLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK  447 (SEQ ID NO: 193)
IgG4   PPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK  447 (SEQ ID NO: 194)
       **:***********:*********:************************:**
```

FIGS. 6A-B

FIG. 6A

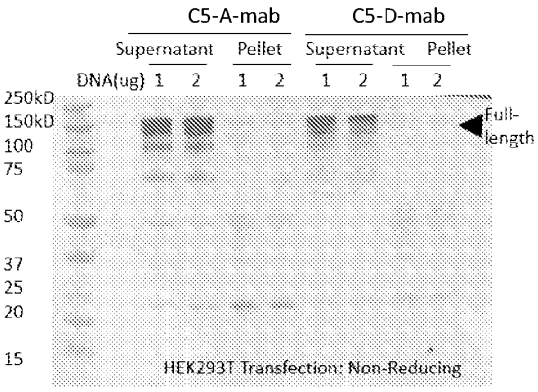
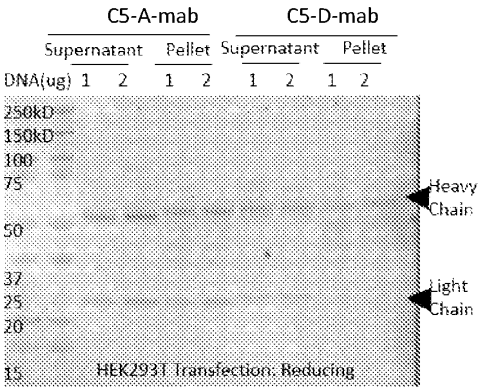


FIG. 6B



- The pellet samples were loaded 2.5x more to the supernatant samples.

FIG. 7A

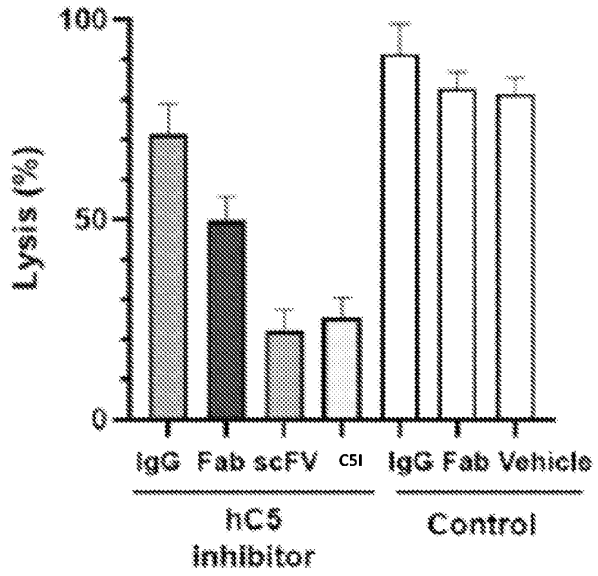

100
50
0
Lysis (%)
IgG
Fab
scFV
C5I
IgG
Fab
Vehicle
hC5 inhibitor
Control

FIG. 7B.

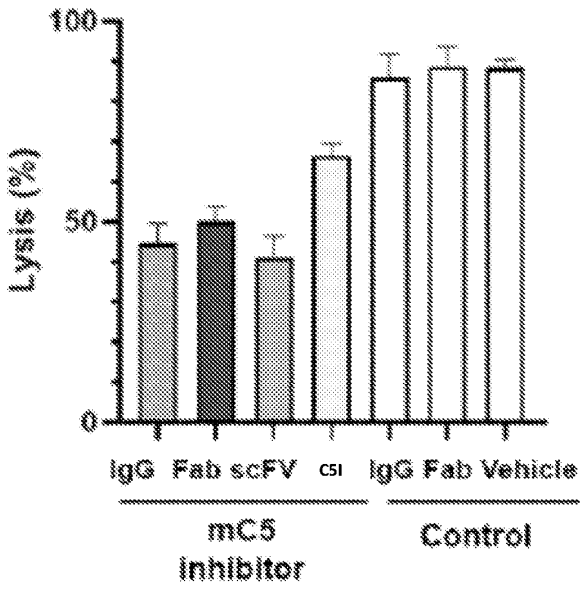
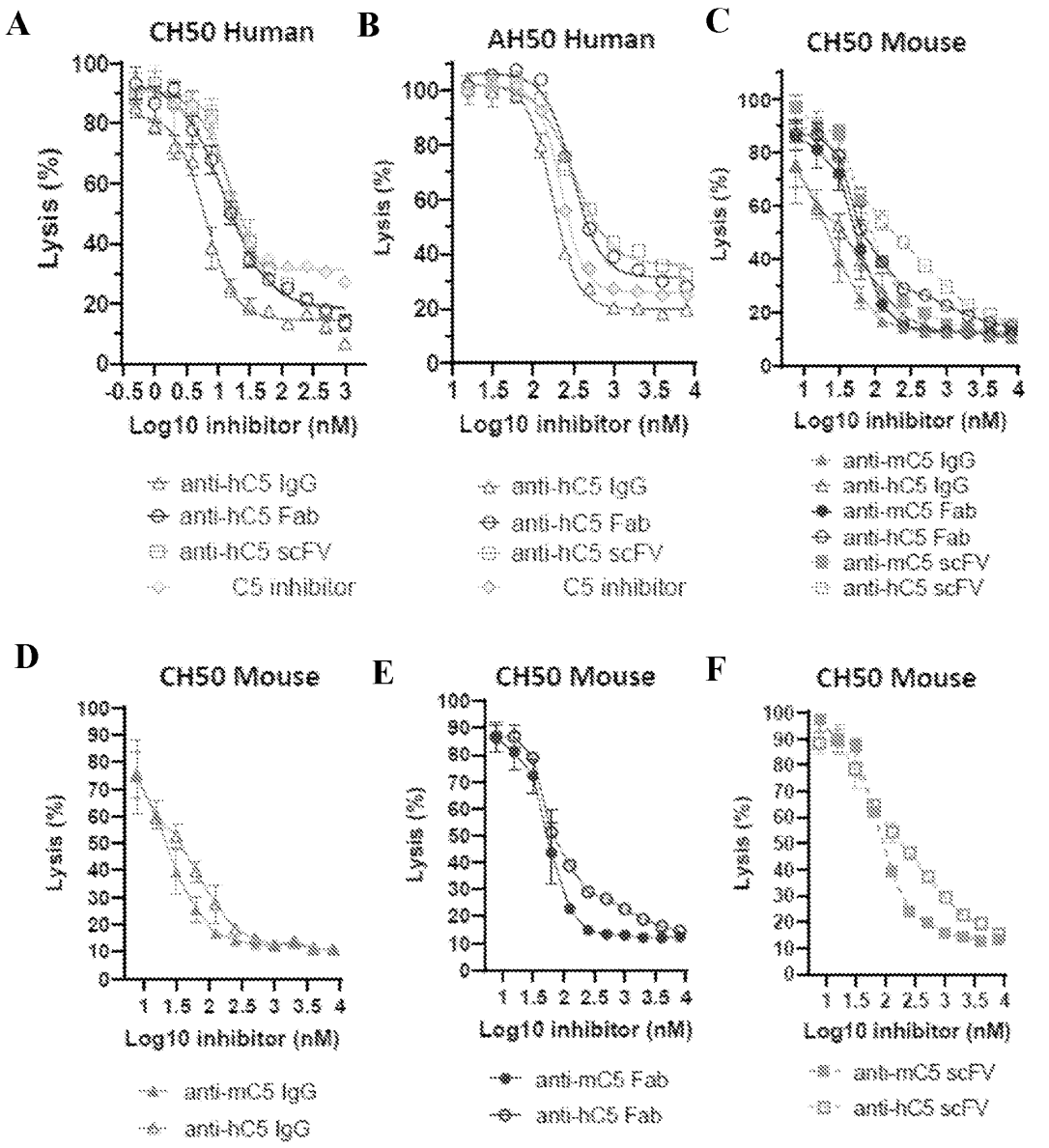
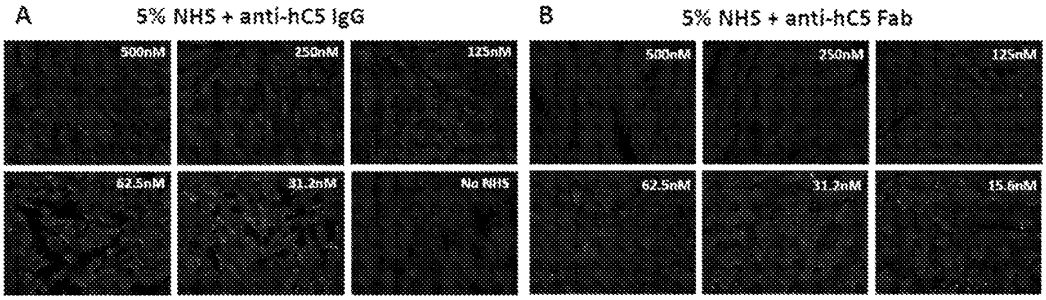
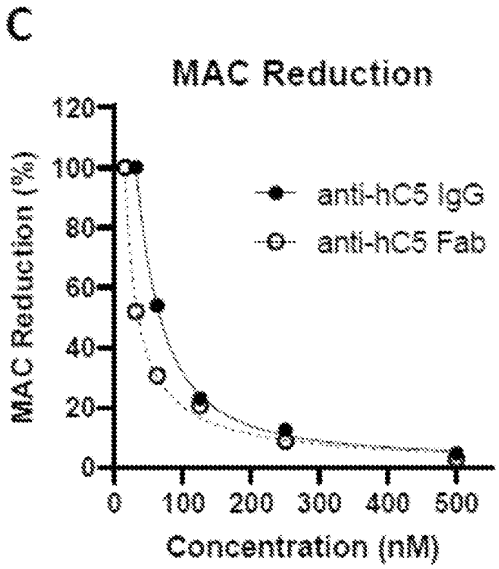

100
50
0
Lysis (%)
IgG
Fab
scFV
C5I
IgG
Fab
Vehicle
mC5
inhibitor
Control

FIG. 8A-8F


A
CH50 Human
Lysis (%)
Log10 inhibitor (nM)
anti-hC5 IgG
anti-hC5 Fab
anti-hC5 scFV
C5 inhibitor
B
AH50 Human
Lysis (%)
Log10 inhibitor (nM)
anti-hC5 IgG
anti-hC5 Fab
anti-hC5 scFV
C5 inhibitor
C
CH50 Mouse
Lysis (%)
Log10 inhibitor (nM)
anti-mC5 IgG
anti-hC5 IgG
anti-mC5 Fab
anti-hC5 Fab
anti-mC5 scFV
anti-hC5 scFV
D
CH50 Mouse
Lysis (%)
Log10 inhibitor (nM)
anti-mC5 IgG
anti-hC5 IgG
E
CH50 Mouse
Lysis (%)
Log10 inhibitor (nM)
anti-mC5 Fab
anti-hC5 Fab
F
CH50 Mouse
Lysis (%)
Log10 inhibitor (nM)
anti-mC5 scFV
anti-hC5 scFV

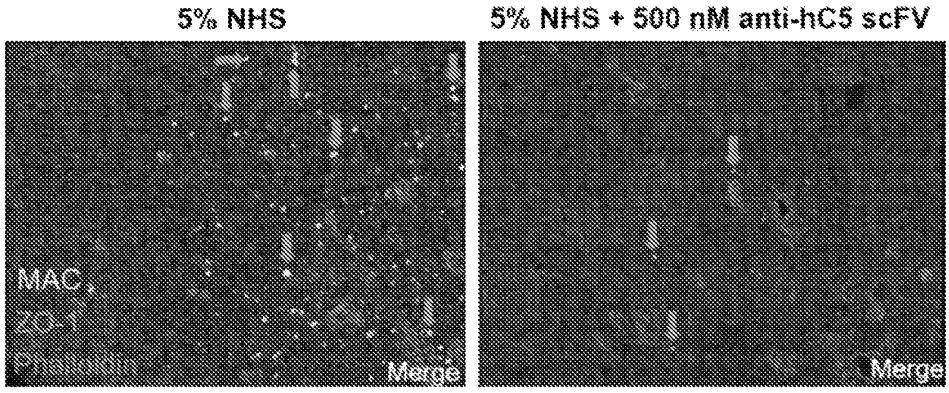
FIGS. 9A-9C


A
5% NHS + anti-hC5 IgG
500nM
250nM
125nM
62.5nM
31.2nM
No NHS
B
5% NHS + anti-hC5 Fab
500nM
250nM
125nM
62.5nM
31.2nM
15.6nM

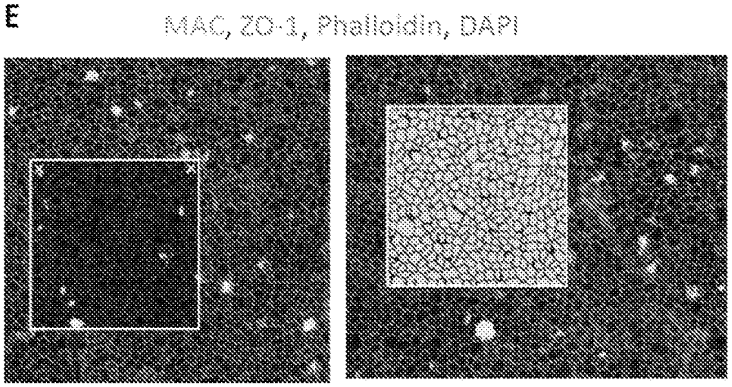

C
MAC Reduction
MAC Reduction (%)
120
100
80
60
40
20
0
0
100
200
300
400
500
Concentration (nM)
anti-hC5 IgG
anti-hC5 Fab

FIGS. 9D-9F

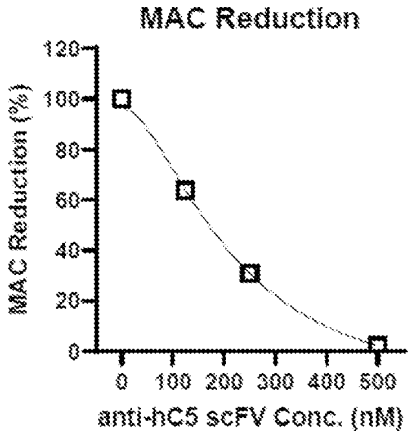
D



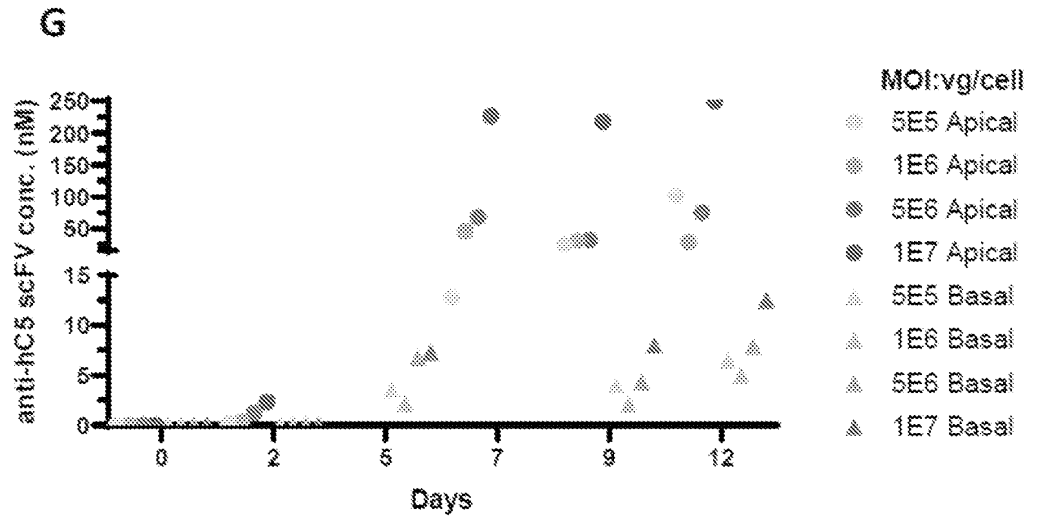
E

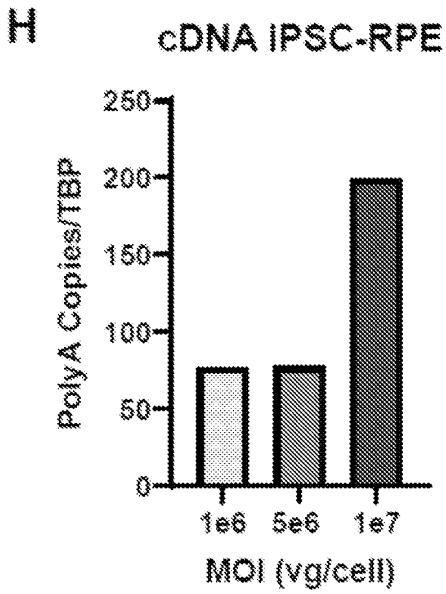


F



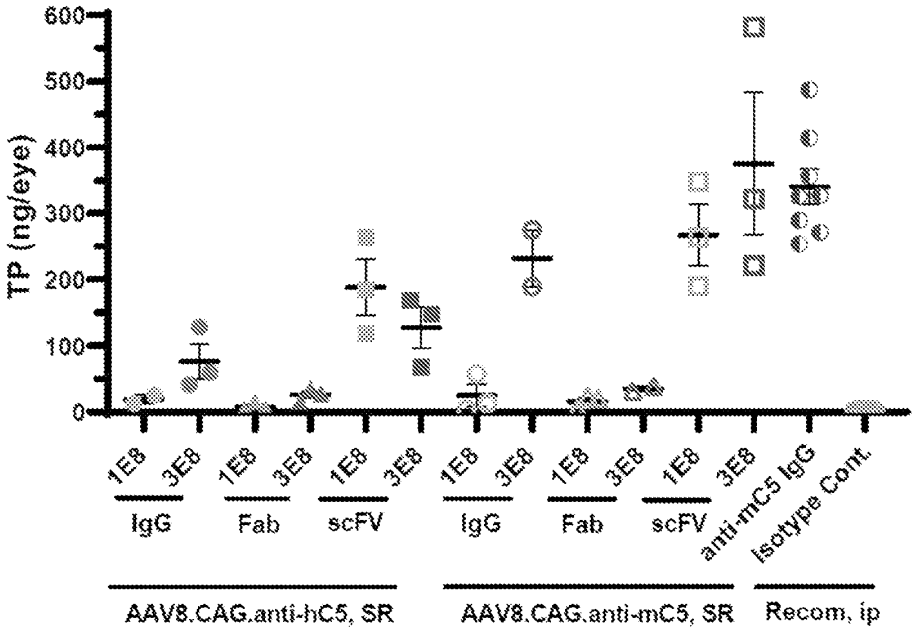
FIGS. 9G-9H


G
anti-hC5 scFV conc. (nM)
250
200
150
100
50
15
10
5
0
0
2
5
7
9
12
Days
MOI:vg/cell
5E5 Apical
1E6 Apical
5E6 Apical
1E7 Apical
5E5 Basal
1E6 Basal
5E6 Basal
1E7 Basal

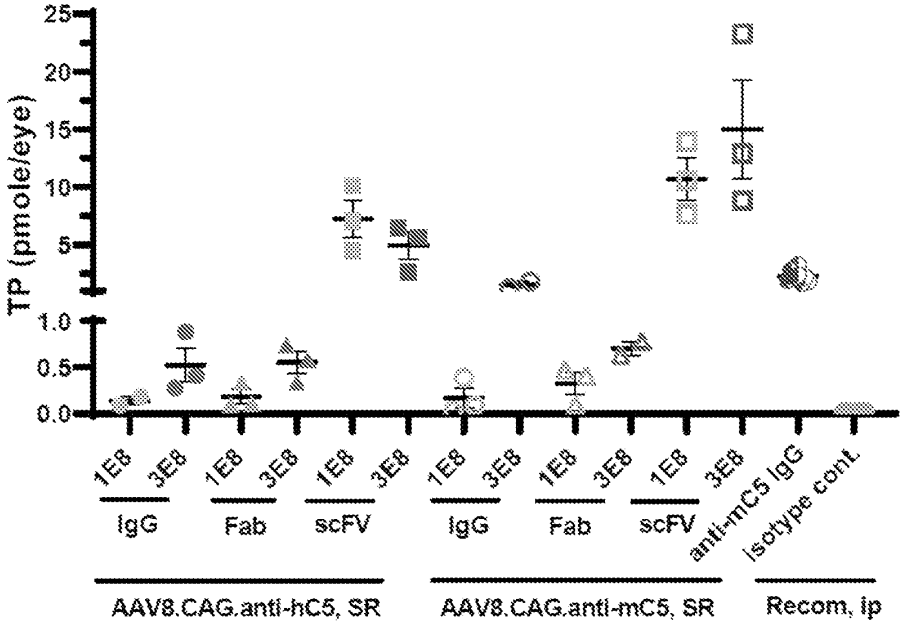

H
cDNA iPSC-RPE
PolyA Copies/TBP
250
200
150
100
50
0
1e6
5e6
1e7
MOI (vg/cell)

FIGS. 10A-10B

A.

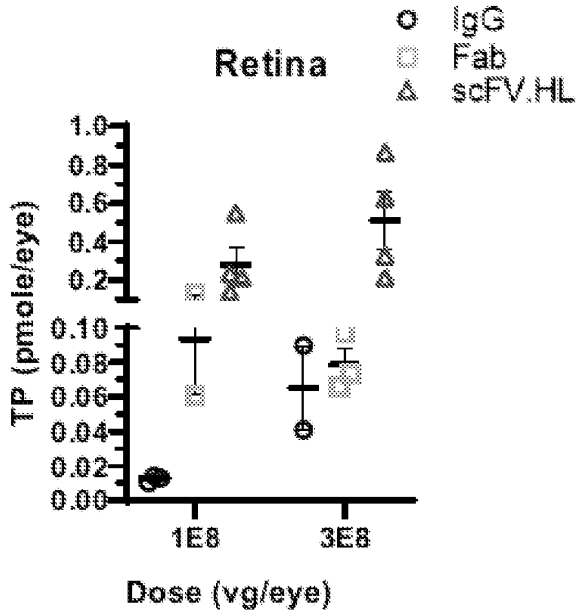


B.



FIGS. 10C-10D

C.



D.

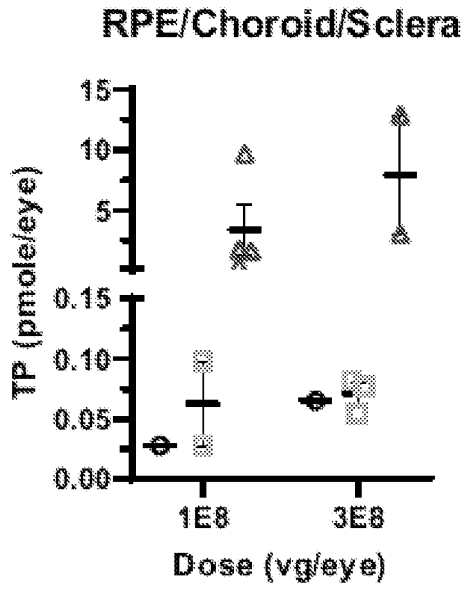


FIG. 11

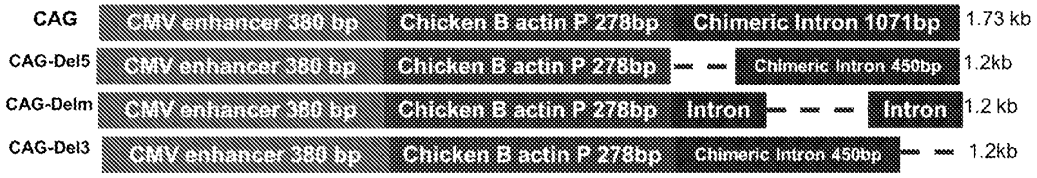
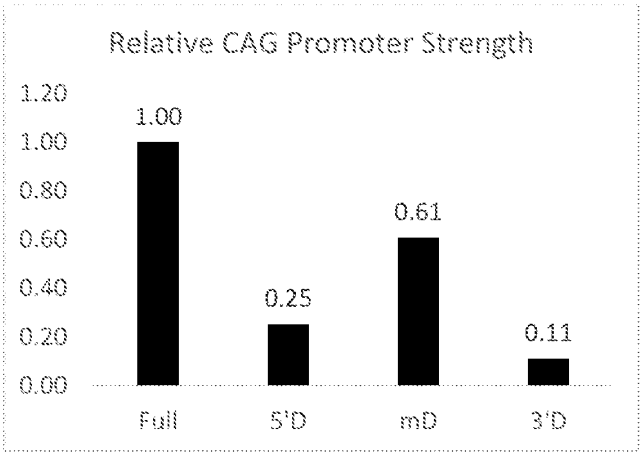
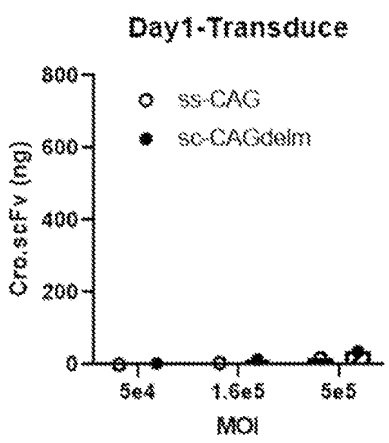

CAG
CMV enhancer 380 bp
Chicken B actin P 278bp
Chimeric Intron 1071bp
1.73 kb
CAG-Del5
CMV enhancer 380 bp
Chicken B actin P 278bp
Chimeric Intron 450bp
1.2kb
CAG-Delm
CMV enhancer 380 bp
Chicken B actin P 278bp
Intron
Intron
1.2 kb
CAG-Del3
CMV enhancer 380 bp
Chicken B actin P 278bp
Chimeric Intron 450bp
1.2kb

FIG. 12

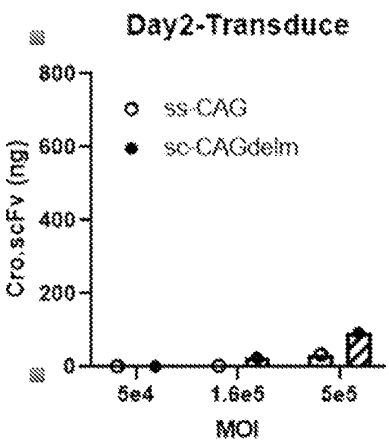

Relative CAG Promoter Strength
1.20
1.00
0.80
0.60
0.40
0.20
0.00
1.00
0.25
0.61
0.11
Full
5'D
mD
3'D

FIGs. 13A-D

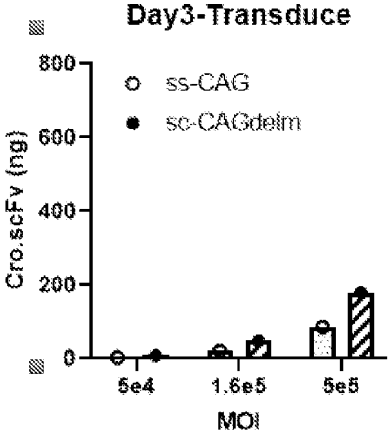
A



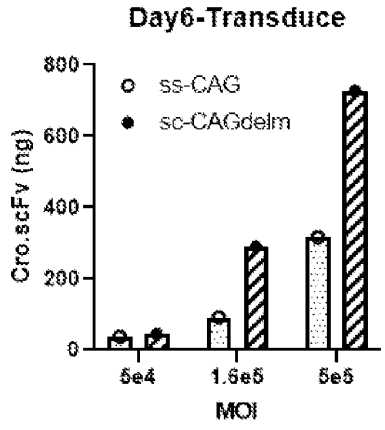
B



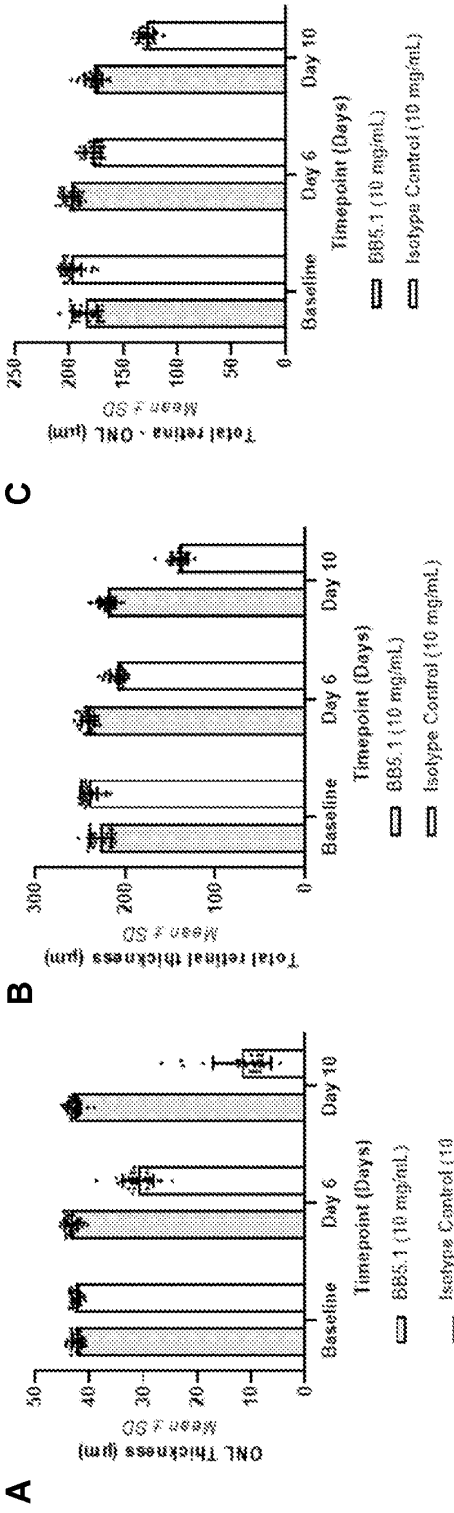
C



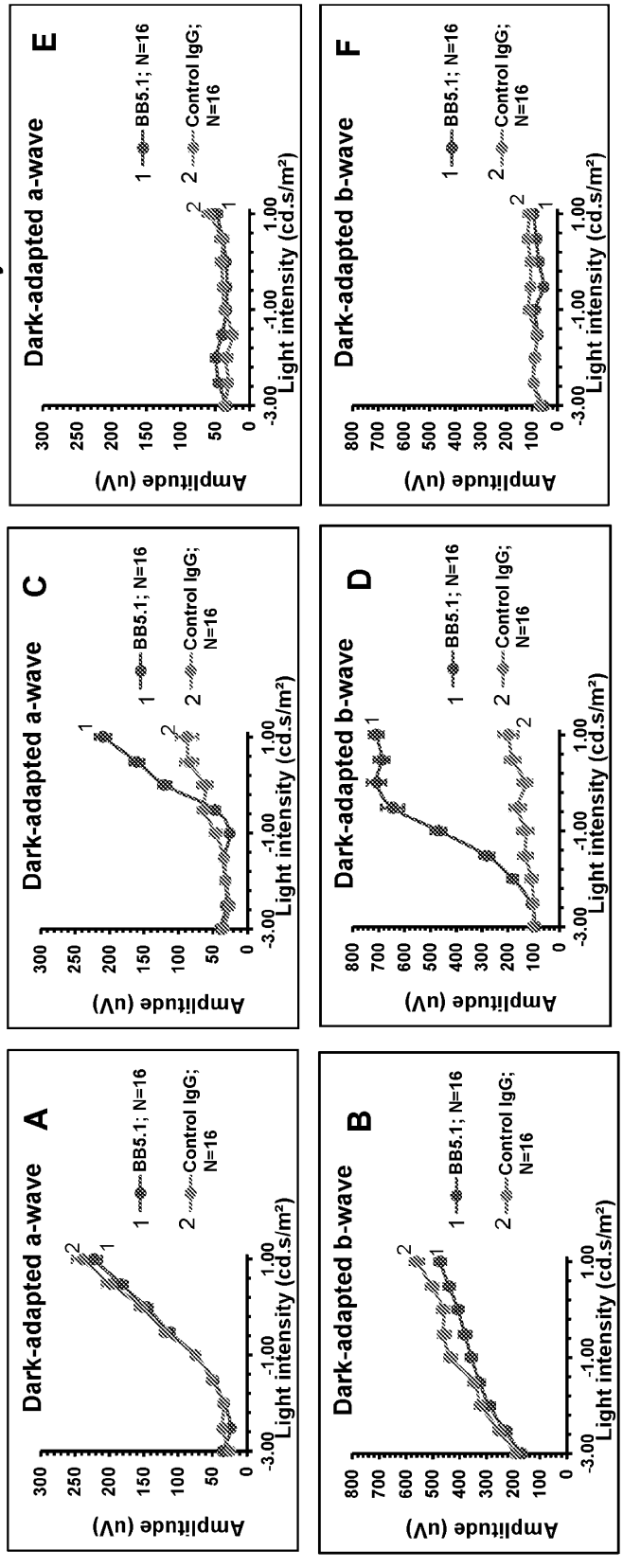
D



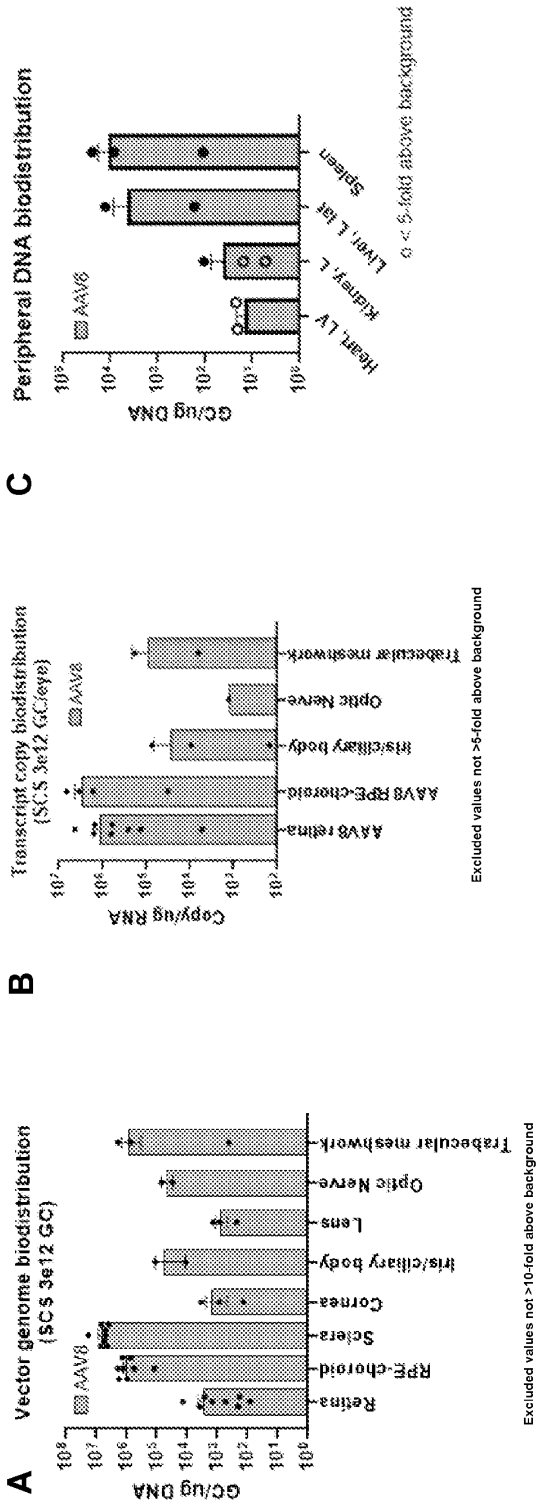
FIGS. 14A-14C


A
ONL Thickness (µm)
Mean ± SD
Timepoint (Days)
Baseline
Day 6
Day 10
BB5.1 (10 mg/mL)
Isotype Control (10 mg/mL)
B
Total retinal thickness (µm)
Mean ± SD
C
Total retina - ONL (µm)
Mean ± SD

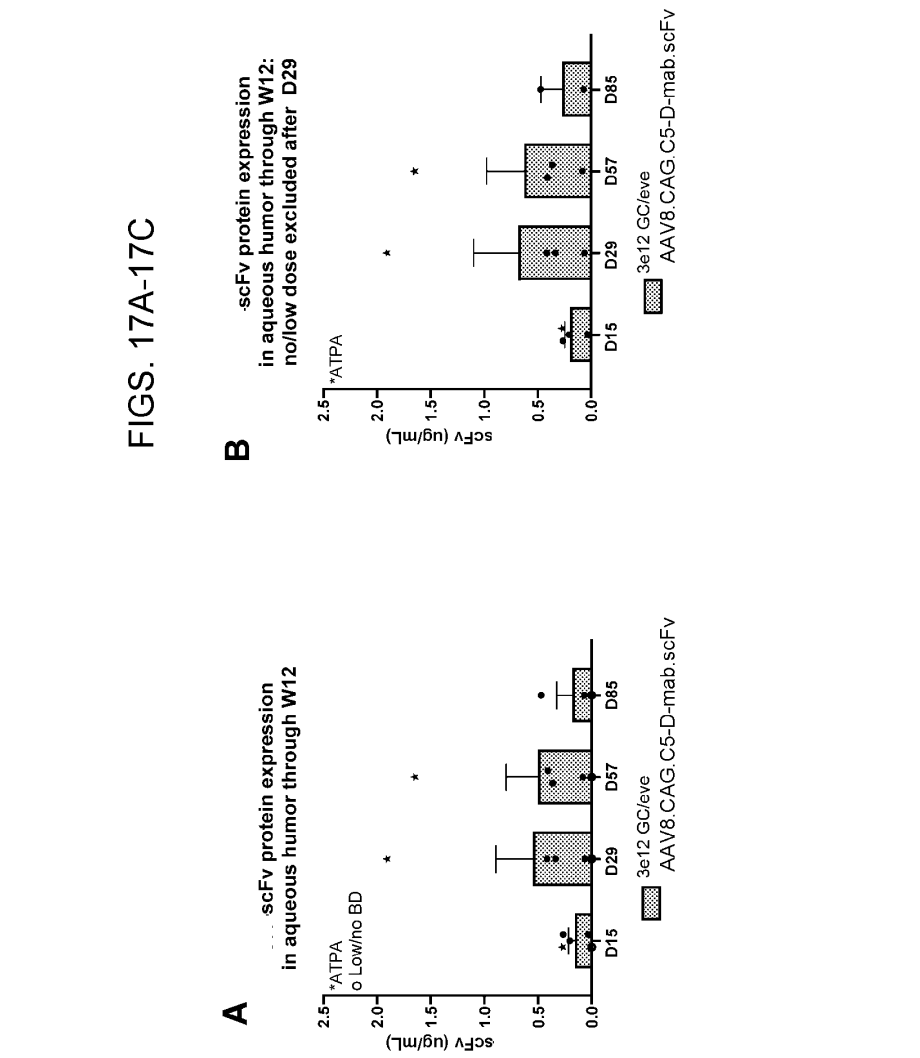
FIGS. 15A-15F


Baseline
Day 6
Day 10
Dark-adapted a-wave
Dark-adapted b-wave
A
B
C
D
E
F
Amplitude (uV)
Light intensity (cd.s/m²)
1 BB5.1; N=16
2 Control IgG; N=16

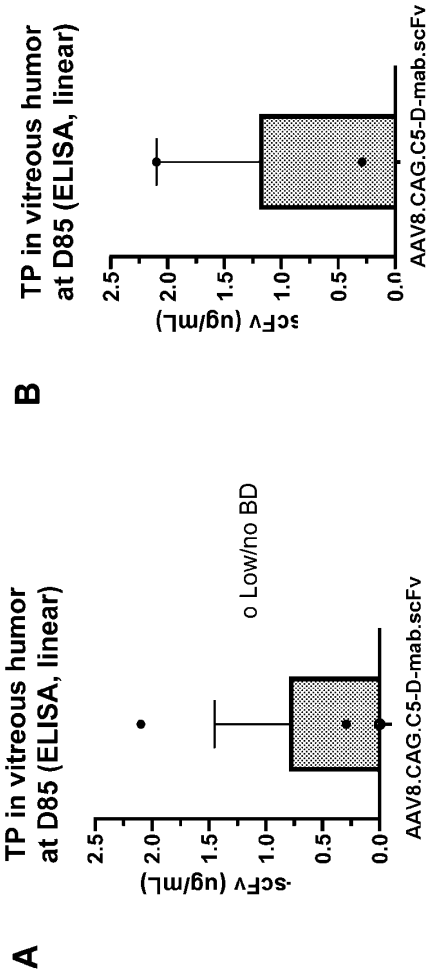
FIGS. 16A-16C


A
Vector genome biodistribution
(SCS 3e12 GC)
AAV8
GC/ug DNA
Retina
RPE-choroid
Sclera
Cornea
Iris/ciliary body
Lens
Optic Nerve
Trabecular meshwork
Excluded values not >10-fold above background
B
Transcript copy biodistribution
(SCS 3e12 GC/eye)
AAV8
Copy/ug RNA
AAV8 retina
AAV8 RPE-choroid
Iris/ciliary body
Optic Nerve
Trabecular meshwork
Excluded values not >5-fold above background
C
Peripheral DNA biodistribution
AAV6
GC/ug DNA
Heart, LV
Kidney, L
Liver, L lat
Spleen
o < 5-fold above background

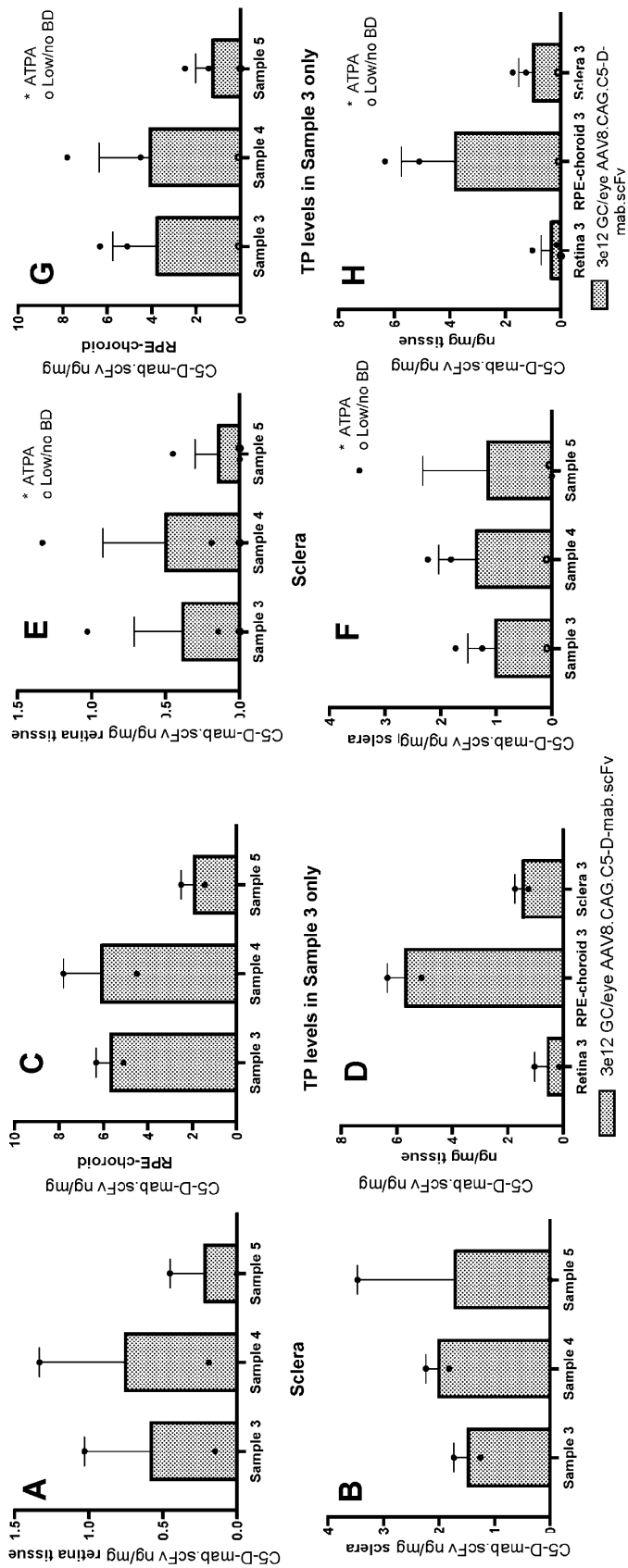
FIGS. 17A-17C


A
scFv protein expression
in aqueous humor through W12
*ATPA
o Low/no BD
scFv (ug/mL)
2.5
2.0
1.5
1.0
0.5
0.0
D15
D29
D57
D85
3e12 GC/eve
AAV8.CAG.C5-D-mab.scFv
B
scFv protein expression
in aqueous humor through W12:
no/low dose excluded after D29
*ATPA
scFv (ug/mL)
2.5
2.0
1.5
1.0
0.5
0.0
D15
D29
D57
D85
3e12 GC/eve
AAV8.CAG.C5-D-mab.scFv
C
Aqueous Humor aC5-scFv levels,
individual animal timecourses:
AAV8
scFv (ug/mL)
2.5
2.0
1.5
1.0
0.5
0.0
D15
D29
D57
D85
Study Day
P0001 AHL#
P0001 AHR*#
P0002 AHL
P0002 AHR
P0003 AHL^
P0003 AHR
AAV8
* low/no BD
# High ATPA
^ not dosed

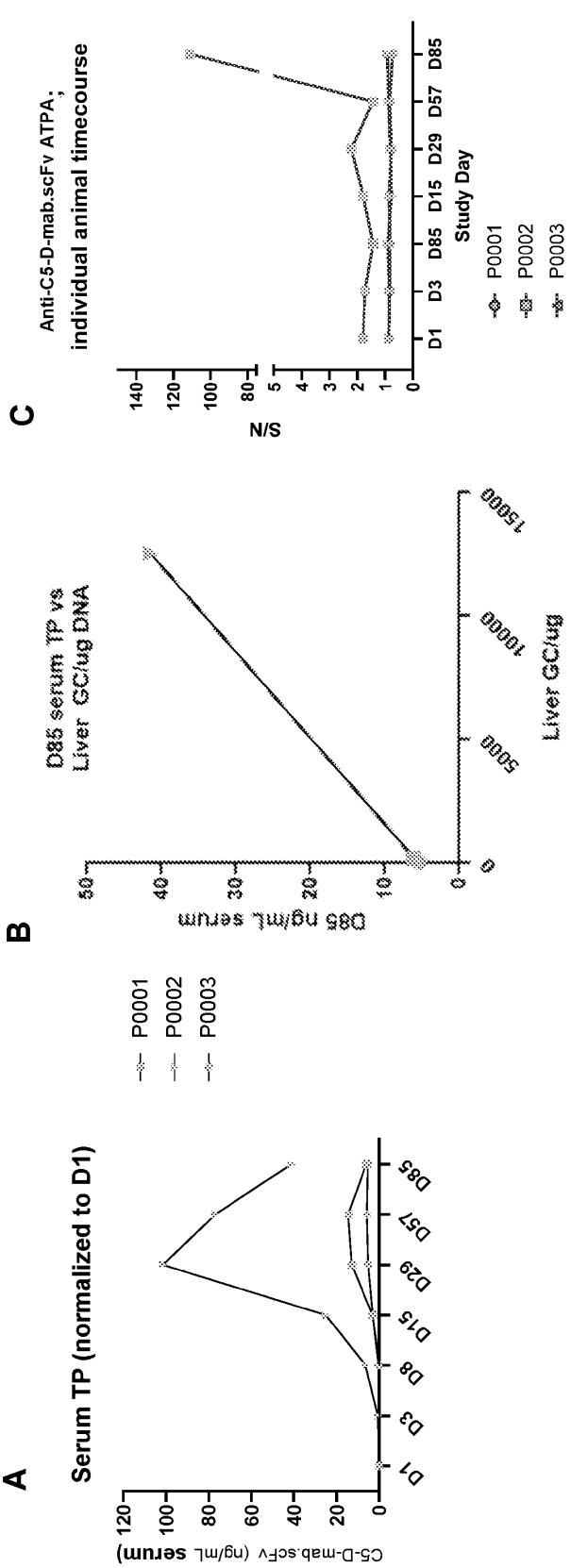
FIGS. 18A-18B


A
TP in vitreous humor
at D85 (ELISA, linear)
-scFv (ug/mL)
2.5
2.0
1.5
1.0
0.5
0.0
o Low/no BD
AAV8.CAG.C5-D-mab.scFv
B
TP in vitreous humor
at D85 (ELISA, linear)
scFv (ug/mL)
2.5
2.0
1.5
1.0
0.5
0.0
AAV8.CAG.C5-D-mab.scFv

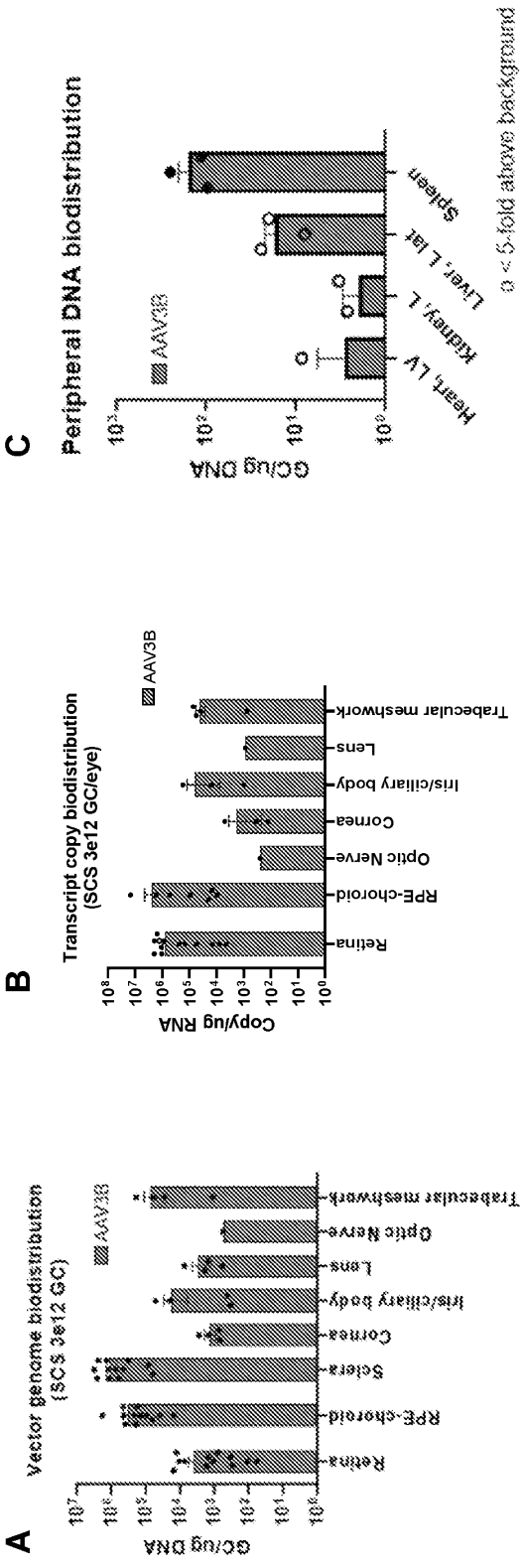
FIGS. 19A-19H


A
Retina
C5-D-mab.scFv ng/mg retina tissue
Sample 3
Sample 4
Sample 5
B
Sclera
C5-D-mab.scFv ng/mg sclera
C
RPE-choroid
C5-D-mab.scFv ng/mg RPE-choroid
D
TP levels in Sample 3 only
C5-D-mab.scFv ng/mg ng/mg tissue
Retina 3
RPE-choroid 3
Sclera 3
3e12 GC/eye AAV8.CAG.C5-D-mab.scFv
E
Retina
C5-D-mab.scFv ng/mg retina tissue
* ATPA
o Low/no BD
F
Sclera
C5-D-mab.scFv ng/mg sclera
G
RPE-choroid
C5-D-mab.scFv ng/mg RPE-choroid
H
TP levels in Sample 3 only
C5-D-mab.scFv ng/mg ng/mg tissue

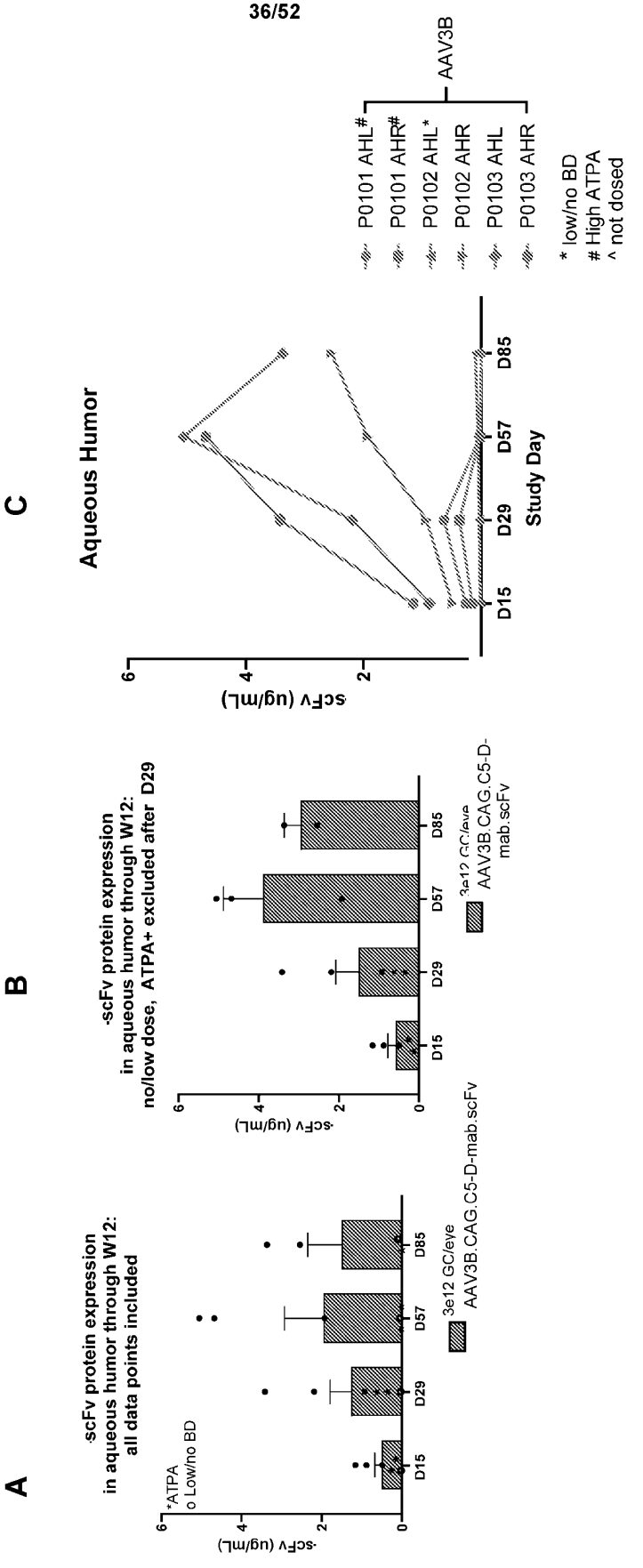
FIGS. 20A-20C


A
Serum TP (normalized to D1)
C5-D-mab.scFv (ng/mL serum)
120
100
80
60
40
20
0
D1
D3
D8
D15
D29
D57
D85
P0001
P0002
P0003
B
D85 serum TP vs
Liver GC/ug DNA
D85 ng/mL serum
50
40
30
20
10
0
0
5000
10000
15000
Liver GC/ug
C
Anti-C5-D-mab.scFv ATPA;
individual animal timecourse
N/S
140
120
100
80
5
4
3
2
1
0
D1
D3
D85
D15
D29
D57
D85
Study Day
P0001
P0002
P0003

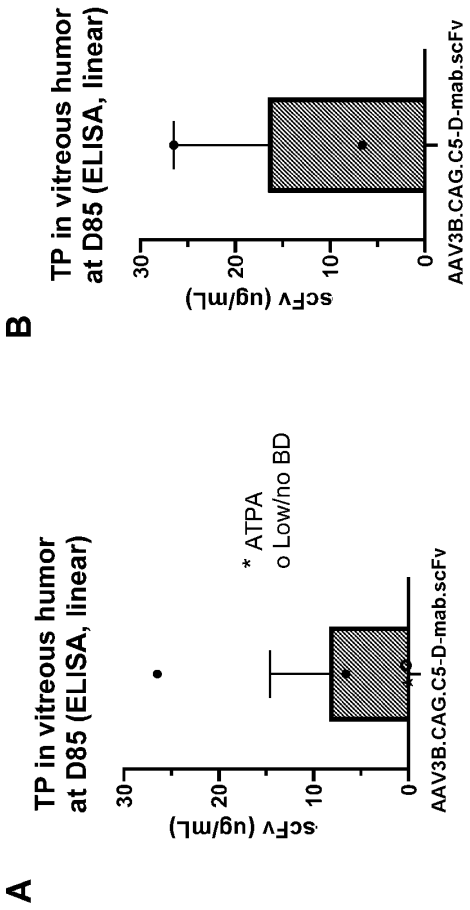
FIGS. 21A-21C


A
Vector genome biodistribution
(SCS 3e12 GC)
AAV3B
GC/ug DNA
Retina
RPE-choroid
Sclera
Cornea
Iris/ciliary body
Lens
Optic Nerve
Trabecular meshwork
Excluded values not >10-fold above background
B
Transcript copy biodistribution
(SCS 3e12 GC/eye)
AAV3B
Copy/ug RNA
Retina
RPE-choroid
Optic Nerve
Cornea
Iris/ciliary body
Lens
Trabecular meshwork
C
Peripheral DNA biodistribution
AAV3B
GC/ug DNA
Heart, LV
Kidney, L
Liver, L lat
Spleen
o < 5-fold above background

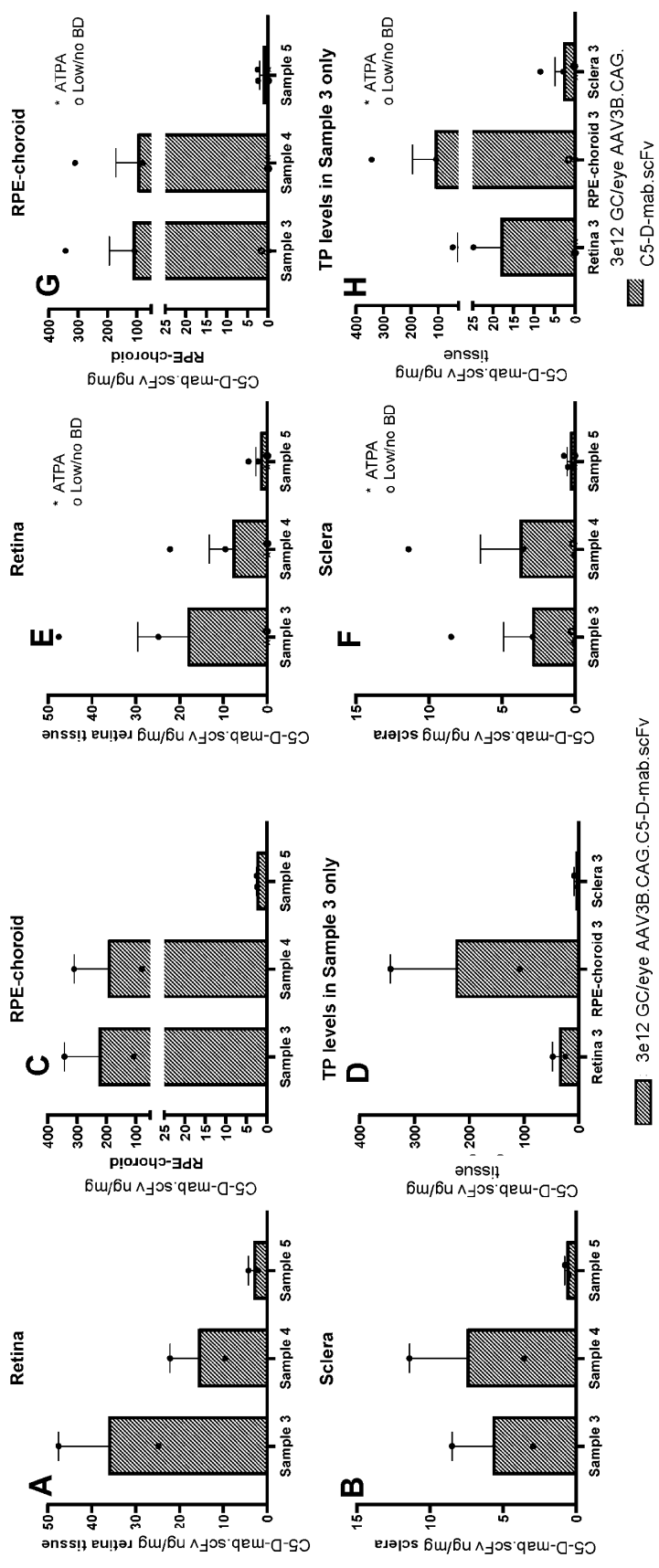
FIGS. 22A-22C


A
-scFv protein expression
in aqueous humor through W12:
all data points included
*ATPA
o Low/no BD
-scFv (ug/mL)
D15
D29
D57
D85
3e12 GC/eye
AAV3B.CAG.C5-D-mab.scFv
B
-scFv protein expression
in aqueous humor through W12:
no/low dose, ATPA+ excluded after D29
C
Aqueous Humor
Study Day
P0101 AHL#
P0101 AHR#
P0102 AHL*
P0102 AHR
P0103 AHL
P0103 AHR
AAV3B
* low/no BD
# High ATPA
^ not dosed

FIGS. 23A-23B


A
TP in vitreous humor
at D85 (ELISA, linear)
scFv (ug/mL)
30
20
10
0
* ATPA
o Low/no BD
AAV3B.CAG.C5-D-mab.scFv
B
TP in vitreous humor
at D85 (ELISA, linear)
scFv (ug/mL)
30
20
10
0
AAV3B.CAG.C5-D-mab.scFv

FIGS. 24A-24H


A
Retina
C5-D-mab.scFv ng/mg retina tissue
Sample 3
Sample 4
Sample 5
B
Sclera
C5-D-mab.scFv ng/mg sclera
C
RPE-choroid
C5-D-mab.scFv ng/mg RPE-choroid
D
TP levels in Sample 3 only
C5-D-mab.scFv ng/mg tissue
Retina 3
RPE-choroid 3
Sclera 3
E
Retina
C5-D-mab.scFv ng/mg retina tissue
* ATPA
o Low/no BD
F
Sclera
C5-D-mab.scFv ng/mg sclera
G
RPE-choroid
C5-D-mab.scFv ng/mg RPE-choroid
H
TP levels in Sample 3 only
C5-D-mab.scFv ng/mg tissue
3e12 GC/eye AAV3B.CAG.C5-D-mab.scFv

FIGS. 25A-25C

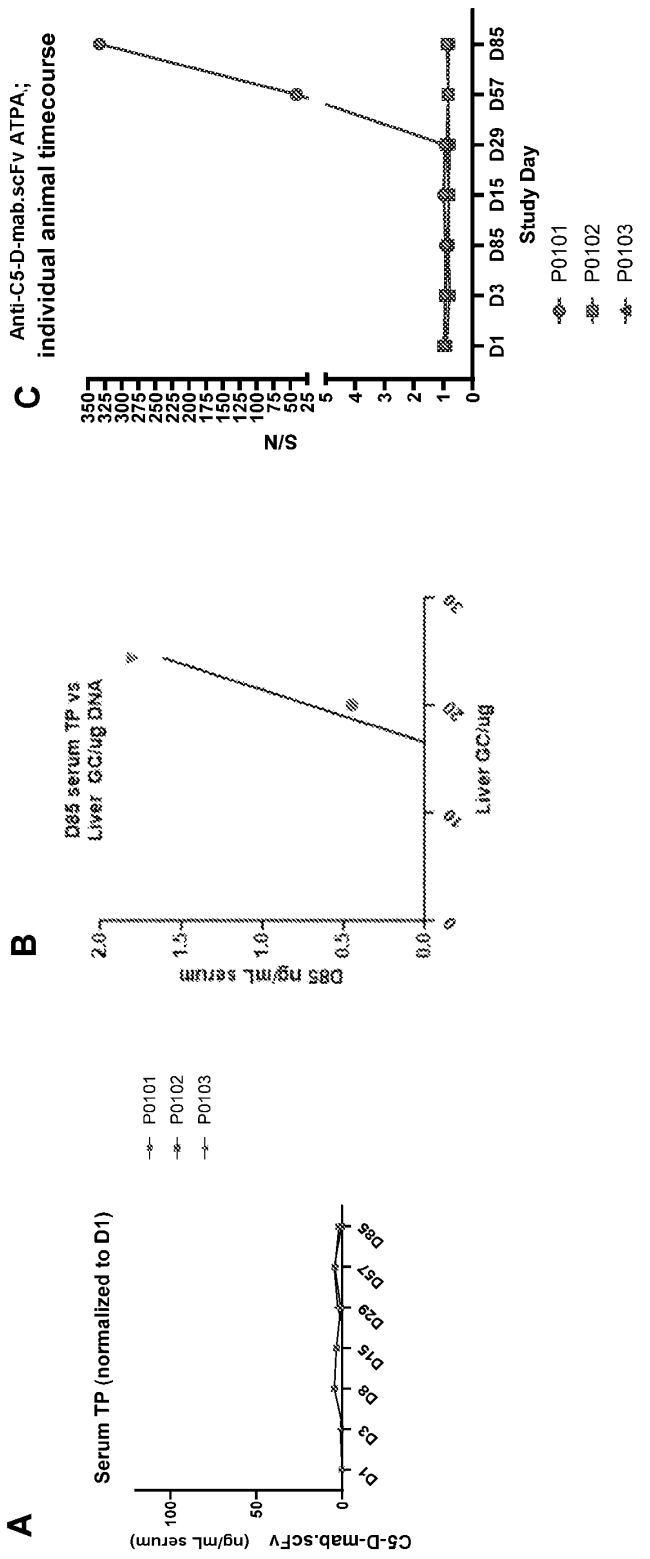
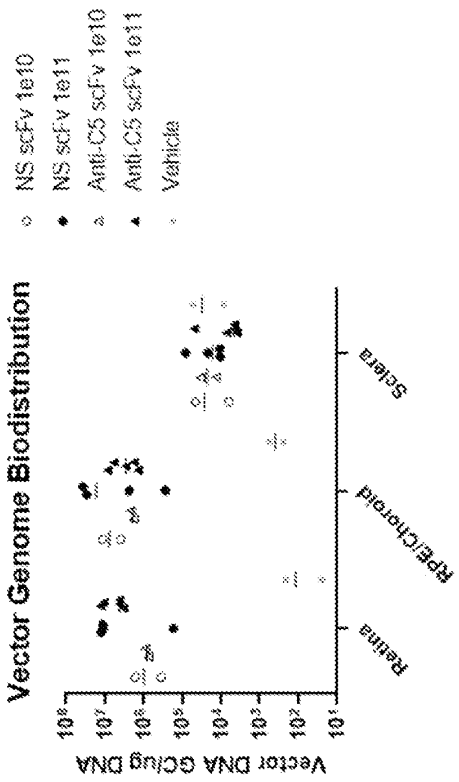
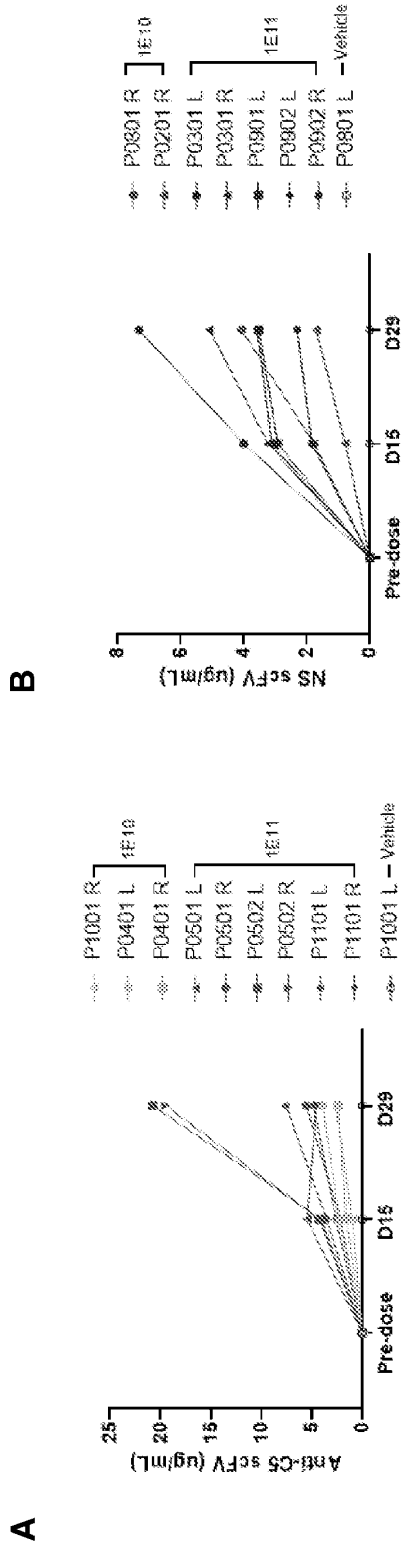

A
Serum TP (normalized to D1)
C5-D-mab.scFv (ng/mL serum)
100
50
0
D1
D3
D8
D15
D29
D57
D85
P0101
P0102
P0103
B
D85 serum TP vs
Liver GC/ug DNA
D85 ng/mL serum
2.0
1.5
1.0
0.5
0.0
0
Liver GC/ug
C
Anti-C5-D-mab.scFv ATPA;
individual animal timecourse
N/S
350
325
300
275
250
225
200
175
150
125
100
75
50
25
5
4
3
2
1
0
D1
D3
D85
D15
D29
D57
D85
Study Day
P0101
P0102
P0103

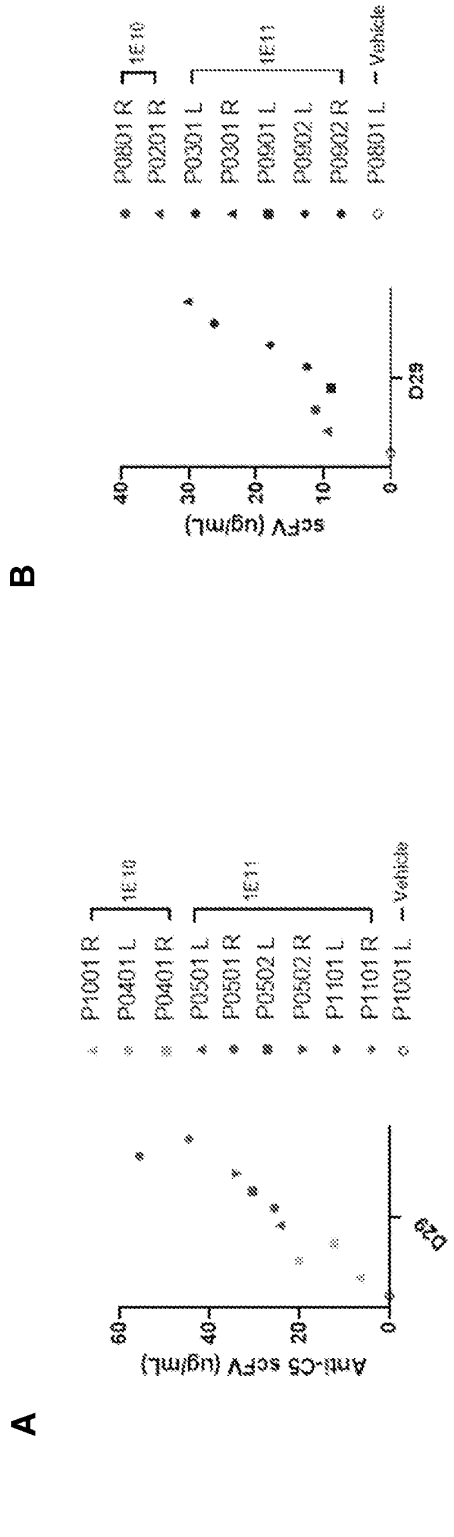
FIG. 26


Vector Genome Biodistribution
NS scFv 1e10
NS scFv 1e11
Anti-C5 scFv 1e10
Anti-C5 scFv 1e11
Vehicle
Vector DNA GC/ug DNA
Retina
RPE/Choroid
Sclera

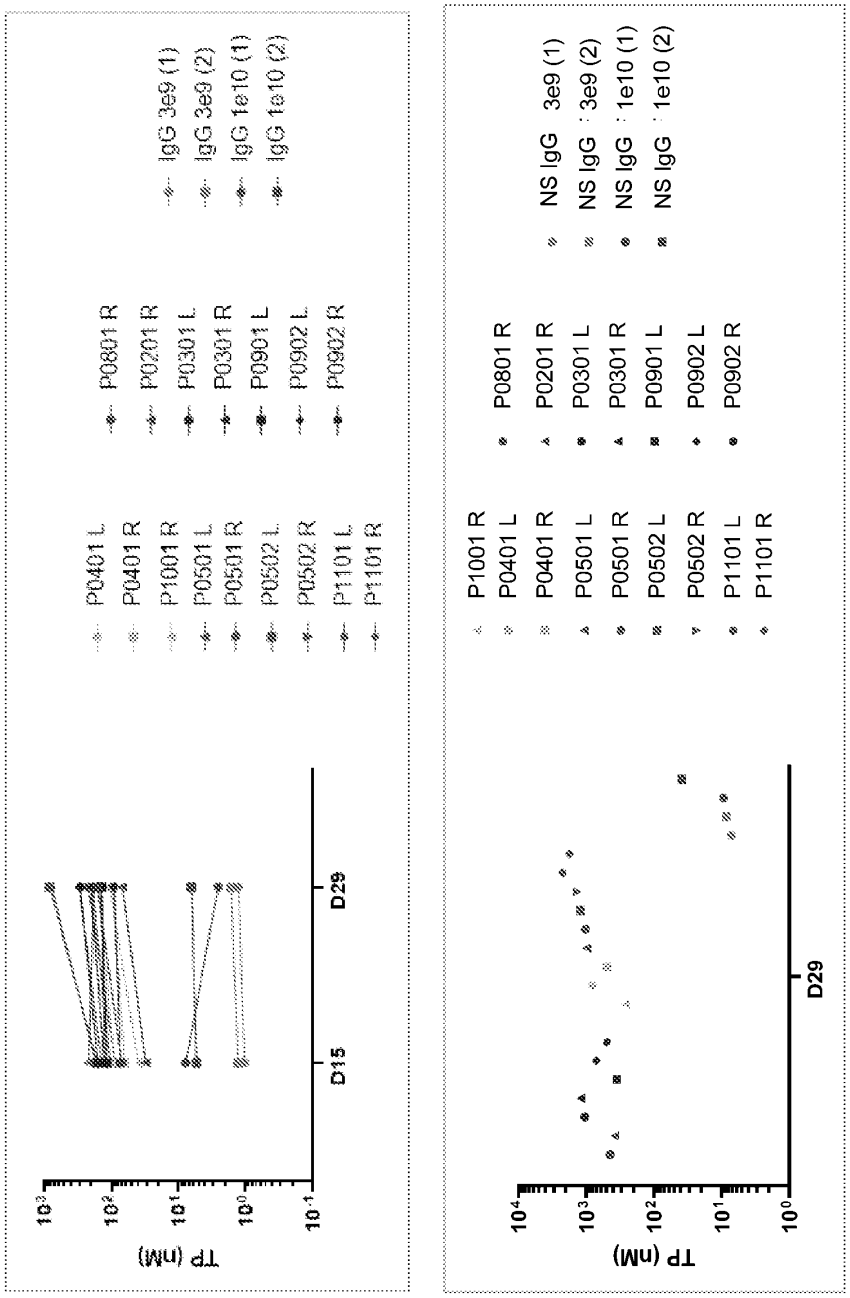
FIGS. 27A-27B


A
Anti-C5 scFV (ug/mL)
25
20
15
10
5
0
Pre-dose
D15
D29
P1001 R
P0401 L
P0401 R
1E10
P0501 L
P0501 R
P0502 L
P0502 R
P1101 L
P1101 R
1E11
P1001 L – Vehicle
B
NS scFV (ug/mL)
8
6
4
2
0
Pre-dose
D15
D29
P0301 R
P0201 R
1E10
P0301 L
P0301 R
P0901 L
P0902 L
P0902 R
1E11
P0901 L – Vehicle

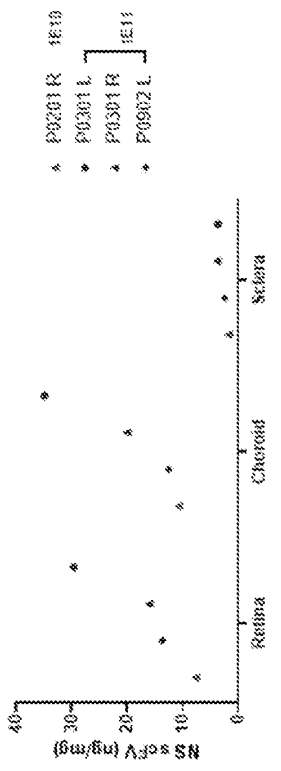
FIGS. 28A-28B

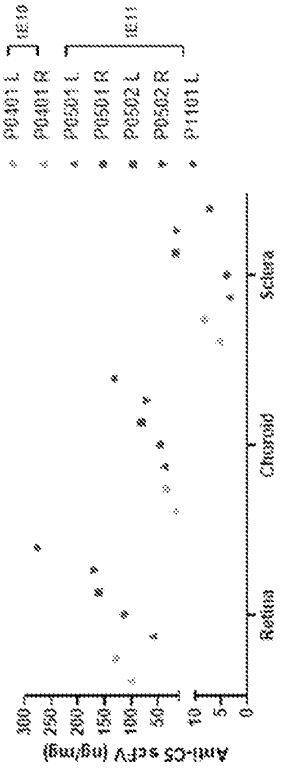

A
Anti-C5 scFV (ug/mL)
60
40
20
0
D29
P1001 R
P0401 L
P0401 R
1E10
P0501 L
P0501 R
P0502 L
P0502 R
P1101 L
P1101 R
1E11
P1001 L
Vehicle
B
scFV (ug/mL)
40
30
20
10
0
D29
P0801 R
P0201 R
1E10
P0301 L
P0301 R
P0901 L
P0902 L
P0902 R
1E11
P0801 L
Vehicle

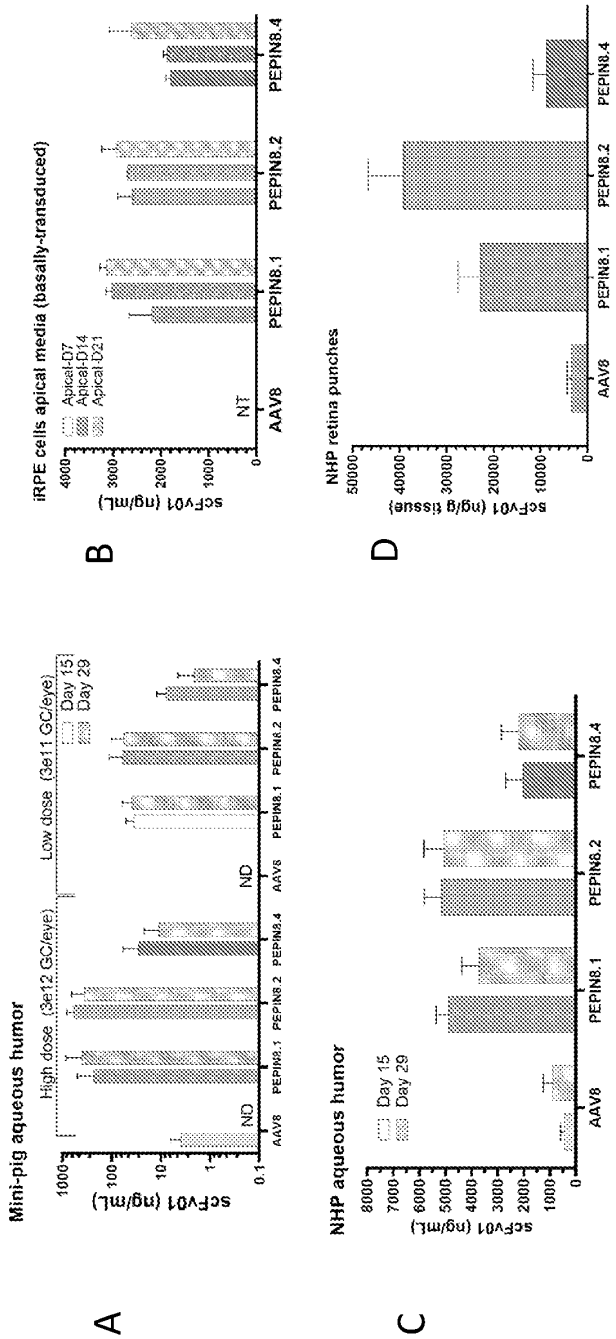
FIGS. 29A-29B


A
TP (nM)
D15
D29
P0401 L
P0401 R
P1001 R
P0501 L
P0501 R
P0502 L
P0502 R
P1101 L
P1101 R
P0801 R
P0201 R
P0301 L
P0301 R
P0901 L
P0902 L
P0902 R
IgG 3e9 (1)
IgG 3e9 (2)
IgG 1e10 (1)
IgG 1e10 (2)
B
TP (nM)
D29
P1001 R
P0401 L
P0401 R
P0501 L
P0501 R
P0502 L
P0502 R
P1101 L
P1101 R
P0801 R
P0201 R
P0301 L
P0301 R
P0901 L
P0902 L
P0902 R
NS IgG 3e9 (1)
NS IgG : 3e9 (2)
NS IgG : 1e10 (1)
NS IgG : 1e10 (2)

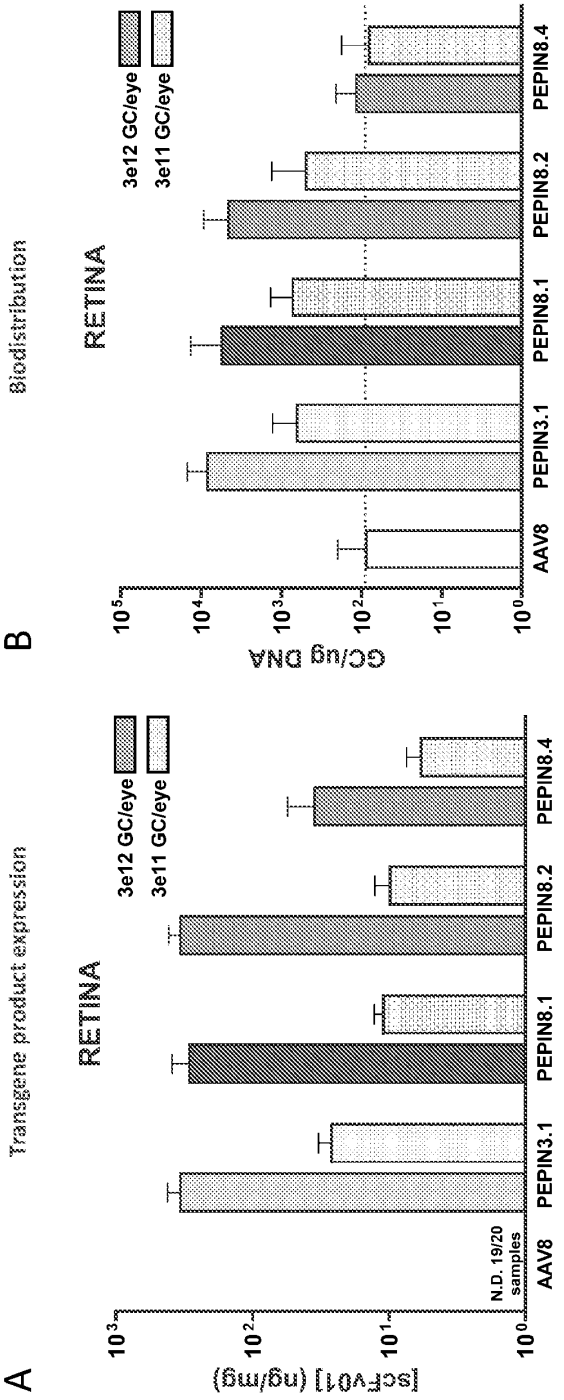
FIGS. 30A-30B


B
NS scFV (ng/mg)
40
30
20
10
0
Retina
Choroid
Sclera
P0201 R
P0301 L
P0301 R
P0902 L
IE10
IE11

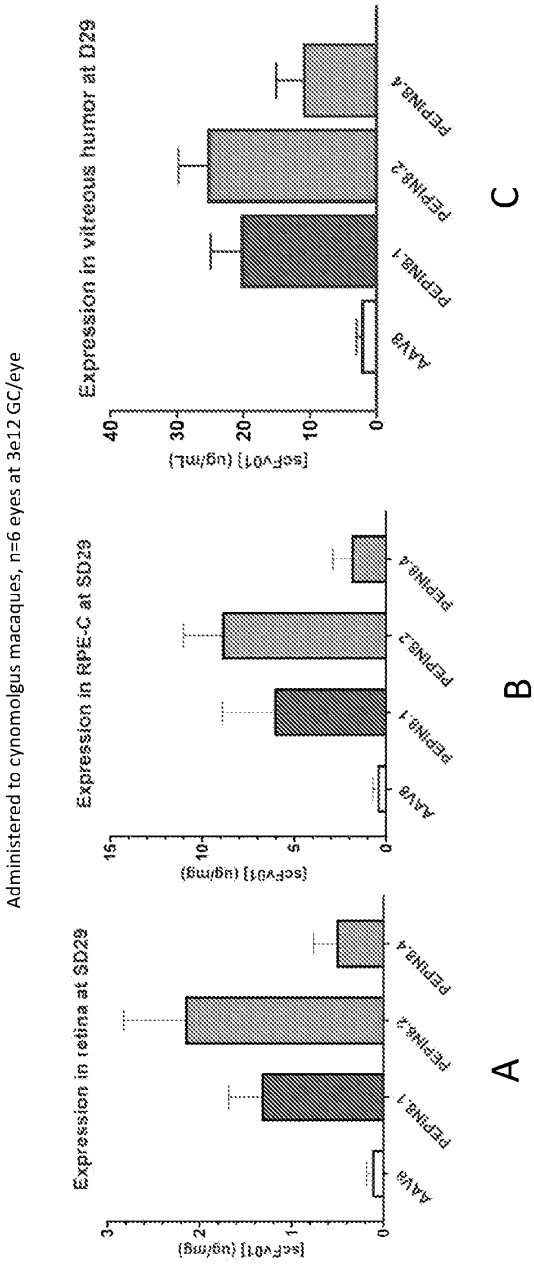

A
Anti-C5 scFV (ng/mg)
300
250
200
150
100
50
10
5
0
Retina
Choroid
Sclera
P0401 L
P0401 R
P0501 L
P0501 R
P0502 L
P0502 R
P1101 L
IE10
IE11


A
Mini-pig aqueous humor
High dose (3e12 GC/eye)
Low dose (3e11 GC/eye)
Day 15
Day 29
scFv01 (ng/mL)
1000
100
10
1
0.1
ND
ND
AAV8
PEPIN8.1
PEPIN8.2
PEPIN8.4
AAV8
PEPIN8.1
PEPIN8.2
PEPIN8.4
B
iRPE cells apical media (basally-transduced)
Apical-D7
Apical-D14
Apical-D21
scFv01 (ng/mL)
4000
3000
2000
1000
0
NT
AAV8
PEPIN8.1
PEPIN8.2
PEPIN8.4
C
NHP aqueous humor
Day 15
Day 29
scFv01 (ng/mL)
8000
7000
6000
5000
4000
3000
2000
1000
0
AAV8
PEPIN8.1
PEPIN8.2
PEPIN8.4
D
NHP retina punches
scFv01 (ng/g tissue)
50000
40000
30000
20000
10000
0
AAV8
PEPIN8.1
PEPIN8.2
PEPIN8.4

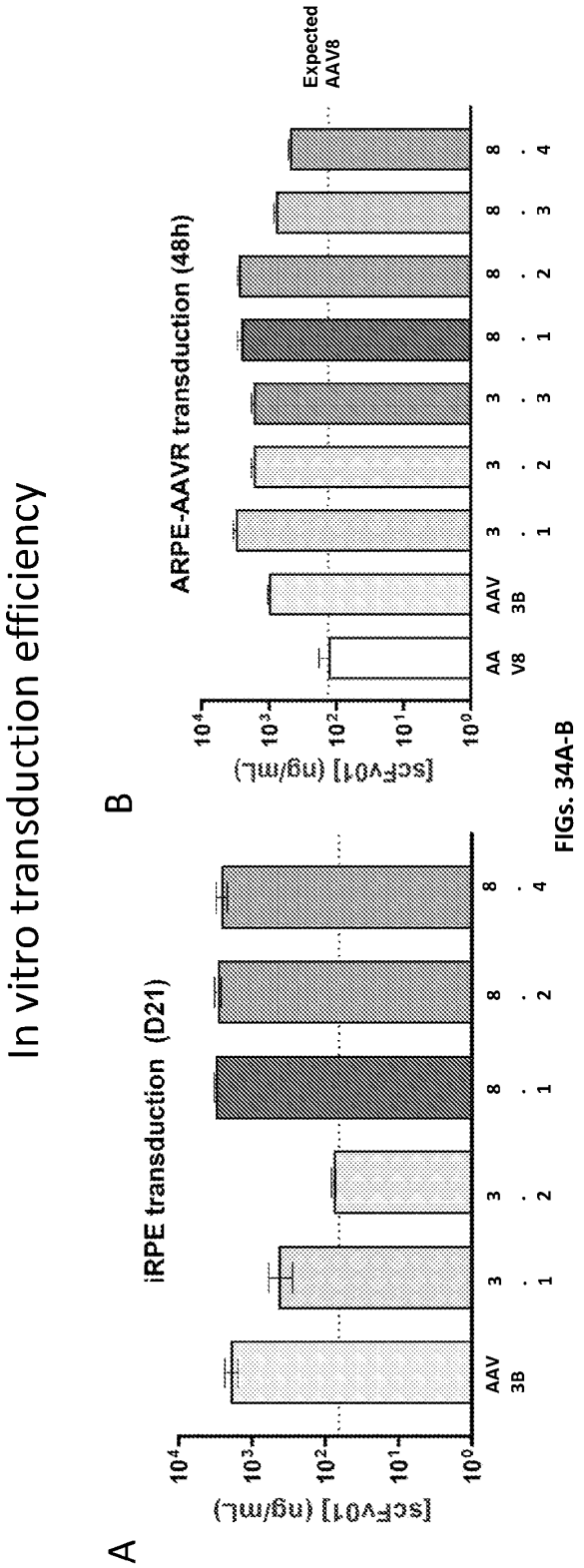
FIGs. 31A-D


A
Transgene product expression
RETINA
3e12 GC/eye
3e11 GC/eye
[scFv01] (ng/mg)
N.D. 19/20 samples
AAV8
PEPIN3.1
PEPIN8.1
PEPIN8.2
PEPIN8.4
B
Biodistribution
RETINA
3e12 GC/eye
3e11 GC/eye
GC/ug DNA
AAV8
PEPIN3.1
PEPIN8.1
PEPIN8.2
PEPIN8.4

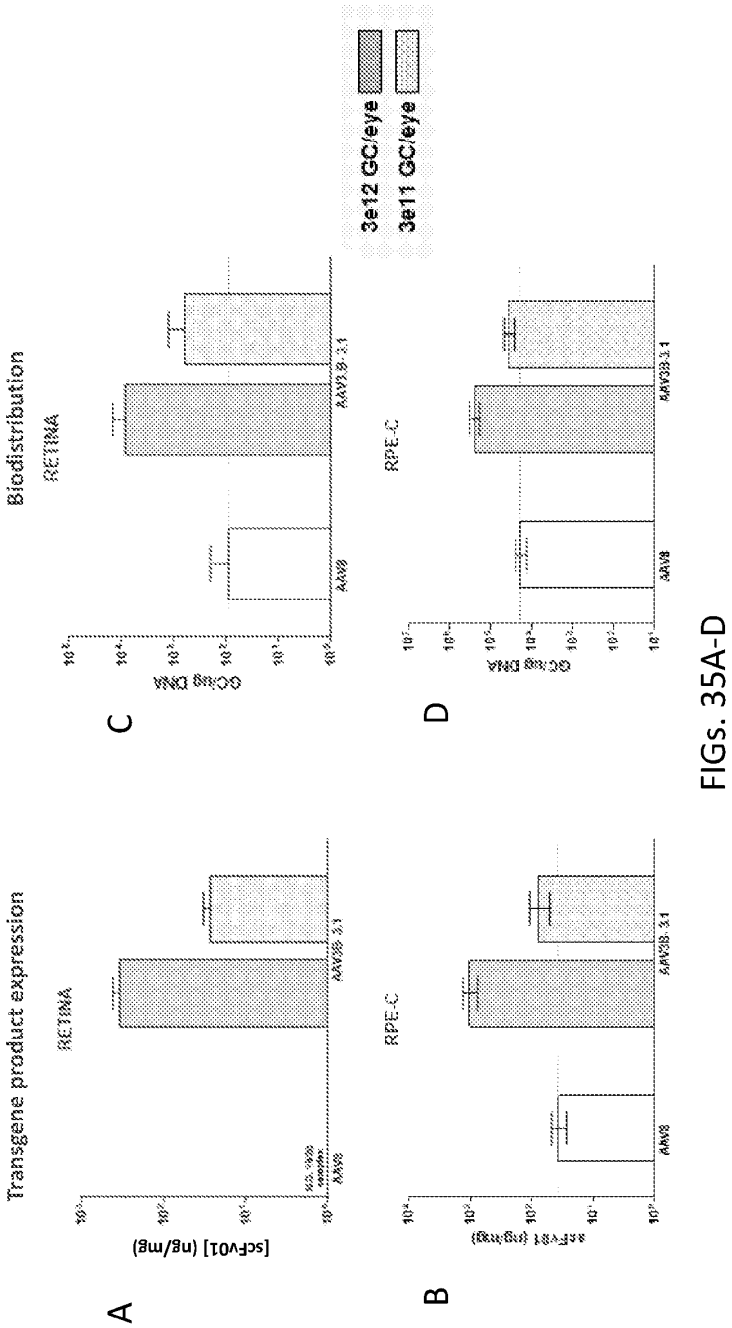
FIGs. 32A-B


Administered to cynomolgus macaques, n=6 eyes at 3e12 GC/eye
Expression in retina at SD29
[scFv01] (ug/mg)
AAV9
PEPIN8.1
PEPIN8.2
PEPIN8.4
A
Expression in RPE-C at SD29
[scFv01] (ug/mg)
AAV9
PEPIN8.1
PEPIN8.2
PEPIN8.4
B
Expression in vitreous humor at D29
[scFv01] (ug/mL)
AAV9
PEPIN8.1
PEPIN8.2
PEPIN8.4
C

FIGs. 33A-C


In vitro transduction efficiency
A
iRPE transduction (D21)
[scFv01] (ng/mL)
AAV 3B.1
AAV 3B.2
AAV 3B.3
AAV 3B.8.1
AAV 3B.8.2
AAV 3B.8.4
B
ARPE-AAVR transduction (48h)
[scFv01] (ng/mL)
AAV V8
AAV 3B.1
AAV 3B.2
AAV 3B.3
AAV 3B.8.1
AAV 3B.8.2
AAV 3B.8.3
AAV 3B.8.4
Expected AAV8

FIGs. 34A-B


Transgene product expression
RETINA
[scFv01] (ng/mg)
AAV8
AAV3B 3.1
A
RPE-C
B
Biodistribution
RETINA
GC/ng DNA
C
RPE-C
D
3e12 GC/eye
3e11 GC/eye

FIGs. 35A-D

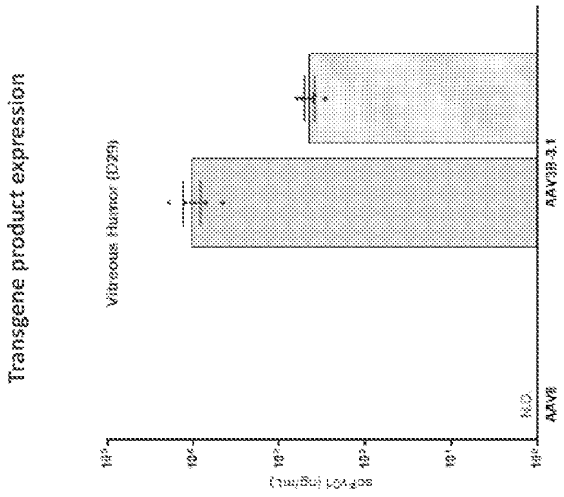
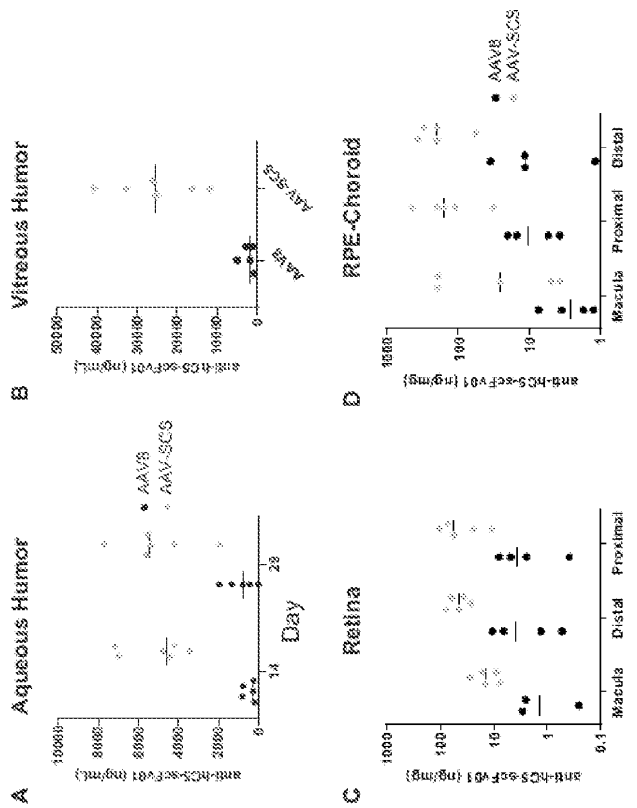

Transgene product expression
Vitreous Humor (D29)
AAV8
AAV3B.1

FIG. 36


A
Aqueous Humor
anti-hCS-scFv01 (ng/mL)
Day
AAV8
AAV-SCS
B
Vitreous Humor
C
Retina
anti-hCS-scFv01 (ng/mg)
Macula
Distal
Proximal
D
RPE-Choroid

FIGs. 37A-D

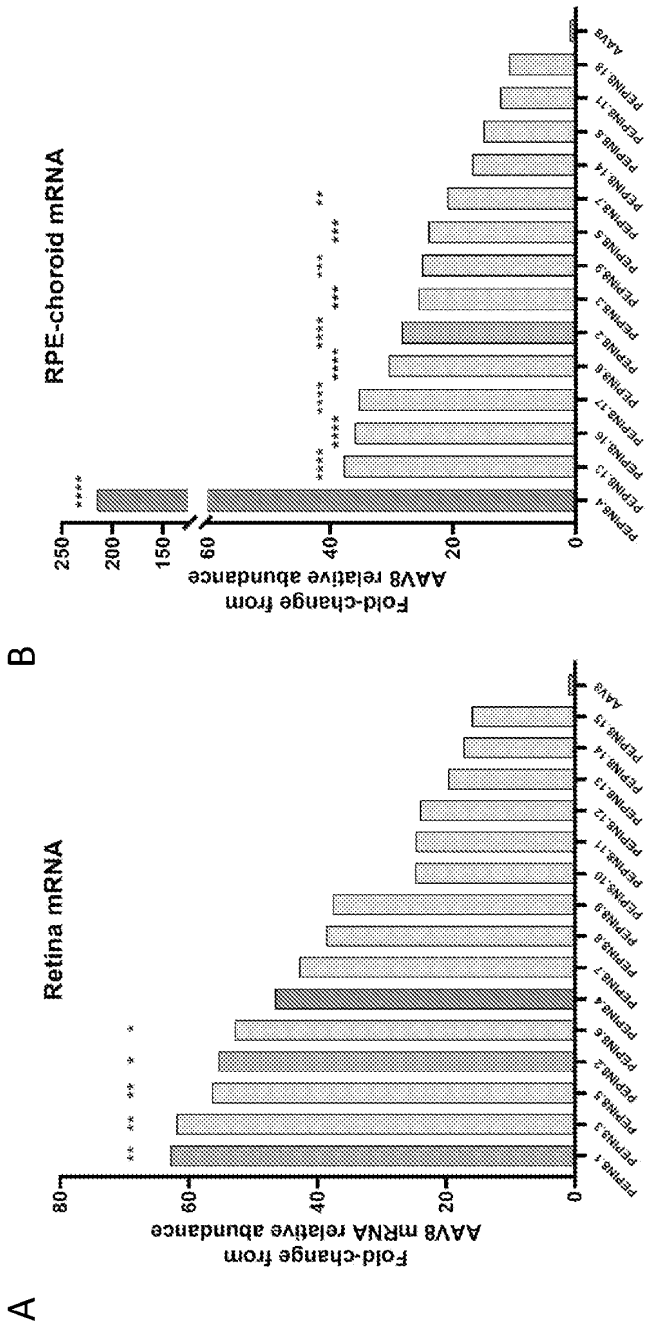

A
Retina mRNA
Fold-change from
AAV8 mRNA relative abundance
0
20
40
60
80
PEPNP8.1
PEPNP8.3
PEPNP8.5
PEPNP8.2
PEPNP8.6
PEPNP8.4
PEPNP8.7
PEPNP8.8
PEPNP8.9
PEPNP8.10
PEPNP8.11
PEPNP8.12
PEPNP8.13
PEPNP8.14
PEPNP8.15
AAV8
B
RPE-choroid mRNA
Fold-change from
AAV8 relative abundance
0
20
40
60
150
200
250
PEPNP8.4
PEPNP8.13
PEPNP8.16
PEPNP8.17
PEPNP8.6
PEPNP8.2
PEPNP8.3
PEPNP8.9
PEPNP8.5
PEPNP8.7
PEPNP8.14
PEPNP8.8
PEPNP8.11
PEPNP8.19
AAV8

FIG. 38A-B