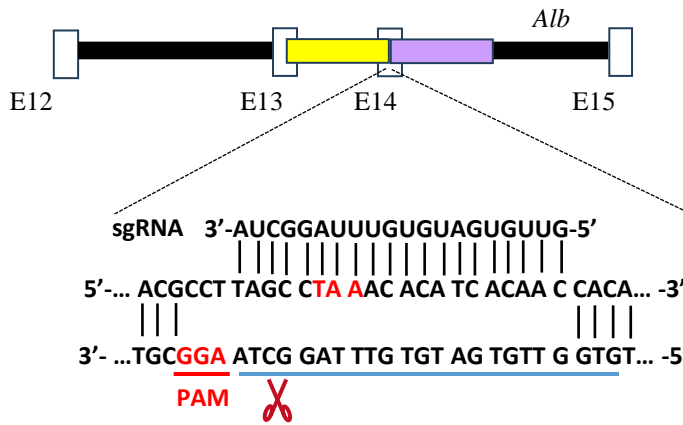


A



B

Indels% of liver gDNA from unedited hemophilia A mouse = 0.09% (background error)

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-Reference
 sgRNA
 TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-98.05% (11937 reads)

Indels% of edited HA mouse liver after injection of F8 donor plasmid only = 0.10% (background error)

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-Reference
 sgRNA
 TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-97.98% (42335 reads)

Indels% of edited HA mouse liver after injection with CRISPR plasmids only = 10.5%

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-Reference
 sgRNA

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC	-87.59% (24415 reads)
TAGATGCAAAGACGCGCTTAACCTAAACACATCACAAACCAC	-2.24% (625 reads)
TAGATGCAAAGACGCGCTTAGCTAAACACATCACAAACCAC	-1.73% (481 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-1.47% (411 reads)
TAGATGCAAAGACGCGCTTAGCTAAACACATCACAAACCAC	-0.76% (212 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.60% (168 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.46% (129 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.30% (85 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.25% (71 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.21% (59 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.21% (58 reads)

Indels% of edited HA mouse liver after injection of CRISPR and F8 donor plasmids = 11.53%

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC-Reference
 sgRNA

TAGATGCAAAGACGCGCTTAGCCTAAACACATCACAAACCAC	-86.48% (38092 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-2.03% (894 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-1.93% (849 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-1.64% (723 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.92% (404 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.84% (372 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.53% (232 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.34% (149 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.27% (117 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.24% (106 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.21% (93 reads)
TAGATGCAAAGACGCGCTTAACTAAACACATCACAAACCAC	-0.21% (91 reads)

Figure S1. sgRNA Design and Indel Frequencies at the Alb Locus. (A) An sgRNA (sgAlb-E14) was designed to target the sequence surrounding the stop codon TAA (shown in red, reverse complement) in Exon 14 of the Alb gene. The red scissors icon indicates the anticipated Cas9 cleavage site, with "PAM" denoting the protospacer-adjacent motif (PAM) for SpCas9, recognized as NGG. (B) Frequencies of indels observed at the Alb locus following in vivo editing in the liver of hemophilia A mice. One week after the injection of editing plasmids, the sequence adjacent to the editing site was amplified from liver genomic DNA and subsequently analyzed using next-generation sequencing (NGS) and CRISPResso2.

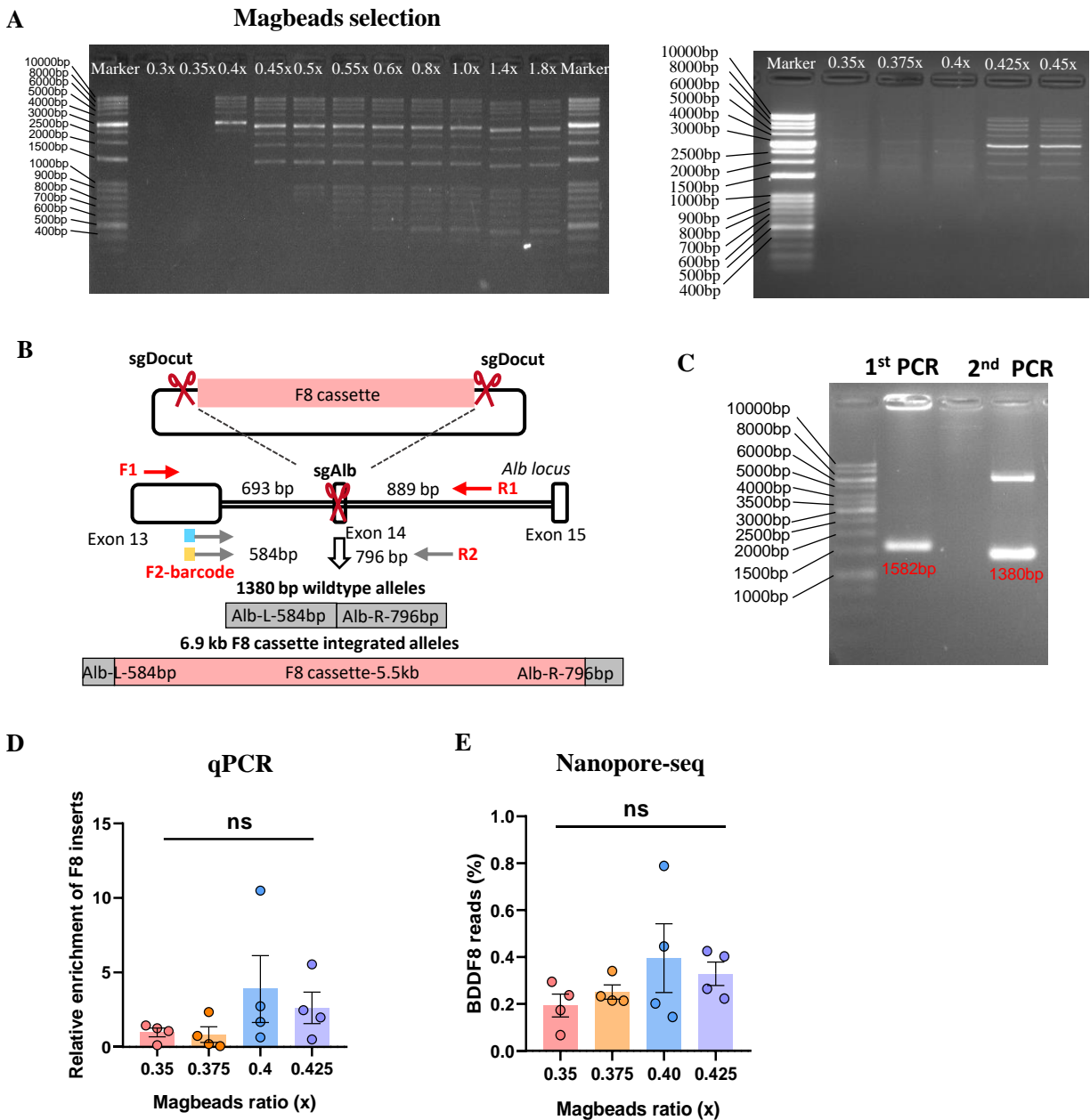
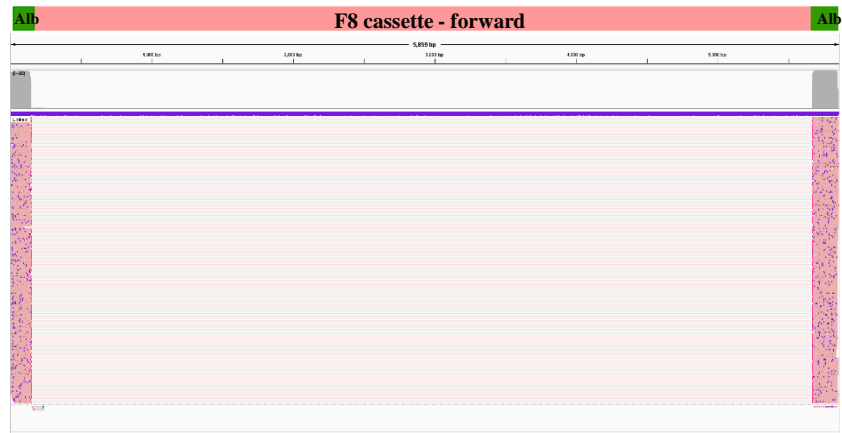
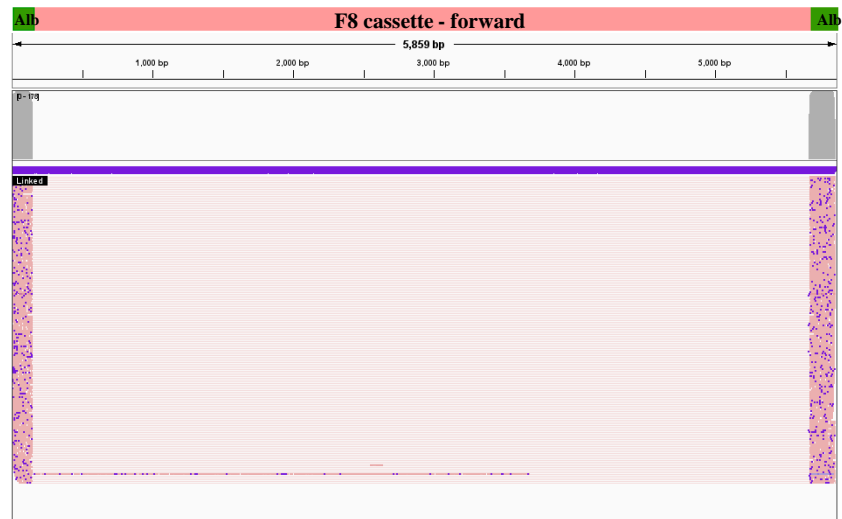


Figure S2. Optimizing Magnetic Beads for the Enrichment of F8-Integrated Alleles. (A) Evaluation of size selection efficiency using various ratios of magnetic beads (0.3x-1.8x). (B) Primer design for nested PCR, depicting expected PCR products, including the 1380bp wildtype alleles and the approximately 6.9kb F8 cassette-integrated alleles. (C) Representative results of gel electrophoresis for the 1st PCR products and the 2nd PCR products, which were amplified from the 1st PCR products after size selection using a beads ratio of 0.4x. The bands corresponding to alleles lacking donor insertion in the 1st and 2nd PCR products were 1586bp and 1380bp, respectively. (D) Relative enrichment of F8 inserts determined by qPCR after size selection using magnetic beads at various ratios. Error bars represent the mean \pm SEM, $n = 4$, and paired two-sided Student's t -tests were performed. (E) Determination of the percentage of both forward and reverse F8 inserts by nanopore sequencing (F8 reads %) in the 2nd PCR products following size selection of the purified 1st PCR products using different ratios of magnetic beads. Error bars represent the mean \pm SEM, $n = 4$, and paired two-sided Student's t -tests were conducted.

Size selection-None



Size selection-Once



Size selection-Twice

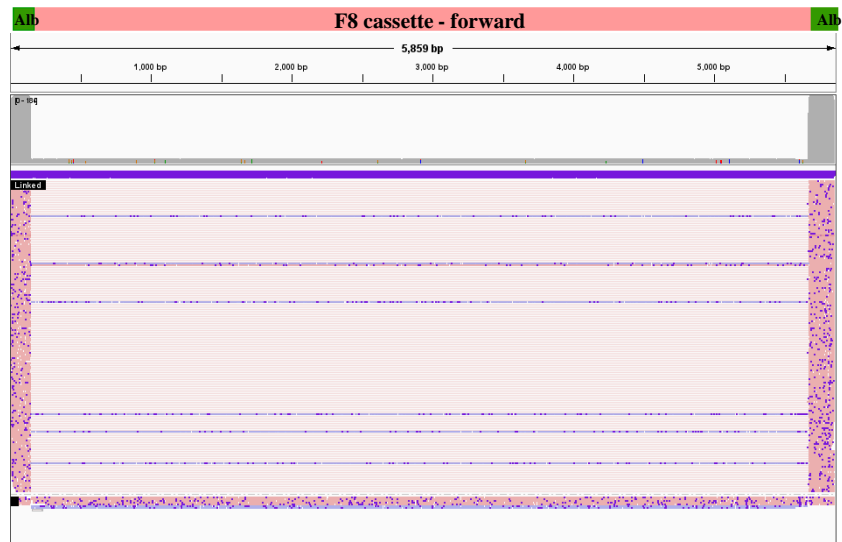


Figure S3. Visualization of Sequencing Results for 2nd PCR Amplicons after Magnetic Beads Size Selection. The reference sequence of the F8 cassette is flanked by 332bp of the Alb genomic sequence. Representative Integrated Genome Viewer (IGV) images display nanopore sequencing results after size selection of the 1st PCR products using magnetic beads 0 (above), 1 (middle), or 2 (bottom) times.

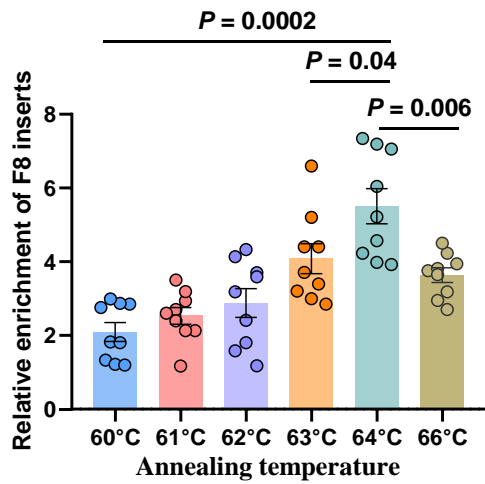
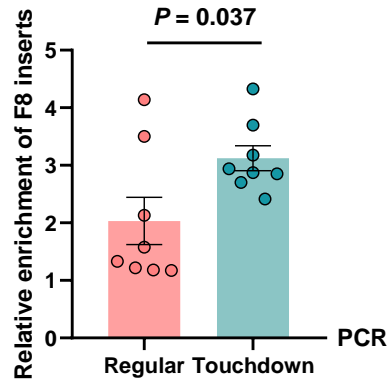
A Optimization of annealing temperature**B 1st PCR program**

Figure S4. PCR Conditions Optimization for Enhanced Amplification of F8 Inserts. (A) Optimization of annealing temperature in the 1st PCR to improve the amplification of F8 inserts. The relative enrichment of amplicons with F8 inserts was determined using qPCR. Error bars represent the mean \pm SEM, $n = 9$, and paired two-sided Student's t-tests were performed. (B) Employment of a touchdown PCR program in the 1st PCR to increase the amplification of F8 inserts. The touchdown PCR program used was 6 cycles of [98°C for 10s, 68°C (-1°C/cycle) for 15s, 68°C for 6.5min]; followed by 25 cycles of [98°C for 10s, 62°C for 15s, 68°C for 6.5min]. Error bars indicate the mean \pm SEM, $n = 8$, and paired two-sided Student's t-tests were conducted.

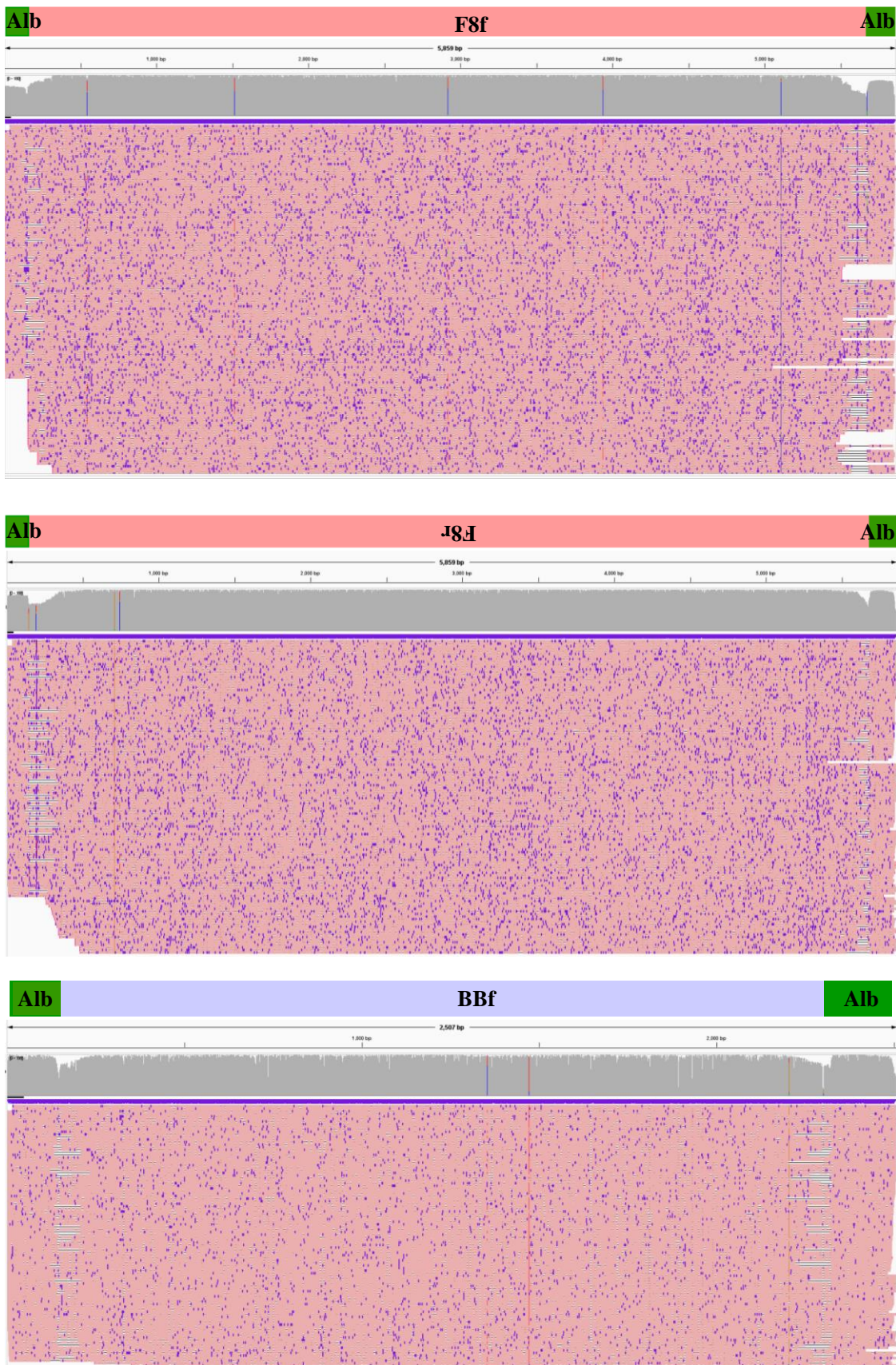


Figure S5. Random 200 reads in the visualization of eight representative insertion patterns of the donor template in Figure 5E. The F8 cassette is abbreviated as F8, and the plasmid backbone is abbreviated as BB. Forward insertions are abbreviated as f, and reverse insertions are abbreviated as r. (continued).

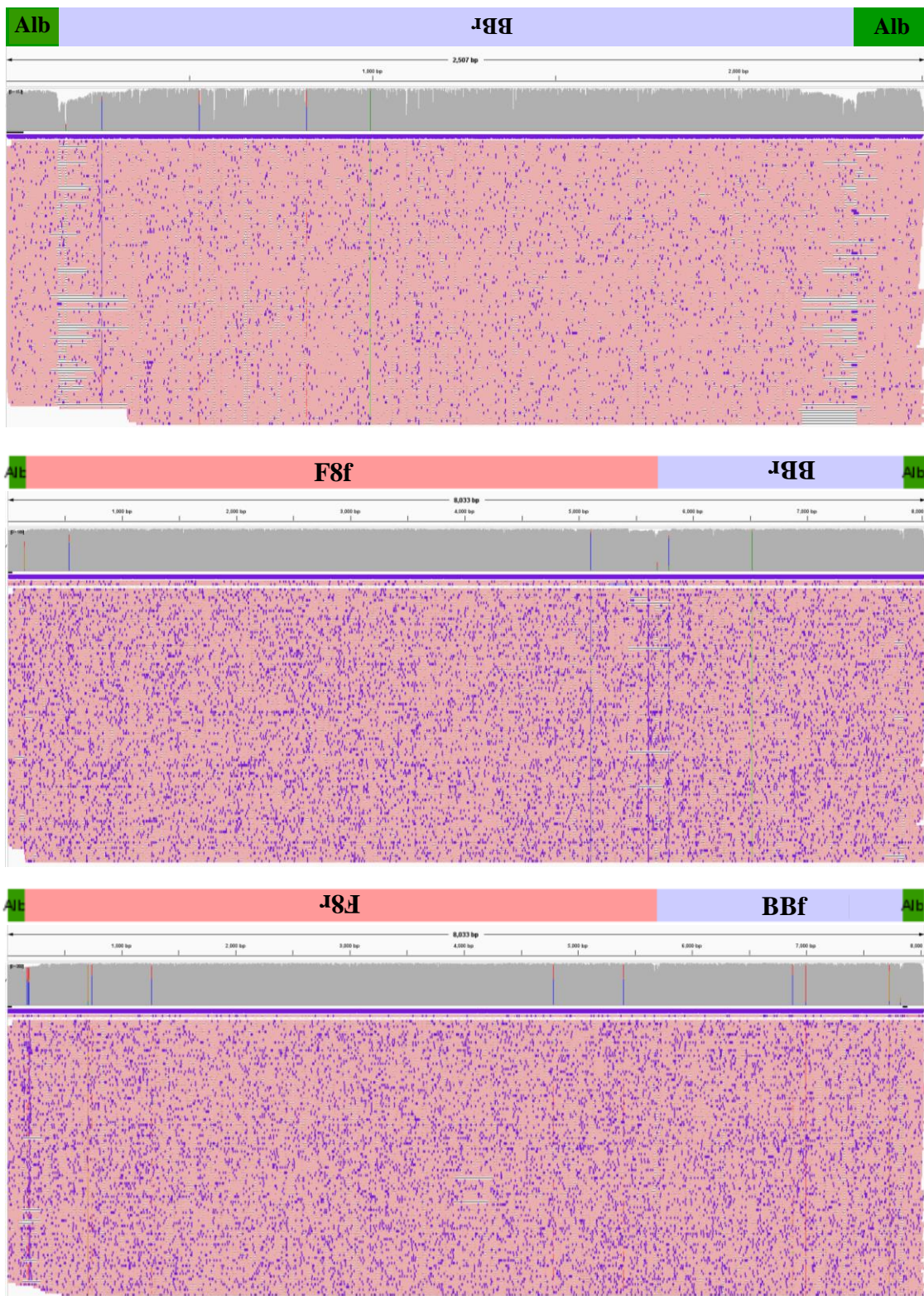


Figure S5. Visualization of Insertion Patterns: This figure presents the visualization of 200 randomly selected reads showcasing eight representative insertion patterns of the donor template, as depicted in Figure 5E. The insertions include components from the F8 cassette (abbreviated as F8) and the plasmid backbone (abbreviated as BB). The orientation of these insertions is also indicated, with forward insertions abbreviated as 'f' and reverse insertions as 'r'. This visualization aids in understanding the diversity and orientation of the insertions at the targeted genomic site. (Continued)

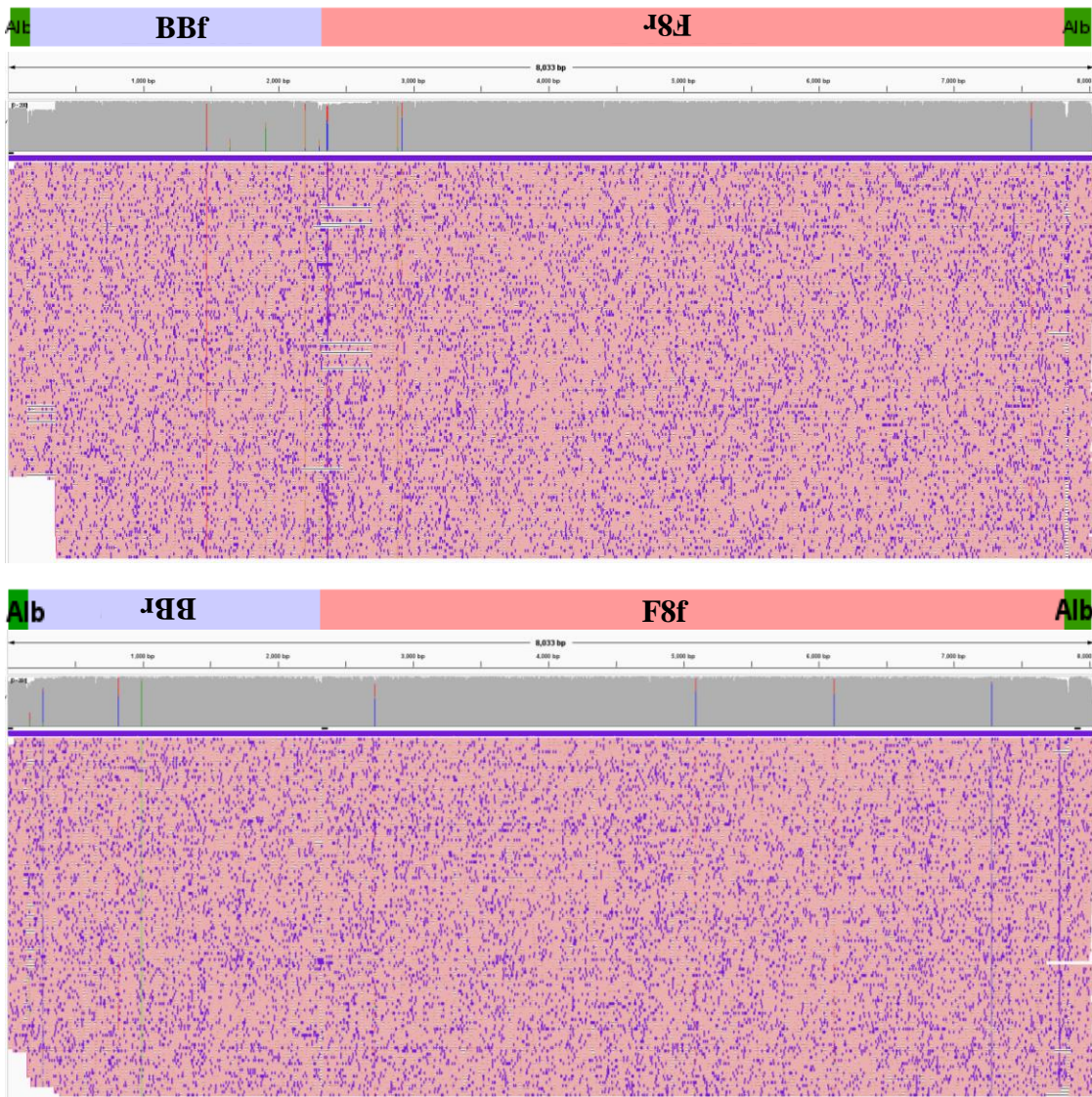
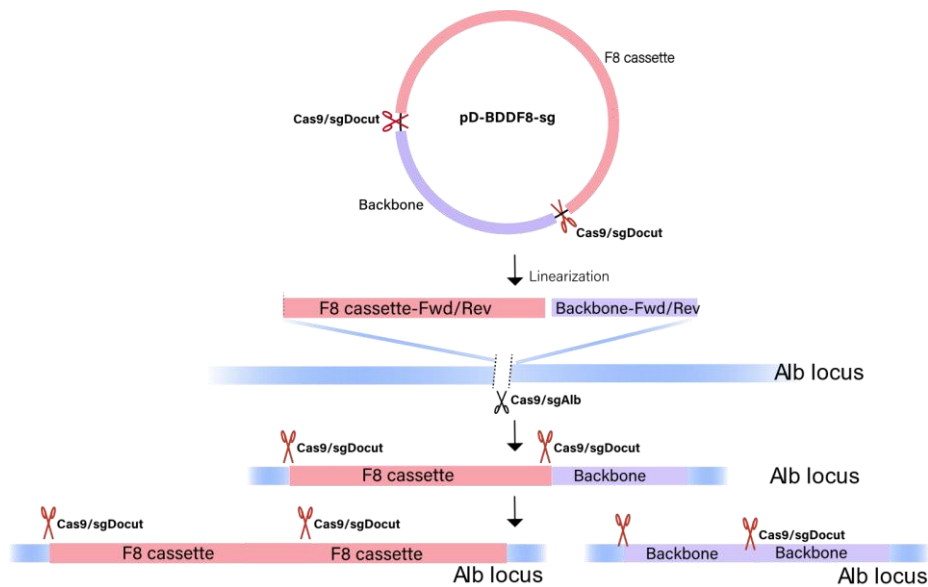


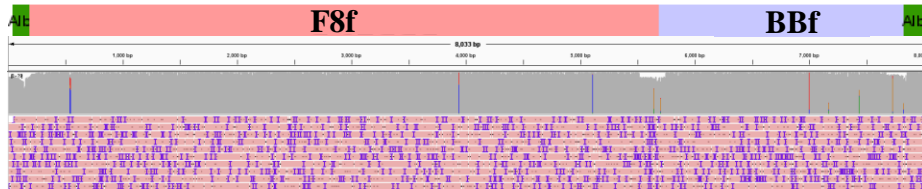
Figure S5. Visualization of Insertion Patterns: This figure presents the visualization of 200 randomly selected reads showcasing eight representative insertion patterns of the donor template, as depicted in Figure 5E. The insertions include components from the F8 cassette (abbreviated as F8) and the plasmid backbone (abbreviated as BB). The orientation of these insertions is also indicated, with forward insertions abbreviated as 'f' and reverse insertions as 'r'. This visualization aids in understanding the diversity and orientation of the insertions at the targeted genomic site.

A Schematic of insertions of multiple double-cut donor fragments

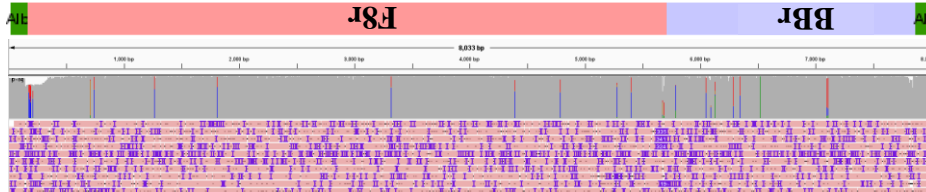


B Additional two-fragment integrations

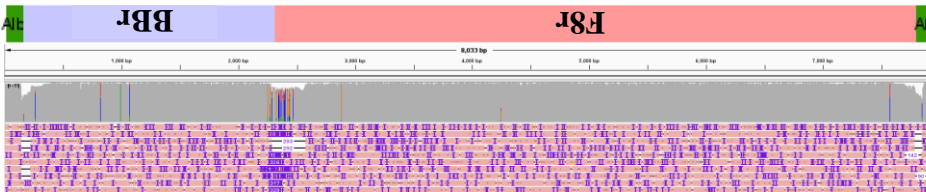
F8fBBf inserts = 0.35%. Shows 10 out of 79 reads.



F8rBBr inserts = 0.24%. Shows 10 out of 54 reads.



BBrF8r inserts = 0.22%. Shows 10 out of 51 reads.



BBfF8f inserts = 0.09%. Shows 10 out of 22 reads.

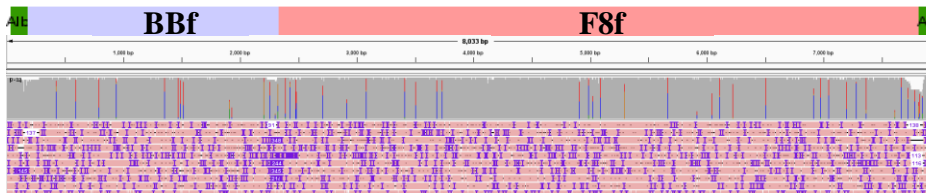
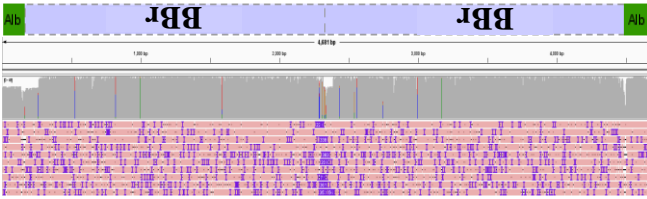
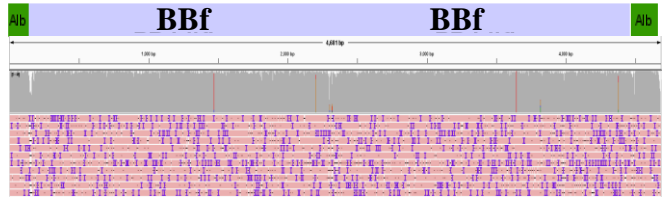


Figure S6. Characterization of Multi-Fragment Insertions from Double-Cut Donor Plasmid Following Cas9-sgRNA Linearization. The orientation of these insertions is indicated, with forward insertions abbreviated as 'f' and reverse insertions as 'r'. (A) Schematic representation of multi-fragment insertions resulting from the linearization of the double-cut donor plasmid. Following linearization, multiple fragments can integrate, albeit at lower frequencies. (B) Visualization of additional two-fragment integrations not shown in Figure 5, including four patterns of F8 and BB insertions in both orientations.

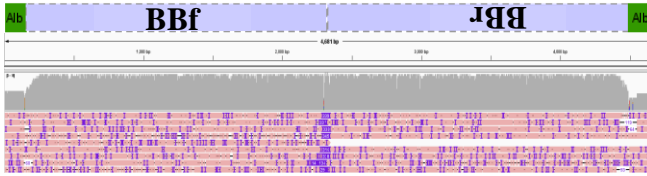
BBrBBr inserts = 0.22%. Shows 10 out of 49 reads.



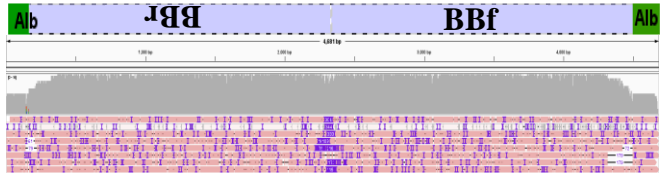
BBfBBf inserts = 0.20%. Shows 10 out of 46 reads.



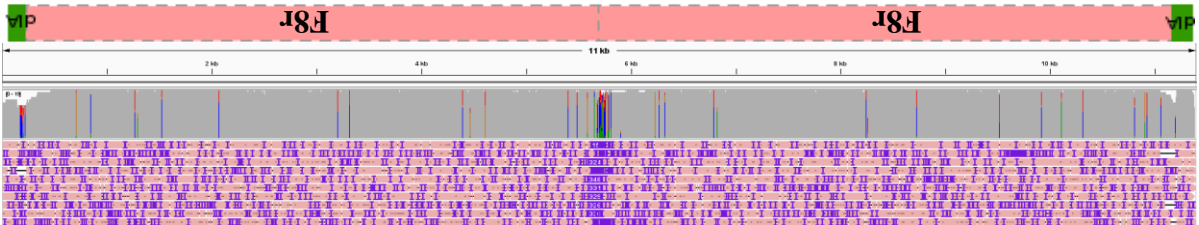
BBfBBr inserts = 0.04%. Shows 9 out of 9 reads.



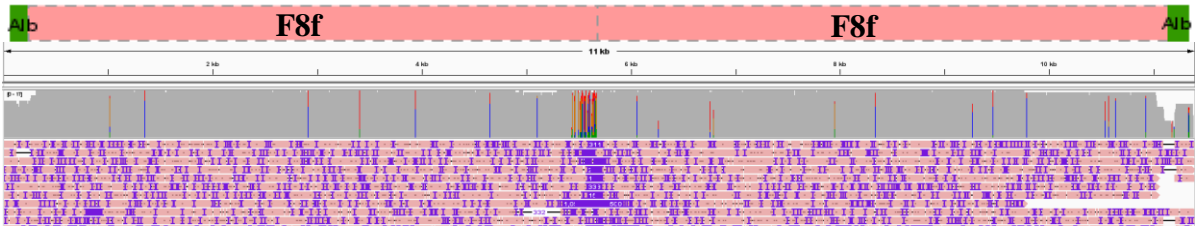
BBrBBf inserts = 0.04%. Shows 8 out of 8 reads.



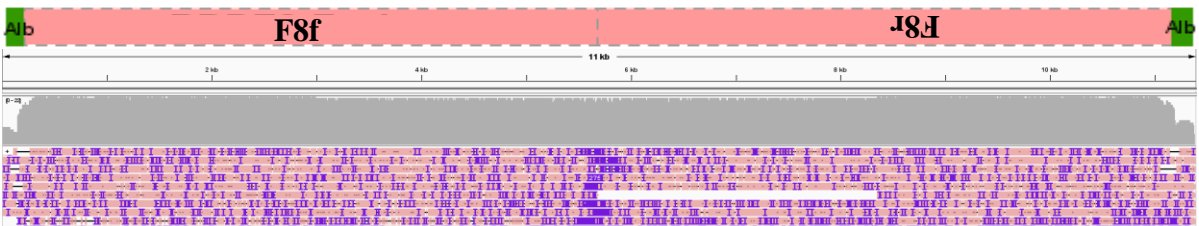
F8rF8r inserts = 0.08%. Shows 10 out of 19 reads.



F8fF8f inserts = 0.08%. Shows 10 out of 17 reads.



F8fF8r inserts = 0.05%. Shows 10 out of 11 reads.



F8rF8f inserts = 0.03%. Shows 8 out of 8 reads.

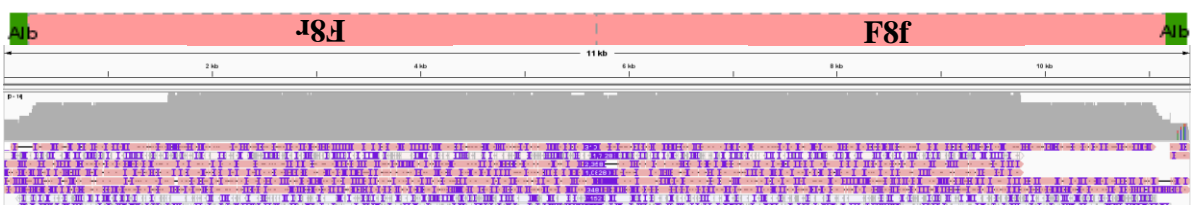
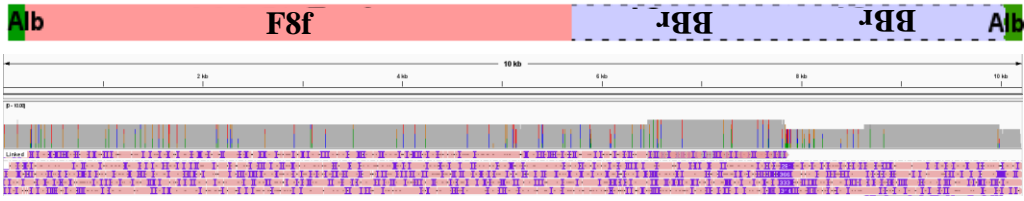


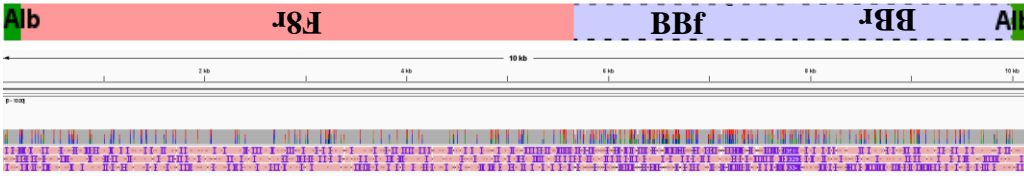
Figure S6B. Visualization of additional two-fragment integrations not shown in Figure 5, including four patterns of F8 and BB insertions in both orientations (continued).

C Three-fragment insertions: BB+BB+F8

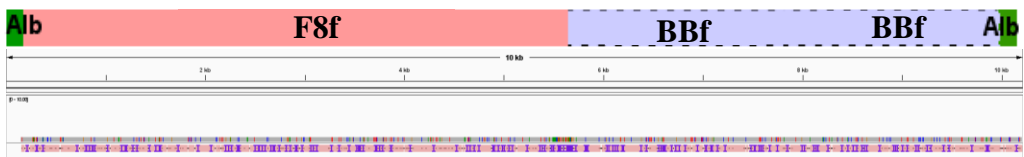
F8fBBrBBr inserts = 0.02%. Shows 5 out of 5 reads.



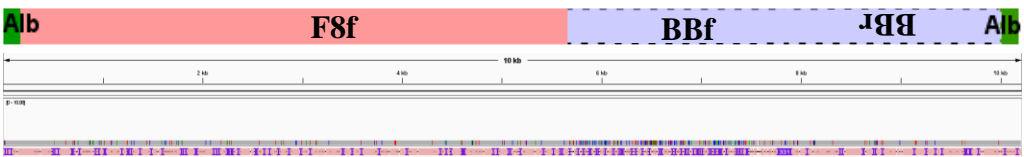
F8rBBfBBr inserts = 0.01%. Shows 3 out of 3 reads.



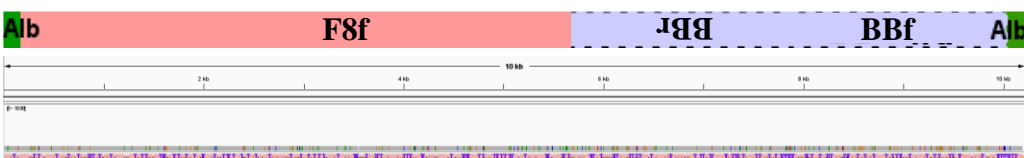
F8fBBfBBf = 0.004%. Shows 1 out of 1 read.



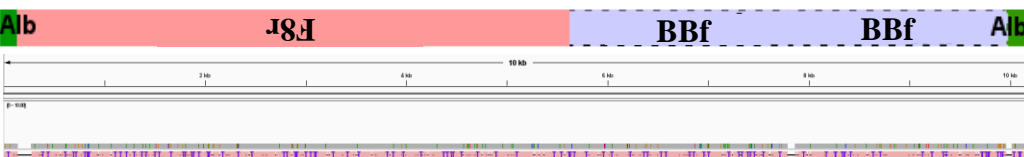
F8fBBfBBr = 0.004%. Shows 1 out of 1 read.



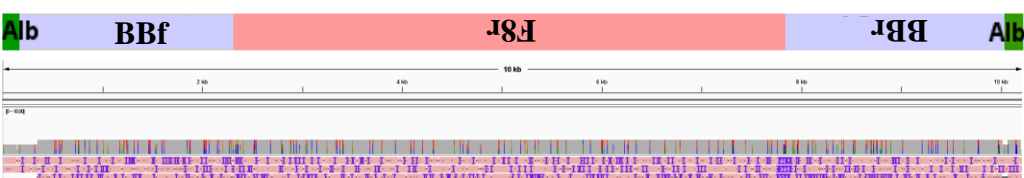
F8fBBrBBf = 0.004%. Shows 1 out of 1 read.



F8rBBfBBf = 0.004%. Shows 1 out of 1 read.



BBfF8rBBr inserts = 0.01%. Shows 3 out of 3 reads.



BBrF8fBBf = 0.004%. Shows 1 out of 1 read.

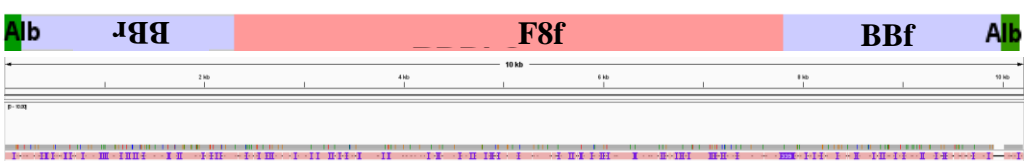
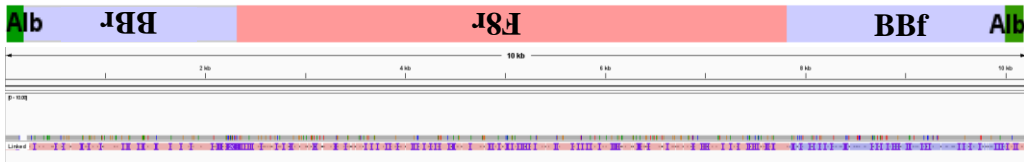
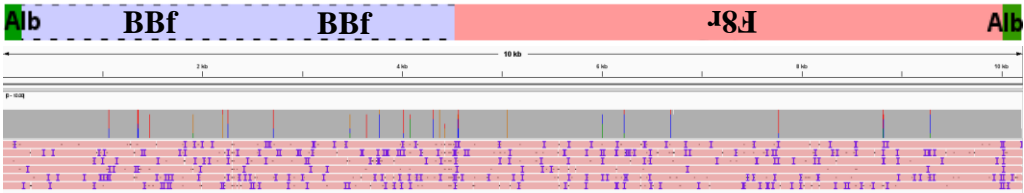


Figure S6C. Visualization of three-fragment insertions, specifically the insertion of two plasmid backbone fragments and one F8 fragment.

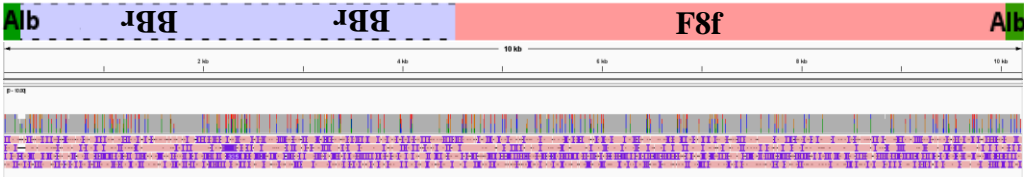
BBrF8rBBf = 0.004%. Shows 1 out of 1 reads.



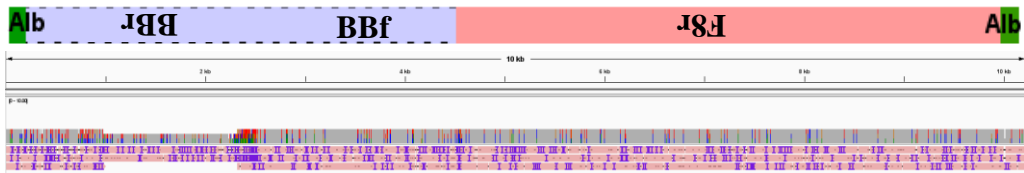
BBfBBfF8r inserts = 0.03%. Shows 6 out of 6 reads.



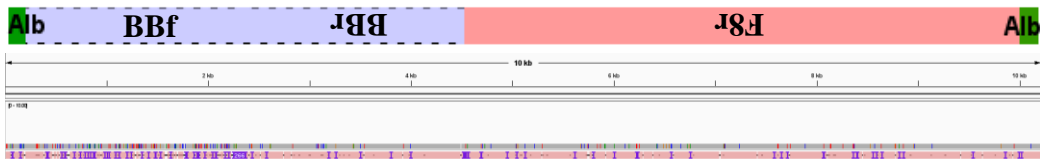
BBrBBrF8f inserts = 0.02%. Shows 4 out of 4 reads.



BBrBBfF8r inserts = 0.01%. Shows 3 out of 3 reads.



BBfBBrF8r inserts = 0.004%. Shows 1 out of 1 reads.



BBfBBrF8f inserts = 0.004%. Shows 1 out of 1 reads.

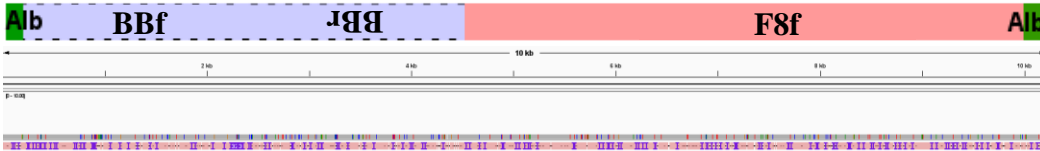
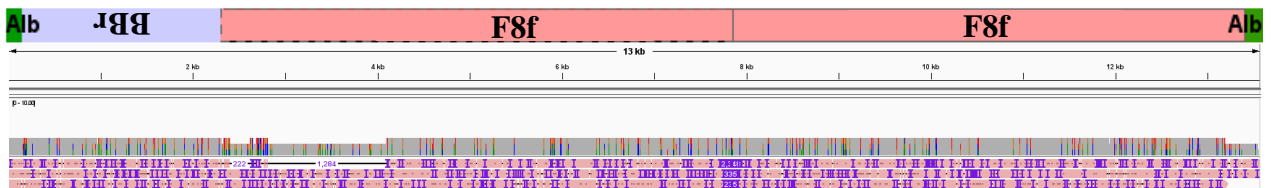


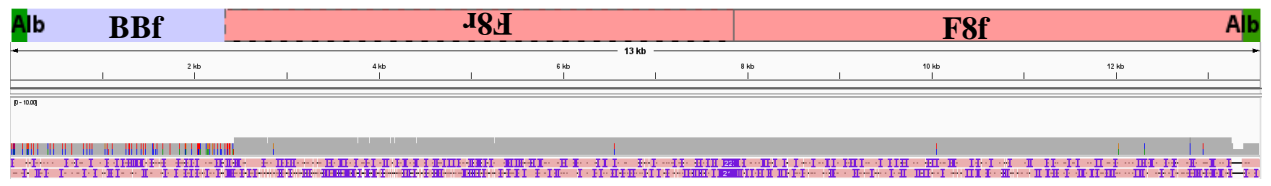
Figure S6C. Visualization of three-fragment insertions, specifically the insertion of two plasmid backbone fragments and one F8 fragment (continued).

D Three-fragment insertions: BB+F8+F8

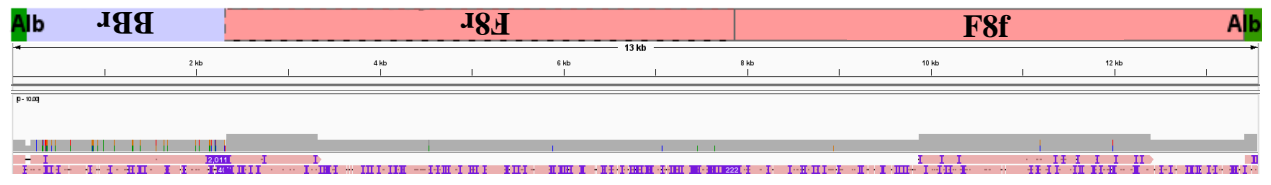
BBrF8fF8f inserts = 0.01%. Shows 3 out of 3 reads.



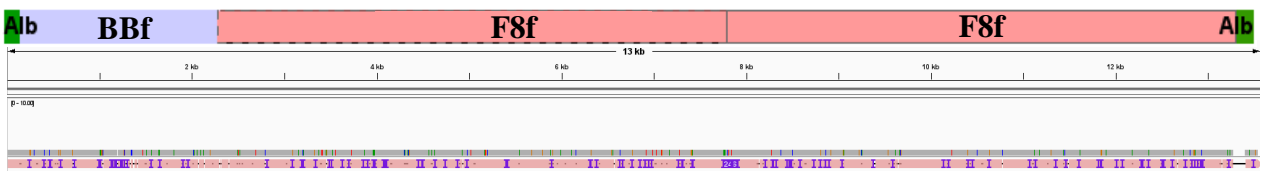
BBfF8rF8f inserts = 0.01%. Shows 2 out of 2 reads.



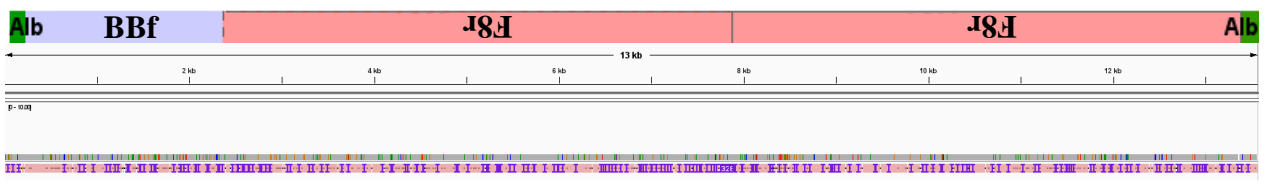
BBrF8rF8f inserts = 0.01%. Shows 2 out of 2 reads.



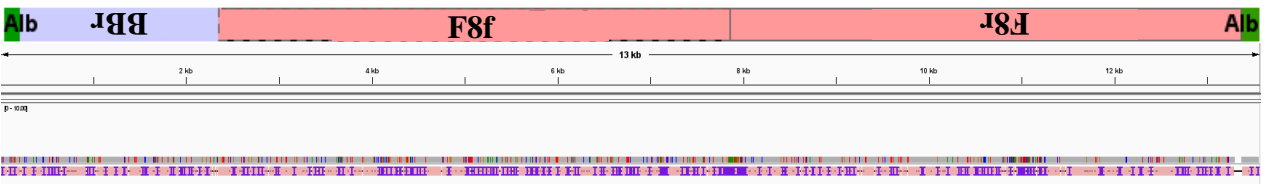
BBfF8fF8f inserts = 0.004%. Shows 1 out of 1 reads.



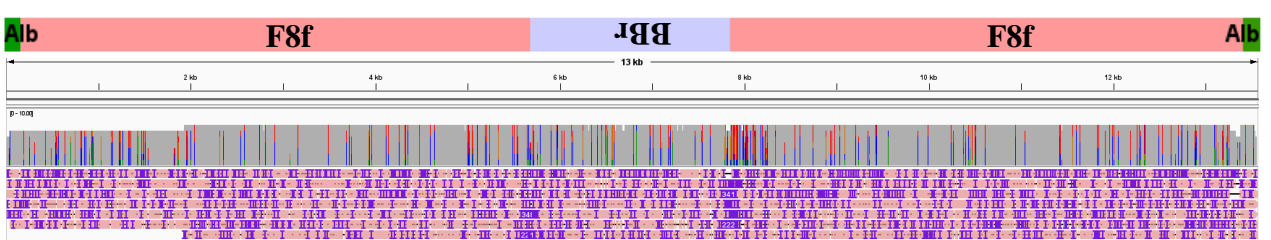
BBfF8rF8r inserts = 0.004%. Shows 1 out of 1 read.



BBrF8fF8r inserts = 0.004%. Shows 1 out of 1 read.



F8fBBrF8f inserts = 0.03%. Shows 7 out of 7 reads.



F8fBBrF8r inserts = 0.03%. Shows 6 out of 6 reads.

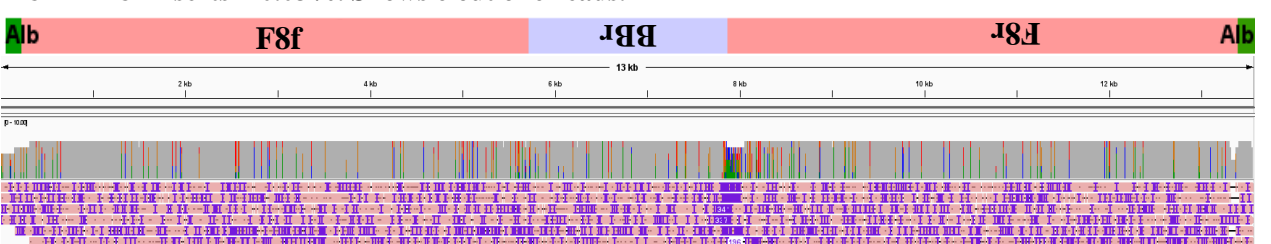
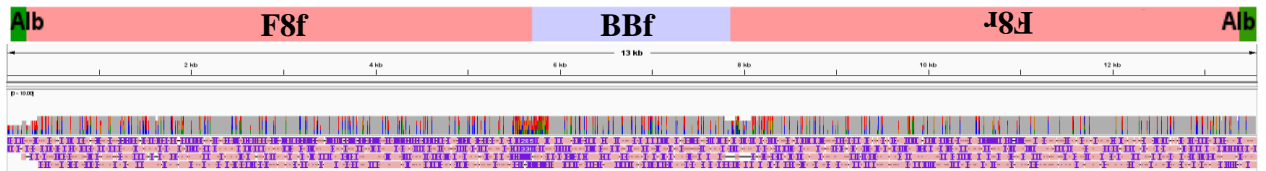
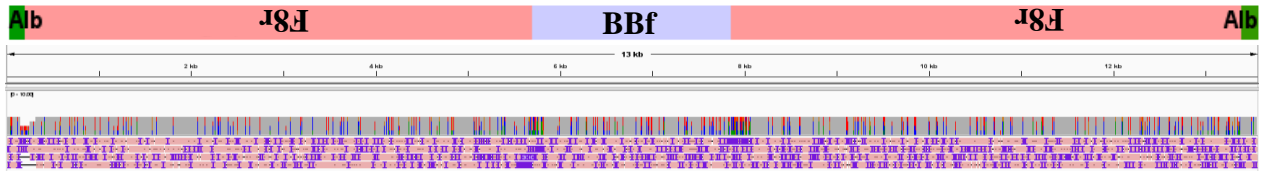


Figure S6D. Visualization of three-fragment insertions, specifically the insertion of one plasmid backbone fragment and two F8 fragments.

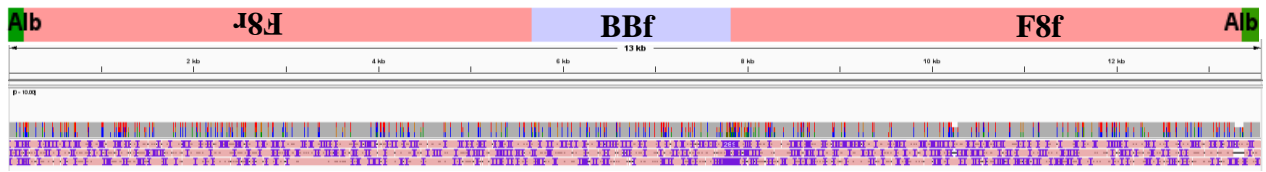
F8fBBfF8r inserts = 0.02%. Shows 4 out of 4 reads.



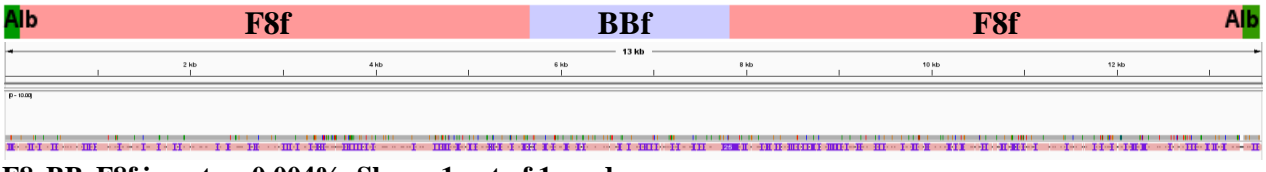
F8rBBfF8r inserts = 0.02%. Shows 4 out of 4 reads.



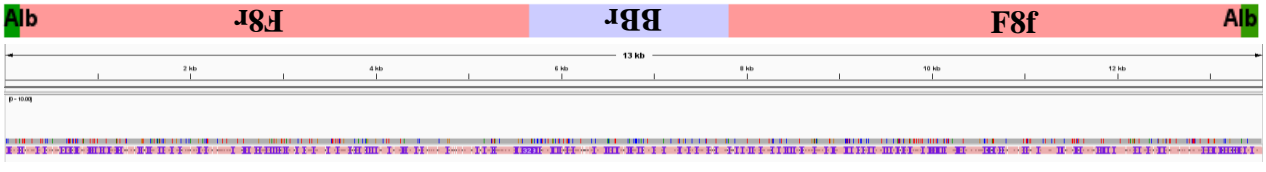
F8rBBfF8f inserts = 0.01%. Shows 3 out of 3 reads.



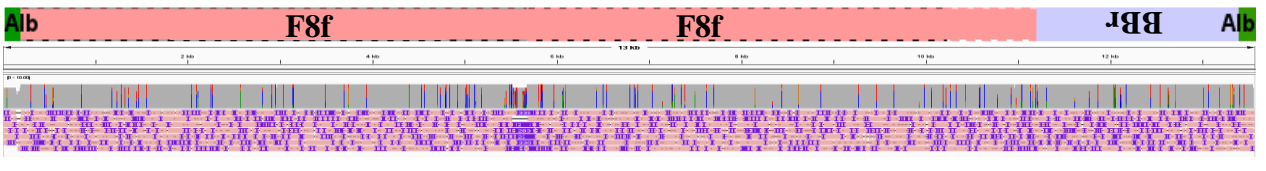
F8fBBfF8f inserts = 0.004%. Shows 1 out of 1 read.



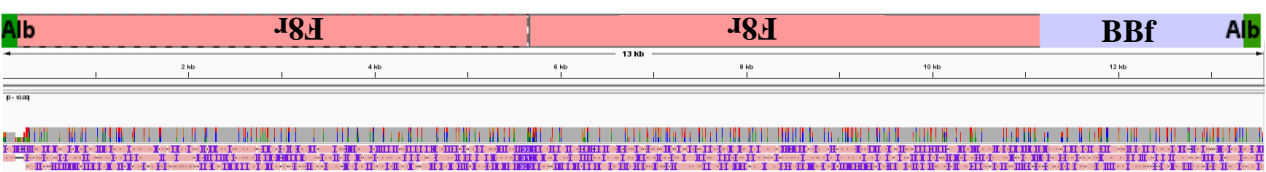
F8rBBrF8f inserts = 0.004%. Shows 1 out of 1 read.



F8fF8fBBr inserts = 0.03%. Shows 7 out of 7 reads.



F8rF8rBBf inserts = 0.01%. Shows 3 out of 3 reads.



F8fF8rBBf inserts = 0.01%. Shows 2 out of 2 reads.



F8rF8fBBr inserts = 0.004%. Shows 1 out of 1 read.

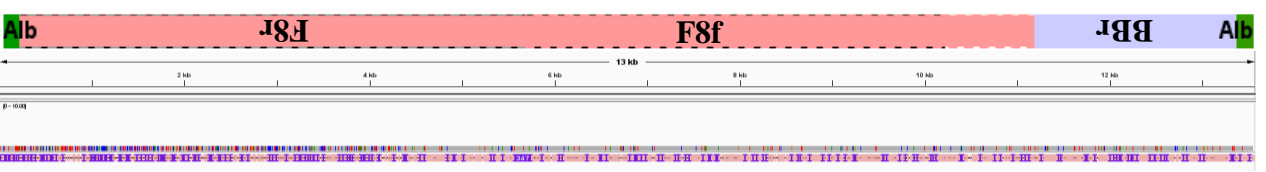
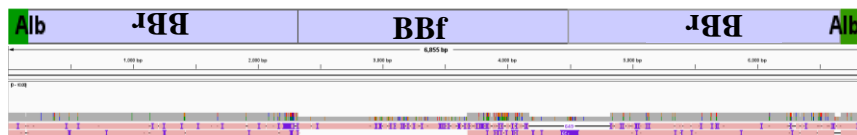


Figure S6D. Visualization of three-fragment insertions, specifically the insertion of one plasmid backbone fragment and two F8 fragments (continued).

E Three-fragment insertions: BB+BB+BB

BBrBBfBBr inserts = 0.01%. Shows 2 out of 2 reads.



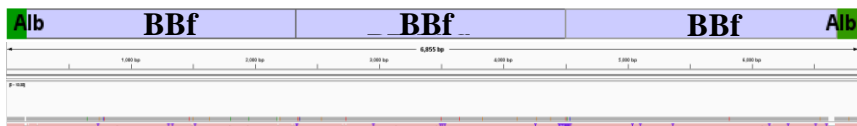
BBrBBfBBf inserts = 0.004%. Shows 1 out of 1 read.



BBrBBrBBr inserts = 0.004%. Shows 1 out of 1 read.



BfBBfBBf inserts = 0.004%. Shows 1 out of 1 read.



BBfBBfBBr inserts = 0.004%. Shows 1 out of 1 reads.



F Three-fragment insertions: F8+F8+F8

F8rF8rF8r inserts = 0.004%. Shows 1 out of 1 read.

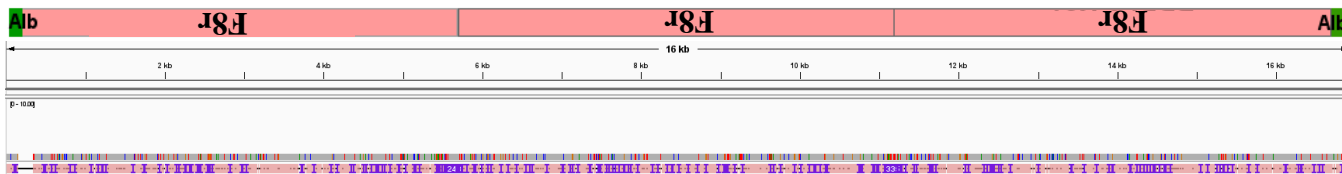
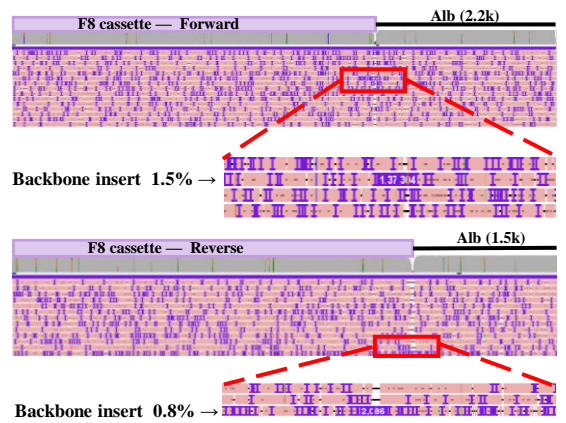
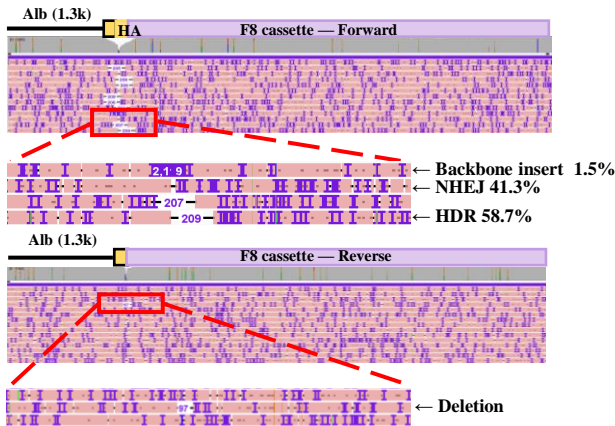
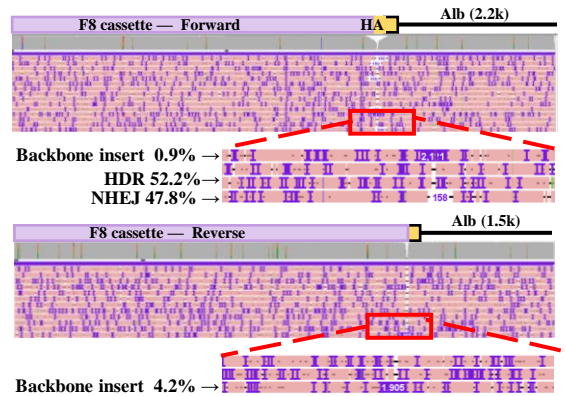
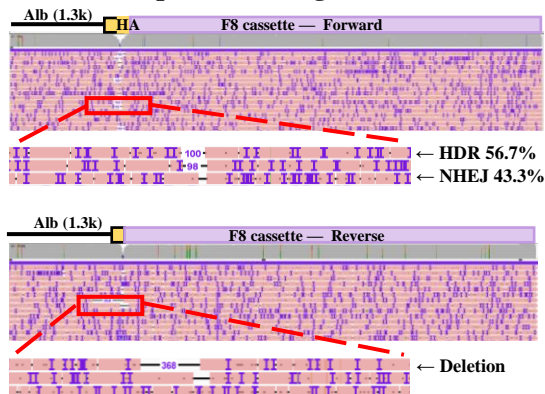


Figure S6EF. The visualization of three-fragment insertions, specifically the insertion of three plasmid backbone fragments (E), and three F8 fragments (F).

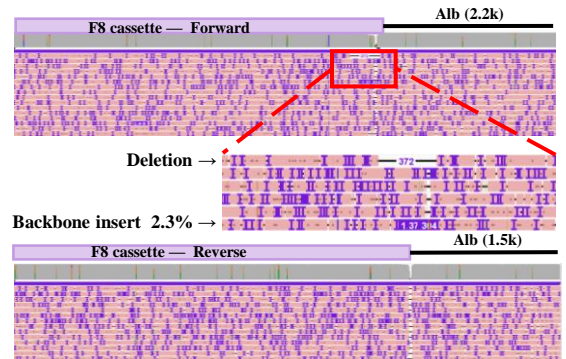
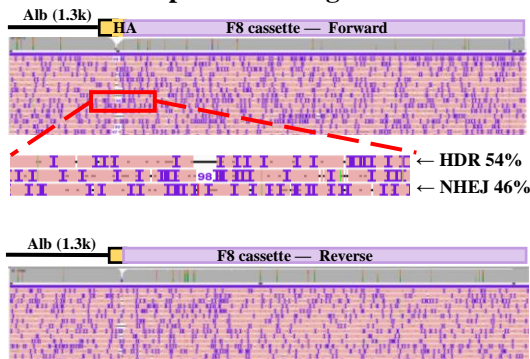
Insertion of pD-BDDF8-sg with HA190-0



Insertion of pD-BDDF8-sg with HA85-130



Insertion of pD-BDDF8-sg with HA85-0



Insertion of pD-BDDF8-sg with HA600-600

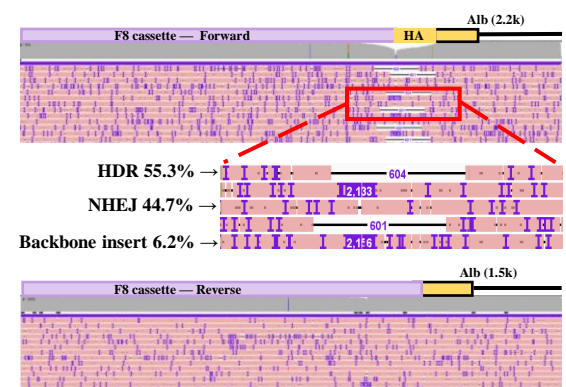
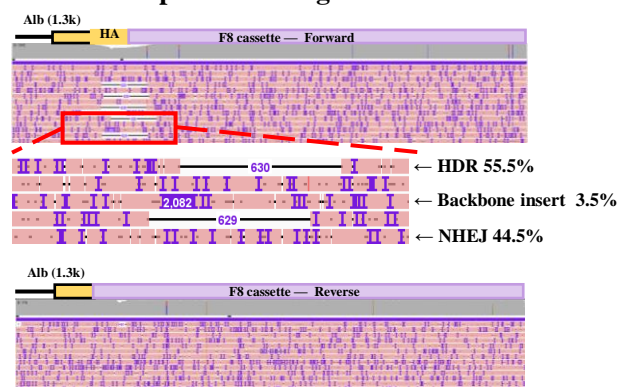
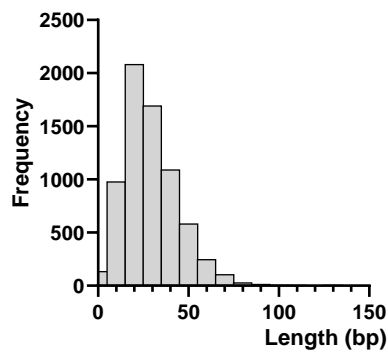


Figure S7. Visualization of PCR Products from Mouse Liver Edited with Donor Plasmids Featuring Various Homology Arm Lengths. Integrated Genomics Viewer (IGV) was employed to display the PCR products derived from mouse liver that had been edited using donor plasmids with different lengths of homology arms, specifically HA190-0, HA85-130, HA85-0, and HA600-600. The figure presents alignments of 15 randomly selected reads for each homology arm length.

A Length Distribution of Deleted Alb Fragments



B Length Distribution of Deleted F8 Fragments

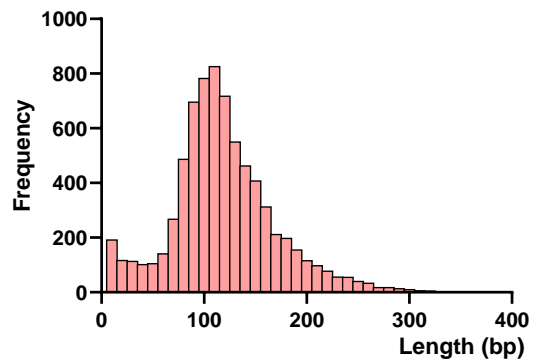


Figure S8. Analysis of Deletion Length Distribution in Junction PCR of pD-BDDF8-sg Inserts with Homology Arm HA85-0. (A) Length Distribution of Deleted Alb Fragments: This section presents the distribution of deletion lengths observed in the Alb fragments within the junction PCR of F8 donor inserts that utilized the HA85-0 homology arm. (B) Length Distribution of Deleted F8 Fragments: Here, the focus is on the distribution of deletion lengths found in the F8 fragments within the same junction PCR of F8 donor inserts, again using the HA85-0 homology arm.

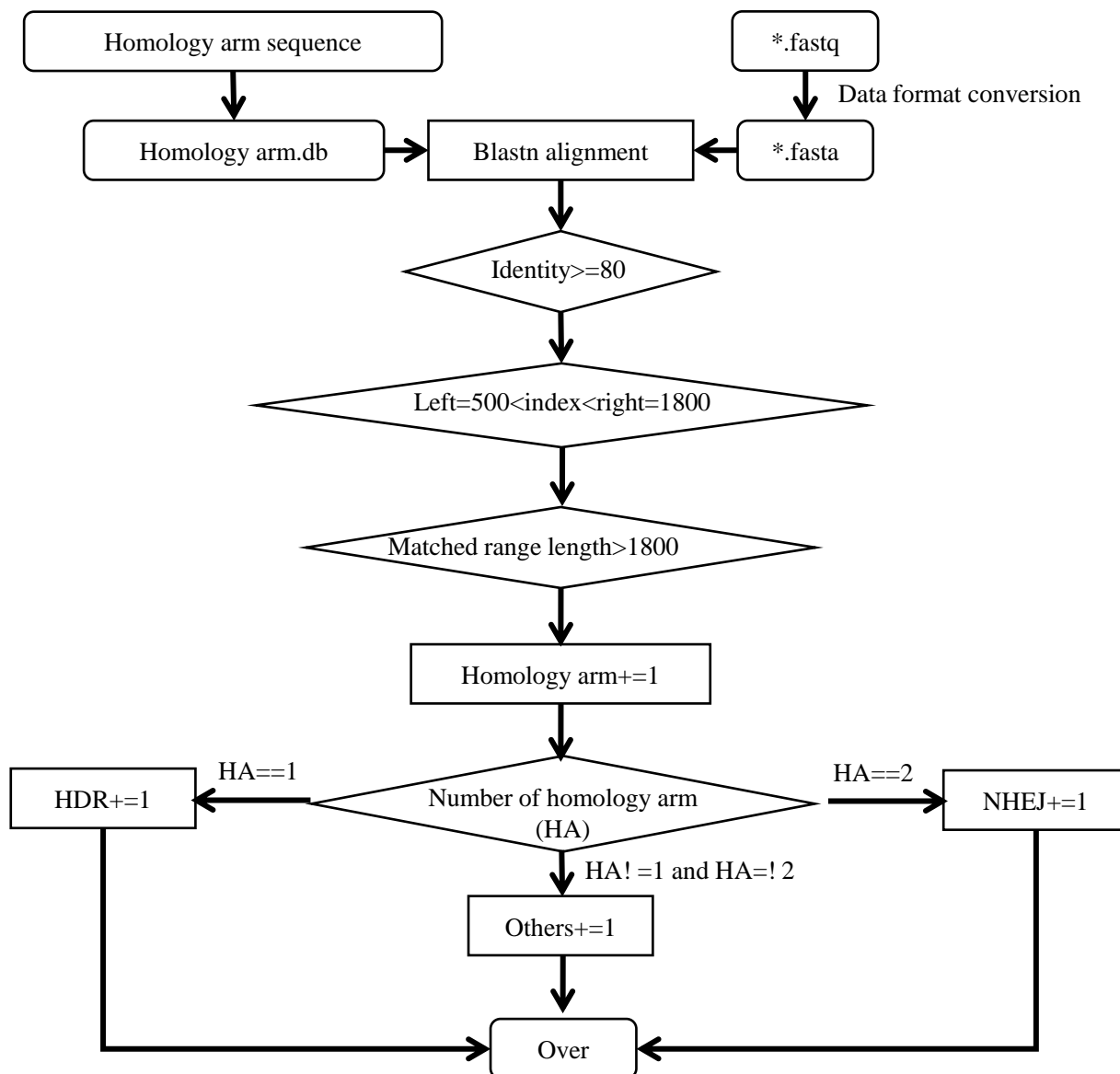
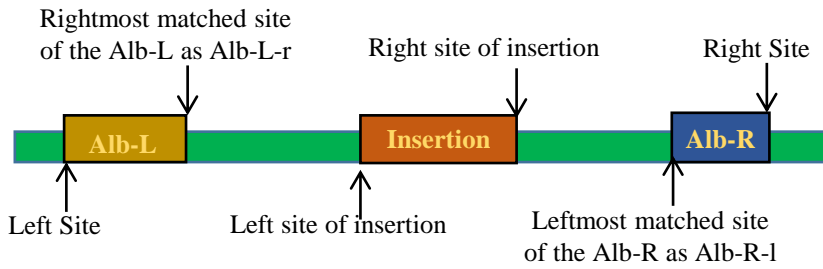


Figure S9. Workflow for Distinguishing Non-Homologous End Joining (NHEJ) and Homology-Directed Repair (HDR) in Donor Insert Analysis. This flow chart outlines the data processing steps used to differentiate between NHEJ and HDR events, with a focus on a donor with 600bp homology arms as a case example. The analysis employs the Basic Local Alignment Search Tool (BLAST) to search for corresponding arm sequences and determine the proportion of inserts mediated by each repair pathway. The steps include:

1. Aligning the homology arm sequences with the sequencing file and selecting reads with an identity score of 80 or more.
2. Restricting the range of alignment to ensure the homology arms are located near the target site.
3. Limiting the length of screened reads to exclude artifacts caused by incomplete Nanopore sequencing.
4. Classifying reads that match up to two copies of homology arms as 'NHEJ' and those matching only one homologous arm as 'HDR'. Reads not meeting either condition are categorized as 'Others'.

The reference sequence used in this analysis was generated by directly inserting the donor with homology arms into the cleaved genomic sequence.

A. Schematic definition of terms used in the data processing



B. The flow chart for processing data to analyze endogenous genomic DNA insertion

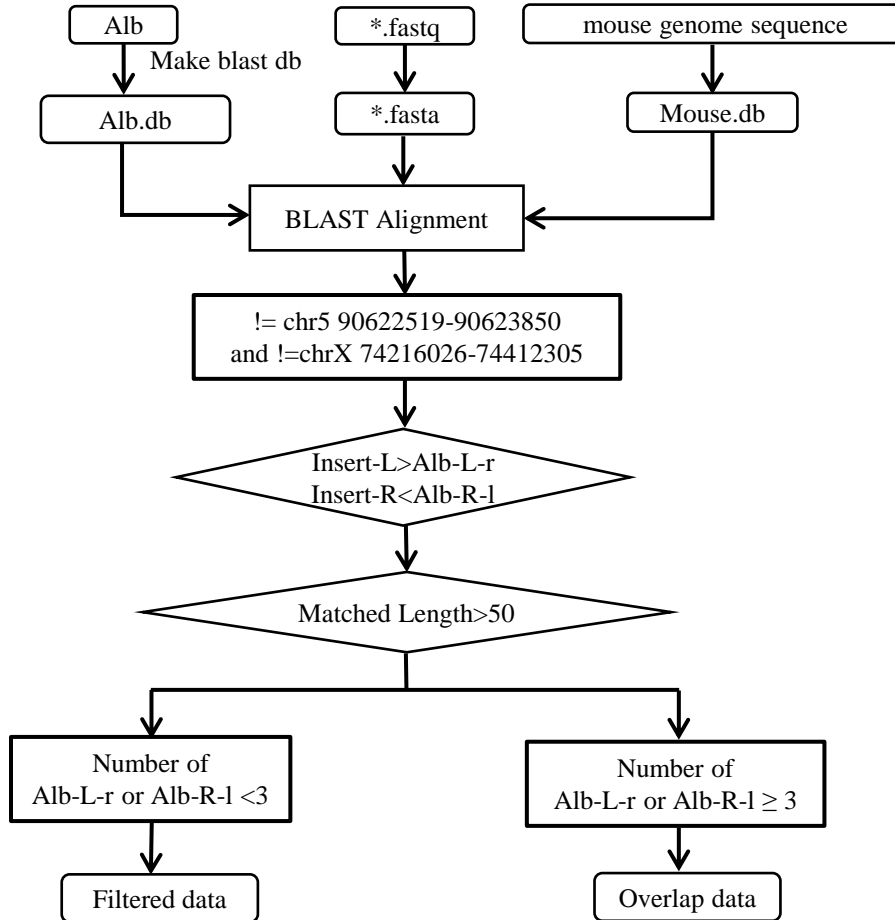


Figure S10. Data Processing Workflow for Analyzing Endogenous DNA Insertion. This flow chart describes the steps for processing data to analyze the insertion of endogenous DNA. It includes the following key components:

A. Definition of Terms:

Alb-L: The upstream homology arm near the cut site.

Alb-R: The downstream homology arm.

Alb-L-r: The rightmost matched site of Alb-L.

Alb-R-l: The leftmost matched site of Alb-R.

B. Steps for Data Processing:

Generation of database files containing the 332bp homology arm sequence (denoted as Alb), the mouse genome sequence, and the LINE-1 sequence.

Conversion of sequencing data format from *.fastq to *.fasta.

Alignment of the sequencing file with the homologous arm sequences and the mouse genome sequence (or the LINE-1 sequence).

Elimination of sequences matching the Alb gene range on chromosome 5 and the F8 gene range on chromosome X.

Limitation of insertions between Alb-L-r and Alb-R-l to ensure endogenous DNA fragments integrate at the target site.

Removal of indexes matched with a length of less than 50bp.

Consideration of occurrences where the number of Alb-L-r or Alb-R-l is greater than three as derived from the same amplicon, counting them as the same type of insertion.

Read #14 Alb-chr3-Alb

TCAATTACGACGAATGCAAGGTAATGTACGTTTACTGTGCATTGCCTATGGCTATGAAGGCAAACTCTAACAGCTCTGGCTAACTCTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #15 Alb-chr4-Alb

ACACCACAAAGCAATGCAAGGCACTGTAGCTTTACTATGTCTATGGCTATGAAGTGCAACTCTAACAGTCTGGCTAACTTTTTAAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #16 Alb-chr4-Alb

AATGCAAGGCACTGCTTTACTATGTCTATGGCTATGAAGTGCAACTCTAACAGTCTGGCTAACTCTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #17 Alb-chr5-Alb

CAGCAATGCAAGGCACTGTAACATTTACTATGTCTATGGCTATGAAGTGCAACTCTAACAGTCTGGCTAACTCTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #18 Alb-chr6-Alb

AGGCTTCTAGCAATGCAAGGCACTGCTAGCTTTGCCATTCAGGTTTCTTTATGGCTGCGAAGTGCCTAACAGCTCTGGCTAACTCTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #19 Alb-chr6-Alb

AGGCTTCTAGCAAGGCACTACATTTTACTATGTCTATGGCTATGAAGTGCAACTCTAACAGTCTGGCTAACTTTTTTCAACATCCATGTTCTTTTTTTTTT

Read #20 Alb-chr6-Alb

ATGCAAGGCAAGGTAACGTTTACTATGTCTATGGCTATGAAGTGCAACTCTAACAGTCTGGCTAACTTTTTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Read #21 Alb-chr6-Alb

CAATGCAAGGCAAGGTAACGTTTACTATGTCTATGGCTATGGCGCAAACTCCAAAGTCCATAAATCTTTTCAACATCCATCATTCTTTGGTTTCAGGGTCCAAACC

Figure S11A. Single Genomic DNA Fragment Insertion: The displayed read sequences show the insertion of a single piece of genomic DNA fragment at the Alb site (continued).

Read #35 Alb-chr11-Alb

GACACGGTAGCAATGCAAGGCAAGTACGTTTACTGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCAAGACGT
CTTAGCCCCAACATTGCAOCAAAGTAGGGAGAATCTCACTTTTTCAAATAAGGAGGCTCATTGAGTGATGTGGCACAATOCCTTTGTTOCCAGCACTCAGGAGGCAGAAGCAAGTGGATCTCTGAGTTTGAGACCAATCTGGTCTATTTAAC
AAGTTCCAGACCAGCCAAAGTTACATAGTGAGCCTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAAACATAATCATAATCATTCTTCTCTAAAACGATCAAGACTGATAACCACTTGACAAGGCCATAACA
GACAAGCAACAGCTGGCACTTTAGGCTTCAAGTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #36 Alb-chr11-Alb

CCGTCAAGCAAGCAAGGCAAGTACGTTTACTGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCA
AAGACGAGACCTGCCTGCTCTGCCTCCOGAGTGTGGGTTAATTTTTTTTTTTTTTTTTTTTTCGAGACAGGGTTCTCTGTGTAGCCCTGAGTGTGGGTTAAAGGCATACCTAGTCTGGTCTGAACTTTTTTTTCT
TTTAAACATGTCTTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAAACATAATCATAATCATTCTTCTAAAACGATCAAGACCGTGATAACCACTTGACAAGGCCATACAGACAAGCACAGCTGGCACT
CTTAGGTTCTCAGTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #37 Alb-chr12-Alb

AGTCAATGAGCAATGCAAGGCAAGTACGTTTACTATGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCA
AAGACGAGACCTGCCTGCTCTGCCTCCOGAGTGTGGGTTAATTTTTTTTTTTTTTTTTTTTTCGAGACAGGGTTCTCTGTGTAGCCCTGAGTGTGGGTTAAAGGCATACCTAGTCTGGTCTGAACTTTTTTTTCT
TTTAAACATGTCTTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAAACATAATCATAATCATTCTTCTAAAACGATCAAGACCGTGATAACCACTTGACAAGGCCATACAGACAAGCACAGCTGGCACT
TTAGGTTCTCAGTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #38 Alb-chr14-Alb

CAATGCAAGGCAAGTACGTTTACTATGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCA
AAGACGAGACCTGCCTGCTCTGCCTCCOGAGTGTGGGTTAATTTTTTTTTTTTTTTTTTTTTCGAGACAGGGTTCTCTGTGTAGCCCTGAGTGTGGGTTAAAGGCATACCTAGTCTGGTCTGAACTTTTTTTTCT
TTTAAACATGTCTTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAAACATAATCATAATCATTCTTCTAAAACGATCAAGACCGTGATAACCACTTGACAAGGCCATACAGACAAGCACAGCTGGCACT
GTTCCATTTGTAGAT

Read #39 Alb-chr15-Alb

GCACCTGCAACAGAGGAGCAATGCAAGGCAAGTACGTTTACTATGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGA
TGCAAAGACGCGCTGCTACTTCCCTTTTAAAGTCTAGTATGGTTTTGTTCAATTCATCACCTGTTGGATGTGCTTTCCTGTTTTTTCTTTAAGGACTTCACTCTGTTGATTGTTTCTTTTTCTTTAAGGACTTGAACCTAAACA
CATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAAACATAATCATAATCATTCTTCCCTAAAACGATCAAGACTGATAACCACTTGACAAGGCCATACAGACAAGCACAGCTGGCACTCTTAGGTTCTCAGATGTGGTC
ATCAGTTTGGGTTCCATTTGTAGATAAGAAACTGAGGTGC

Read #40 Alb-chr16-Alb

ACTAGACCAGCAATGCAAGGCAAGTACGTTTACTATGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCA
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TGTGTCATCAGTTTGGTTCATTTGTAGATAAGAAACTGAGC

Read #41 Alb-chrX-Alb

GCACCTCAGGCTCTAGCAATGCAAGGCAAGTACGTTTACTATGCTGTCATGTCATGATATTGCTGCAACTCTTAACAGCTCTGCTAATACCTTTTCTAACATCCATCATTCTTTTGTTCAGGGTCCAAACCTTTGTCACTAGATGCA
AAGACGAGACCTGCCTGCTCTGCCTCCOGAGTGTGGGTTAATTTTTTTTTTTTTTTTTTTTTCGAGACAGGGTTCTCTGTGTAGCCCTGAGTGTGGGTTAAAGGCATACCTAGTCTGGTCTGAACTTTTTTTTCT
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AAGCACAGCTGGCACTTTAGGTTCTCAGTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAACTGAGGTGC

Figure S11A. Single Genomic DNA Fragment Insertion: The displayed read sequences show the insertion of a single piece of genomic DNA fragment at the Alb site (continued).

Read #42 Alb-chr10-chr3-Alb

CCAAATGCAAGCAATGCAAGGCACGTACGTTTACTATGTCATTGCCTGTGGCTGTGAAGTGCAAATCAACAGCTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTCAGGGTCCAAACCTGTCACTAGATGCAAAAGCGCCT
AGCATCCGCTGACCATCTTTGAACTCAGATAATCACAGCCAGGATGACTCTCAGGGTGTCTCTCCATCCAGTGTGGCCAGAGTGTGTCAGAAAGGTGGACTCAAAGCAAAAGGAGGATCATACCACTGAGTGTCTCCAGGATTTT
AGGCTAGTAAAAAACAACAACTAAATAGTAAATAACCTAATGATGTAGCAGAGGAGCTAGATGCACAGAGAGGGGAGAGTCTCGGGTCAAGGCAATAATCTCTAGATGAGATTTTACCTAGCAGAAAGGAGTCTTAAACCATC
CAACACCAACCTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATATCATTTTTCTTAAACGATCAAGACTGATAACCAATTTGCAAAAGAGCCATACAGACAAGCAGCAGCTGCACTCTGGAGTCTTCAGCTATGTCAT
CAGTTTGGGTCATTTGTA

Read #43 Alb-chr2-chr9-chr13-Alb

GCACACTAGCAATGCAAGGCACGTACGTTTACTATGTCATTGCCTATGAGTGCAGAAATCCACAGCTCTGCCAATCTTTCTAACATCCATCATTCTTTGTTTCAGGGTCCAAACCTGTCACTAGATGCAAAAGCGCCT
TAGCTTGCCTGAGAAAAGGAAAGCAAGAGGAGATGATGAATGCCATGGCATGAGTGTCAAGGTCACACAAAACACATCTCTGCTCTATTACATGGATCCCAATGTGAACCTTAGGTCCTCAGGCTGGCAGAAAACAATGCT
TCCTCTGGCATCTCACCAGCACAACATTTAAACATGTAAGAGAGGGATTGCCAAATATCAACAAAGAAAGAGGAGGCTCAAGGGAGGGAAAGAGCCTGGGGCTCTCTGAAGGTCAGTGCAATCTTTACAGCTTTGGAACCAATGGTCCAG
TGCCCTCTCACCACCAATATTTCTCTGTTATGACCAGAAATGTTCTCAGATGCTACCAAGCTTAAGGAGCTCTCTTTGTCAGACAGCAGCAGGCGGAATACTACAGGACTCTTTGCTGTCTGGCTCTTTATCACACTACATGTTCTC
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AGACTGATAACCAATTTGACAAGAGCCATACAGACAAGCAGCAGCTGGCCTCTTAGGCTTCCAGTATGGTCATCAGTTTGGGTCATTTGTAGATAAGAACT

Read #44 Alb-chr5-chr1-chr2-chr8-Alb

GCACCTGTAGTCAATGAGCAATGCAAGGCACGTATGCTTTACTATGTCATTGCCTATGAGTGCAGAAATCCCAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTCAGGGTCCAAACCTGTCACTAGATGC
AAAGAGCGCTTAAACACCGTGGATCTATGTCACAGTGTGTGTTACTATGCACTGAAGATTCTGGCTTAGTACAAGCAGTAGAGGTAATCTAGAATATAGATACTTTCTGGACAACCATACTAGGAACAGCGCAAAGTAAATGCTA
TGCTATAAACATGCACCAATTTAAATCTGAGTGGGAGCATCTGGCAAGTACTGACTTATAAGTTTATAAGGAGACTGTTCACCTTGCCTCTAAGTAGGTAATGTATAATTAATTTACAAAATGACTTGGAGAAACCCAAAGCA
AAGGAATGTAATAGTTTTATGAAAAAATAAATCTAGAAATTTTACAGTGTGCATGTCCAAATAGGTCACCCATGTTTACACATAAATGCAATAAAAAAGAAAATCACTGCTACTGTTTCCTAGTAATCAATAAATGACTC
TAGAGATTTAAACAATTTCAAGTTAAACAAAGTATAGGTGATAGGTTTCAAATTTGCCAAGGAACTACTATGTAACATTTCTCTATGTAACATACAGACATAAGACAGTGCATCTGCTGAGGCTCTGCTTGAGTACTGCATAC
ATAATTTGGCAGGCTGCTTTGCTCCAAGTACCGCAGTGGAGCTGCAAAATGAAAGGAAAGTGCCTGCAACAGGGGAAATGTATTGAGCAGTATTAATAAAAAAGAGGAAATGGTTTAGGAGAAAATGTCACAACTTCACTCTGGAC
TATGTTGCAAACTAGCTCTCAAGTCAGTACCTAAATCTGTTCTTATGCTGTTCATCAACCCCTTCTGACTGAACTATCAAGCTGCTGCTGCTCTATTTTAAATGTTTCTGAAAAAATAGGACAGCAGTTTAACTTAGCC
ACAAAAGTTGAAGCAACATTAATTTAAAAAATAATGTTCACTAACAGAAATGCACGGTGGGTTCTCTTCAAGCAGCTACTGTTGTTTTCTGTAATCCATAGTCTCTACACCTTACTCTAAGGCAGATCCAAATGCTGTGCTGG
CCAGCCTGTCACCAAGTTTATACAGAAATGATGCAATACTGGAGTATGAATGACTAATTTAAACAGTGGAAAACTCTAATAAAGAACCCAAATCTGCAAGATCTAAGCAGATAGGTTTTCTGTAAGAAAATAATGAAAG
CTATGCTTTTGATATCCTAATGACTATTTTTAAATAAAAATAGGCTTAGATTTAAATTACTGAATAATTTAAATCAAACTCTGCACTCTCTTTTCCCTACTGTTTCTATATTTGATGTGCCATAAAGGCTCAGCTCATATGT
CTACTTTATTTGGGGTTTTAGACTTAGAACCATAACTATACATTTTTCTTTATGAATTACTTACATCTGGTTTTGGTTATAACAGCAGAAAAATGAGTAAGACTGCCATAATAGGTTTACTGCTGTGAACAGATACCAAGCAAA
GGCAAGTCTTATGATGAAAACAAATTTAAATTTGGGGTACTGACAGGTTGAGAGGTTGAGTCCATATCATCAAGTGGGAAACATGGCAGTATCCAGGACAGCAGAGCTGAGAGTCTATATCTTCAACAAAGGCTGCTAGGGGAGAAGA
CTGACTTCAAGGCACCCAGGGGGCCCAAGCCACACCCAGTGCACACCTACTCCAAGTGTCAACCTATTTCCAACAGGGCCACCTCCGGGAGCCACTCCCTGGGTCOAAGAAATCCCTTAAACCATCACAAAGCAAAATC
TATTTATGTTAGCTTACCACATAGTATGTTCTGAGGAAATAACTCTCTGCTCAACATGTGCAAAAGATGCTATATTAACAAAGGTTGACAGAGTCCATCTGATCAAGGGGATCAAAAATGGAAGGGAGTGGGAAGTCA
AAATATCACTTTTTCAGATGATATGATAGTATATATAAGTGAOCCTAAAAATTCACAGAGAACTCTTAAAAOCCATAAAACAGTTTGGGCAGTAGCTGGACATAAAAATAACTCAAACAAGTCCAGTCTCTTTCTCTCTTTTTTTTT
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GAAGATCTCAGAGGACACATCTCCATGCTCAAGTATTGGCAGATCAATAAGCAAAAATGGCTATCTTCCAAAAGCAATCTACAGATTCATGACACACCCATCAAATTTCAACTCAATCTTCAACAAATGAAAGGAGCAATTTGC
AAATTCATCTAGAATAACAAAAAACCTAGGATACAAAACCTCTCTCTCAAGGATAAAAGAACTCTGGTGAATCACCATGCTGCACTAAAGTTTATTACAGAGCAATTTGGTAAAAAAGTGCATGGTACTGGTATAGAGACAGACAAG
TAGACCAATGGAATAGAATGGAAGCCGAAATGAAACCCACACCTATGTCATGATCTTCAGACAAGGAGCTAAACCCATCCAAATGAAAGAAAGACAGCATGCAACAAATGGTCTGTAACAACTGGTGTATCATGCAAGAAG
ATGOGGATCGATCCATCTCTCTGACTAAGGTCAAATCTAAATGGATCAAAGAACTTCACATAAAACAGAGACACTGAAACTTATGAGAAAGTGGGGAAAAAGCTGAAGATATGGGCATCAAGAAATCATGCAACCTCAGG
CAACTATCTGGGACTAAAAACATGATCATAAATCATTTTTCTTAAACGATCAAGACTCAACCAATTTGACAAGAGCCATACAGACAAGCAGCAGTTGGCCTCTCTGAAGCCTCAAGTATGTCATCAGTTTGGGTCATTTGCGAGATA
AGAACTCAGGTGCTC

Figure S11B. Multiple Genomic DNA Fragments Insertion: The illustrated read sequences demonstrate the insertion of multiple pieces of genomic DNA fragments at the Alb site.

Read #49 Alb-F8-chr7-Alb

TCAATGAGCAATGCAAGGCACGTACGTTACCGGATGTGTCATTGGCTATGAAGTGCAAATCTGGAGACGCTCTGCTAAGACTTTTCAACATCCATCAITTTTGTGTTTCAGGGTCCAAAACCTTGTCAGTATAGGTTTCATC
TGTTGATGGCCAGATAAATTTGGTCTTTGTACTCTTACCAGTTGGCAGGGCCATTTGTTCAAAATTTGACTTTTCAAACTCTGTCATGGGGTGGGCACTAAGGAGCATACCAGTCTCTCTCAGCAGCAATGTAATGTACCAAGTT
TTAGGATGCTCTTTGGCACTGAGCGAATTTGATAAAGGAAGGAGGTTGTCATCATCAAACCTGACCACATCCATTTACAGAACTAGTAAGATCATCATAGTCTTCGCTTTTCATCATCTGCTAGTTGGGGTTCTTTGGA
CAGCTGTTGACTTTGCATAAATCCATGCTCATGTTGGTGGGAAGATAATGACAAAACAGTAGAACTGTGAGGTGTCATCAAGAGTGGTGGAGCATAGGAAGTTATGGCGAGATTTCCAAAGGACGCTGGCGATGGTCTCA
GCACAAGAGTGGCCACTTCCAGGAATATTGAGTGCACTTCAGGAAGCGGTGCCCATTCATCAGATGCCAATAGACTGATTTCTGTGGCATCCAACTCAGACTGGCAGAGAACTGTTTACATAACCAATTTGATGGTGGATTCAGGC
CAGGCCCTGGAGAGATGCAGATCCCATCTGCATCAAGGAGTTCTTTGTTCTGAGTGCCAACTTTCTTTCATCAAATAACAGAAAAGTAGTATAAATTTGTGCAAAAGTCTGTGCCCTTTCTGGCCAACTCTCTCTCACATA
CGAATAGGGCTCCACCAGCAATTCAGTCTTTTACCAGTTGCACATGAGAAAGATATGAAGTAGGAAGGCACAGTGGTCCAGAGCCATTTGGACATTTCTTCCAGGACTGGCAGACATATGATGGCTTCCACAGGGAAGACTTTA
TCAATCTCTTTCTCCCTTTGACTGGTGTGATCATCATATTTCAAGCTCCTCAGAAAGCTTTCCAGTAGGAACAGACACCAACAGCATGAAGACTGACAGGACGGGAAGCCATGTTCTTAGTAAATTAACACTGTATATAAACCAGCTGGA
TGTAGGACTAGCAGACCCATCCAGGGTGGCTGGCTGAGTGTCTTAAGTGTACCGTAAACCACAAACAGAGTCTTTTGTACAGACTGAGGTGTTGAATGAAAGATTTTGTACTTAGGAGGAAATCTTGGCTCCACAGGCAGCT
CACCGAGTACTTTGACATAGTCCCACTACAGTCCACTGCACCCAGGTAGTATTTAGAAGAGGCTGGCTATGTACAGAGCTACCCATTCACCCCTTCTCAGAGAGCTCAAGTGTTCGGTAACTCTGTTTCACTTTTGTGATTT
GTTGTTGTTAGACAGATCAAGCATTCAGGTACTGCAGACTCCCGCTCAGGATCTGGGTAGCTGGAATTAAGTGTGCATAGCAAGTCTATGTTGCCATATATAAAGTAAAAATACAAATGGAAAATCAAAAAGGTGATTA
TGACTTGCACCAACATATTAGTCAATGCAAAAGCAAGCCATCTCAGGTTAGCAACTCCAAAATCTGGCCCTCTGGCCAGCTCAGATGCTCTTTGAGTCAGATGCTCTGGCCAGGGTGGTACATTTCTCAGTATGAATGAATCTAATG
ATATTAATTTATATAGCAATATAAACAATGGGGTTAAGATGTACATAGTACAGCTGCAAGTACACACACTTGAACACACATGCACATGCACACATAACAGGATACTCAATAAAAACTGGAAAGTCAACAAAATTTTTTCACTGTTA
TCACTACTTATATTCAGATAGCTAATCTATGTTATGTTCTAAACAGACACTTAGAATGGGTGGCTCAGATGCAAGCTGGAAGTGAAGCAATATATAGACAAATTCACATTTGAGAGTCATGAGATGGTAACTTTTCAATTA
TAAATTTGGATGAACACATCACTAATTTGAAACAATCTTTCTCCAGTACTATACTGGGACTTAAAAACATAATCATATATTTTTCTAAAACCATCAAGACTGATAAOCATTTGCAAGAGCCATACAGACAAGCACAGCT
TACTTTAGGCTCCAGTATGCTATCAGTTTGAATTTCAATTTGTAGATAAGAAAAC

Figure S11D. F8 and Genomic DNA Fragments Insertion: The depicted read sequence showcases the insertion of both F8 and genomic DNA fragments at the Alb site.

Read #50 Alb-F8-chr3-BB-Alb

GAATCAGGCAGCAATGCAAGGCACATGGTTTTACTATGCTATTGGCTATGATACAAAATCTAACAGTCTGCTAATACTTTTCAACATCCATCGTTTCTTTGTTTTCCAGAGGGTCCAAAACCTTGTCAGTATGCAAAAGCGC
CGGGAGCTGCATGTGTCAGAGAGTTTTCTACGTCATCTTGAACACTTGCACAGGGCAATAGGATCATATAACAGOCATACCACATTTGTAGAGGTTTTGCCCCCTTTTAAAGCCTCCACCTCCCTGAACTGGAAACATAAAATGAA
TGCAATTTGTTATTTGTTAACTTTGTTGCGAGCTTATAATGGTTACAAAATAAAGCAATAGGCATGCAAAATTCACAAAATAAAGCATTTTTCTGCAATCTAGTTGTGGTTTTGCOCAACTCATAGTATCTTATCATGTCTGGATCCGC
CCAAAAGGAGATCCGACTCGTCTGAGGAGGCAAGGCGAGACGGGAGGCGGAGGCGGAGCAGGCGGGAAGGAAAGGTCGCTGGATTTGGGGGCGGAAGGGACGTAGCAGAGAACTCCACGAGAAATCCAGGTGGCAAC
ACGGGGGAGCAGOCATGGAAGGACGTTGGCTTCCGCAACAACAGCTGTCAAGTGCACACAGCTGAGCCCTGTCCAGCAGCGGGCAAGGGGAAAGGATAGCGGAAGGTTCCGCGCTGGCAATAGGGAGGGGGAAAGCGAAATGCC
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TGCGGGCCGAAACCTCCATCTCAGGGCAATCTGGTGCACCCAACTCTGGGAGGTGAATTCAGGTAGCAGGTGATGAAAGGTTGAGGAGTTCACCAAGCTGTGAAGGACTCTGATTTCCCTGAAAACCTTTACTTTTGCATTT
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CCTTCTCAGGTAATCTACTTGGGACTTAAAAACATAATCATATATTTTTCTCCAAACGATCAGACTGATAAOCATTTGCAAGAGCCATGAAACCAAGCACAGCTGGCCTCTAGGCTTCCAGTATGCTCATGGTTTGGTTGCCA
TTTTG

Figure S11E. F8, Plasmid Backbone, and Genomic DNA Fragments Insertion: The exhibited read sequence displays the insertion of F8, plasmid backbone, and genomic DNA fragments at the Alb site

cgactcgagactcgagccccgggtactctgccagcagagcttgcaccaaccccgaagggtccacacgggactccccagggaccctaagacctctggtgagtgatcacagtgcc
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ggtgggcaggggagtggggtgggtggatgggggacttttggatagcattggaatgtaaatgagttaaatcaataaaaaatggaaaaaa

Figure S12. The consensus sequence of L1MdA_I in the LINE-1 family.

Read #1 Alb-L1-Alb @6054e536-fd9d-4ce6-bf33-b065bed95978

GGCACCTCAACTCCTGAAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTATGAAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCA
AACCTTGTCTAGTAGTGAAGAGCGCTTAGTCAAAATTTAGAAATTTTAGGGTCTTATATATACATATCATATCATCTGCAAAAAGTGATATTTGACTTCTCTTTTCAATTTGTATCTCCTTGATCTC
CTTTTGTGTGCGAATTTGCTCTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATATACATTGACAAGAG
CCATACAGACAAGCGCAGCTGGCACTCTTAGTCTTCACTATGGTCATCAGTTTGGGTTCCATTTGTA

Read #2 Alb-L1-Alb @88a19c42-27f1-4911-b00a-1e132a1b9c61

ACATGAGGAGCAATGCAAGGCACACTTTGTTTACTATGTCATTGCCTATGGCTATGAAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCCAAACCTT
GTCCACTGTAGTCAAAAAGAGCGCTTAGTCAAAATTTAGAAATTTTAGGGTCTTATATATACATATCATATCATCTGCAAAAAGTGATATTTGACTTCTCTTTTCAATTTGTATCTCCTTGATCTC
GTACCACTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATAGCAAAAATTTGACAAGAGCCATACAGACAAG
ACCAGCTAACTCTTAGTCTTCACTATGGTCATCAGTTTGGTGGGTTCCATTTGTAGATAAGAAAC

Read #3 Alb-L1-Alb @d5a82961-5d4f-4c2e-b8e2-232b26dbf4d8

TTACCTGATTACCTCAAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTATGAAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGT
AAACCTTGTCTAGTAGTGAAGAGCGCTTAGTCAAAATTTAGAAATTTTAGGGTCTTATATATACATATCATATCATCTGCAAAAAGTGATATTTGACTTCTCTTTTCAATTTGTATCTCCTTGATCTC
CAGCTCAAACTTTGCTCTTAATACTTACAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCACAATCATTTTTCTAAAAAGTCAAGACTGATAACCAATT
GCAAAAGGCATACAGACAAGCAGCTGGCACTAACAAGAGTCTTCACTATGGTCAATGGTTTGGAGTCCATTTGTAGATAAGAGCTGAGGTGC

Read #4 Alb-L1-Alb @0d0a64cb-40d1-46c7-bbae-5601d14b962e_R

CCTTACGTCGAAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTAAGAGTGCAAATCCAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCCAAACCTTGTCA
AACCTTGTCTAGTAGTGAAGAGCGCTTAGTCAAAATTTAGAAATTTTAGGGTCTTATATATACATATCATATCATCTGCAAAAAGTGATATTTGACTTCTCTTTTCAATTTGTATCTCCTTGATCTC
TTGACACCTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATAACCAATTGACAAGAGCTTT
TTCATACAGAGAGACAAGCAGCTGGCACTCTTAGGCTTCACTATGGTCAATGGTTTGGAGTCCATTTGTAGATAAGAAAC

Read #5 Alb-L1-Alb @845b268b-2288-4aa5-b915-53780c9fa804_R

AGTCAATGAGCAATGCAAGGCAGTACGTTTACTAGTCAATGGCTATGGCTAAGAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCCAAACCTTGTCA
CTAGTCAAAAAGCGCTTAGAGCTGGATATAAAATTAACCTCAAAAGTCAATGGCTTCTCTACAAAAGATAACAGGCTGCAAAAAGATAAGAAACAATACCTTCTCAATAGCTCACAATAA
TATAAAATACCTTGGTGTACTAATAAGCCTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATAACCAATT
ATTCTACAAGAGCCATACAGACAAGCAGCTGGCACTCAGTCTCATGACTGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #6 Alb-L1-Alb @9aca963b-8fb1-4709-905c-f0ba2759f766

GAGCCATAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTAAGAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCAAAGCCATTTCTTTGTTTTCAGGGTCCAAACCTGTA
TAGATGCAAGAGCGCTGGGAAGTAGACAATAAAGAAACCCAAAGCATGAGCAACGCTGAAGATAGAAACCCTAGGAAAGAGATCTAGAACCATAGATGCGAGCATCAGCAACAGAAATACAGAAATGG
AAGACAATCTCAAGGTGCAAGAGATTCCATAGAAACACTCTAGCTTACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATAACCAATT
CTGATCAAGACTGATAACCAATTGACAAGAGCCATACAGCCAGACAAGCAGCTGGCACTCTTGGAGTCTTCACTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #7 Alb-L1-Alb @92f1ed7a-d649-470f-bc21-3215f61678e1

GGCTGACAGAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTAAGAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCATCATTCTTTGTTTTCAGGGTCCAAACCTTGT
TCACTAGATGCAAAAAGCGCTTAGATAGATCTTATTAATAAATGGACTTCCCAACCCAAAACCTATCAAAAAGACAAGGAAGGCACTTCAATCTCATCCAAAGTTAAAACTTTCCAGAGGAACCTTCCAAATCTG
AATATCTATGCTCCAAATGCAAGGCAGCCATTCATTAAGAGACTTTTAGTAAAGCTCAAAAGCATTACCTCATACACAATAATAATAGGAGACTTGGCTACTTTTCAATCAATGGATAGATCTGCTG
CAGAAAACTAAACACATCACAACCACAACCTTCTCAGGTAACATACTTGGGACTTAAAAACATAATCATAATCATTTTTCTAAAAAGTCAAGACTGATAACCAATTGACCAAGAGAGCCATACAGACAG
CACAACCTAACACTCTGAGGCTTCCATGATGATCATTGGGTTCCATTTGTAGATAAGAAAC

Read #8 Alb-L1-Alb @7a05acea-6e10-403a-bfd9-d05e5b25ef5c_R

ACCACATCAAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTAAGAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCCAAACCTTGT
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ACCAGCTGGCAGCTTAAATGTTCACTATGGTCACTAGTTTGGGTTCCATTTGTAGATAAGAAAC

Read #9 Alb-L1-Alb @05d5093e-f9d6-4514-8d26-c3a74881845f

ATTACCTCAGCAATGCAAGGCAGTACGTTTACTATGTCATTGCCTATGGCTAAGAGTGCAAATCTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTTCAGGGTCCAAACCTTGT
CACTAGATGCAAAAAGCGCTTAGTCAAAAATGATCCCCACAGTGGTCAATTTGATGGTGCAAAAGAACTAAAACCATCCAGTGTATAAAGACAGCATTTCAGCAAAATGGTGTGACAGTATCATG
TAGAAGAATGCAAGCTGATCCATTCTATCTCTGTACAAAACAGTCTAAGTGGATTAAGGAAGTGCATAAAAATAGAGACACTGAAACTTATAGAGGGGAAAAGTGGGAAGACCTCAAAGATGTGAG
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GGTGACAGCAGTCTGTGGGATGAGAGAGGAGAACACTGCTCCATGCTAGTGGATATTGGCTGGACAGCCACTGTGAAAATCAGTTTGGCATTCTCAGAAAAATTTGTCATAGTTTCTACT
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AGACACTATTGGGATGCCAATTAACCTTGTGGCAGGACCTAACATAGCTGTCTCCTGAGAGGTTCTGACGGTCTGACTAATACAGAAATGGATGCTCAGCTCATCCATTAGATGGAGCATAGG
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GGATGTGAAAATTAGCAAGGACTTTAGGATTTGCATCTCATGGCCGCAAGGAGCTGACATAGTAAACGTAAGTGCCTTGCATT

Figure S13. (A) The representative read sequences display the insertion of a single LINE-1 fragment at Alb.

Read #10 Alb-chr1-L1-Alb @450abd0c-3536-4496-b7d3-78d412798077_R

ATGC AAGGCAAGCTTAAGCTTTACTATGTCATTGCTTATGGCTATGAAGTGAATCTCAACAGCTCTGCGAGAAGCTTTCTAACATCCATGATTCTTTGTTTCCAGGGTCGGTACCTTTGCTACTAGATGC
AAAGACGCCTTAGCGTGCACAGGGTCAAGTCAATTGGAGGTGAAGTGTCCATAAGGTCCTAATTAACCAAAAATCTATCTCCAATTGATATAACCTTTATAAAGAAAAATATTAGTTTACTCCAAATGAT
TTCAGTGCAGTGAAGGCCAAACAATTTCCAAAGCAAATGGACTCAAGAAACAAGCTGGAGTAGCCATTATATGGATAAATCTACTTCCAAACCCAAAGTTATCAAAAAGACAAGGAGGGACACTTC
ATACTCATCAAAGTAACTCTCCAGAGAACTCTCAATTCCTAAACACATCAACCCAACTTCTCAGGTAAGTACTACTTGGGACTTAAAAACATAATCAATAACTATTTTCTAAAAAACCATCA
AAGACTGATAACCATTTGACAAGGCCATACAGACAGTACCAGCTGGTACTCTTAGGCTTCAGTATGTCATCAGTTTGGGTCCATTTGTAGATAAGAAACTG

Read #11 Alb-L1-chr15-Alb @c7c6b1ba-fd1e-4ca1-aded-92dd0734e698

GCACCTGCAACAGAGGAGCAATACGAAGGCAGTACGTTACTATGTCAGAGCTGCTATATGAAACATGAAGTGAATCTCAACAGCTCTGCTAATCTTTCTAGCATCCATCTTTCTTTGTTTCA
GGCTCCAAACCTTTGCTACTAGTACGAAGAGCGCTGCTACTCTCTTTTAAAGTCTAGTATGGTTTGTTCATTTCCATCACCTGTTGGATGTGCTTCTCTTTTCTTAAAGACTTCTACTCGTGT
TGATTGTGTTTCTCTTTCTTTTAAAGACTTGTAACCTTAAACACATCAACCCAACTTCTGAGTAACTATCTGGGAATAAAAACATAATCTAATACTTTCCCTAAAAACGATCAAGACTG
ATAACCATTTGACAAGGCCATACAGACAGGACCAGCTGGCCTCTTAGGCTTCACATGTGTCATCAGTTTGGGTCCATTTGTAGATAAGAAACTGAGGTGC

Read #12 Alb-L1-chr17-Alb @9df79b4a-32fc-4a67-b4d7-d517944ee53e

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GAAAATATTTCTGTCTCAAAAACTCTCAGGAGAAAAAGACAGGGCCCTACTCAGAGTGAAGGGCTGGGGAAAAACAATTTCCAAAGCAATGAGAACTGGAGTAGCCATTTAATAT
GGATAAATCGACTTCAACCCAAAGTTATCCAAAAAGACAAGGAGGCGCTTCTATCCATCAAGGTAAAACTCTCAAGAGAGGAAGTCTCAATTTCTGAATATCTACGCAACAAATGCAAGGGCAG
CCACATTCATAGAGACACTTAGTAAAAACAAAGCATACATGACCTCACACAATAATAGTGGAGGAGCTTCAACACACCCTTTCTCAAAGGACAGATGTGAAACAGAACTAAACAGGGGACACA
GTGAAACTAACAGAAAGTTATGAACAAGAGCAGAAATCATAGGCATTTGGCCAAAACCTTCTGATGACTCACTTTGGCCATCAGCAACTGGTCAAGTCAATGATCAATGATCAACCATCTTCTTTAAAA
GATTTATTTGTTTGTGTATACGAGTATACTATAGCTGTCTTCAGACACATCAGAAAATGGGCATCAGATCCATGTCAGATGGATTGTGAGCCACCATGTGAATGCTGGGAATGGACTTAGGACCTCTGG
AAGACAGTCAAGTCTTAACTGCTGAGCTTCTCTCCAGCTTATACCATCTCATTTGATATAGATGCTGTGCTGTCATGCTACTTATGTTTGTGTGCATAATAACTTAGCTCATGATGG
GCAGCTCTGAGTGCATGTTAACTAGCAGCATTTGCAAAATGTCAGTTCCAGTACAGGCCAATGAGGCAAGCTGTCTTAAAGGGAGAATGATTTGTTGTGCAGATACCGGTAGAGCCTGTTCC
AAAACTCAAAGGCTTTTCTGTGATTACCTATTTGATTAAGCAAGCTCCAAACAGCTTCCCGCTTGTGTCATGACCTCAAGTACCATTTGGGTCTGCTGGATCATGTCATCCAAAGGTTAGAACA
GCCCTGCAGTAGCCTGGATCTGTTGAGGCTCTCTCTGTCAGGCCCCACAAAACTAACAGCTTCCAAAGTCAATGATATAGGCTGGAGTAAACAAACCCATGTGAGAGTTGTAATGCTCCAGAA
GCCAAATAGACCCACTAACATTTGCTCTTTCTTTGGTGGGGGGGGTGGGTCACTGCAATTTATTTCTTACATACAAGAAATCTCTGCTGCTCCCAACACCCTGGACTTCAAGGGATTTCT
TGCTGTTGAGACAGTCTTTGAAATTTTCTATCTCTGATTTCTGATTTACTACATATCTGTTATTTCAATGATAGTAGTACTGATGACTGGTCCAGCATAATGCTCAATATAAATGGCCAAATGG
ATATTTTGTGGAAGAGTACAGCAATCAAGTCTCTTAACTAAGTTATGACACAGAACAGGAGAGTCTATATCTCTGAGTAAAAGTGTAAAGGATCTAAACACATACAGAAAAGGCCAACCTTC
TCAGGTAACATGCAAGGACTTAAAAACATAATCATAACTATTTCTTAAAAACGATCAGACTGATAACCATTTGACAAGAGCCATACAGACAGGACCAGCTGGCCTCTTAGGCTTCCAGTATGGT
ATCAGTTTGGGTCCATTTGTAGATAAGAAACT

Read #13 Alb-L1-chr1-L1-Alb @d2d48a3f-5803-4c82-b0fc-7af9a078f5e7_R

CAACAACACTGCAATGCAAGGCAAGCTTACTATGTCATTGCTTATGGCTATGAAGTGAATCTCAACAGCTCTGCTAATCTTTCTAACATCCATCTTTCTTTGTTTCCAGGGTCCTAAACCTT
TTGATTCATCTTATCTCTGTTACAAGCTCAAGACTAAGCAGATCAAGCACTCCACATAAAAACAGAGACACTGAACTTATAGAGGAGAAAGTGGGAAGAGTCTCGATGATATGGGCACAGAGAAAAATCTGTAACAGCACT
AGTGGTGTGCTGTGAAGATGCAACATGGAGCCCTCAAAAAATTAAGCTTCAATAAAGAAAGGAGCAGTGTCAATAGCAACAACAGTGGGAAAAATCTTCCAACTCCTAACCAATAGAGGATAATATCCAAAT
TATTCAAAAGCTCAAGAAAGTTAGAACAAACCAAAATACCCCTATTTTAAAAATGGGATACAGAGCAAAAGAACTCTCAACTGAGGACTCCAAATAATGTGGGAAGCCAAATAATCTCAACTCTTAGTCATCAGGAAATG
CAATCAAAAACCCCTGAGATCCACTCACACAGTCAAGTGGCTAAGTCAAAAATCAGGTGACAGCAGACTGGCAAGATGTAGAGAGAGGAGTCTCTCCATGCTGGTGGGATGCAAGCTGGTCAAAAACACTCTGAAAAATC
TGTTTGGTGTGCTCAGAAAATGGACATAGTACTATCAGAAGATCCAGCAATCTCTCTCTGGGCTGTACTGAGAAGTCTGCAACTGGTAAATGACAGCTGCCACTATGTTTATAGCAGCTTATTTATAAAGCCAGGAGTGGG
GAGAGAGGCCAGATGCTCCAAACAGAGGAGTGGATACAGAAAAATGTGGCAGCTTTACACAATGGTGTACTACATAGCTATTAAGCAACAATGAATTTATGAAGTTCTAGACAAATGGAGTGTAGGATCTCAAGTGGATTAAC
TCAATCAAAAAGACTCATGATATGATGACTGATAGTGGATATAGCCAGTACTGCGAAATCCAAAGATAGCTTTGCAAAAATATAGAAATCAAAAAGAGGACCAAAAAGATGATGATGCTCTCTATAGAGGGGG
GAGCAAAATCACTAAGGAAAGTTACAGAACAGTTCAGACAGAGACTGAAGAAATGACATACCAAGATGGCCCACTGGGATCCATCCCAATAAACACCCAGCAACACTATGTAGACACCAACAGAGCTTGTCTGC
AGGACTGATATAGTGTCTCTGAGAGGCTCTGCCACTACCTGCAAAAATACAGAAGTGGATGCTCAGAGACTCCATTTGGACAGGAGCTAGAGGAAGTATCCAGAGGCTGAAGGGGTTAGTAGGCCATAGAGAAACAAAAATATAACT
AACCAGTACACTGAACTCCCTGGAAAGTAACTACCAATCAAGAAAACATATGGTAGGATCATGTTCTAGCTGCATATGATGATAGGATGGCTAGTCACTTAAATGGGAAGAGAGGCTTGTGCTGTGATGTTCTATGCCCCAG
TATAGAGAACTTCCAGGGCCAGGAATTTGGGGAGTGGGTAGGTTGGGGAGCAGGGGATAGGGGAAAGGGATAGGGGATTTTGGTGGGAACTGGAAGGATAAATCAATTTGAAATGAAGAAAAATGAAA
TGGGCTCAGAGCTAAACAAGAAATGCTCAAGTGGAGAAATCAAAAGCCCAAGAGCACTAAAGAAATGTTCAACACTCTTATGATGAGGAAATGCAATCAAAAACCCCTGAGATCTCACTCCAGCAGCTGATGATGATC
AAAAACTCAGTGAACAGCAGATGTGGGAGATGTGGGAAGAGGGGAGCTCTCCATTTTGGTGGGATGTAACTAATAACAACACTTGGAAATGCAATAGCCTAGCATAACAGACTACAGAAATCCAGCTA
TGATCCAGTATACTACTCTGGGCATATACCCAGAAAGTGTCTCAACATGTAATAAGGACACTGCTTACTATCTATAGCAGCCTTATTTATAATAGCCAGAAAGTGGAAAGAAACCCAGATGCTCCAAACAGAGAAATGGATACAG
AAAAATGGGCACTTACACAATAGAGTACTACTCAGTTTCTTTTAAATGATGAATCATGAAATTTCTAGGCAAAATGGAACATAAATCACTGAGTGAAGTAAACCAATCAAGAAAGACACATAGTATGATCACTGATGAT
AGTGGATACTATGTTTCAAACTCCAAATACCCAAGATACAATCTCAGACACCACATGGAAGCTTAAACACATCAACCAACCACTCTCAGGTAACATACTCTGGGACTTAAAAAACATAATCATAACTTTTCTTAAAAACGGAT
CAAGACTGATAACCATTTGACAAGGCCATACAGACAGCACCAGCTGGCCTCTTAGGCTTCCAGTATGTCATCAGTTTGGGTCCATTTGTAGATAAGAAACT

Read #14 Alb-chr5-ch1-chr2-L1-Alb @6cbc53de-41a9-4812-9844-df95ef5c762b

GCACCTGCACTAGACAGCAATGCAAGGCAAGCTTACTATGTCATTGCTTATGGCTATGAAGTGAATCTCAACAGCTCTGCTACTTCTAACATCCATCTTTCTTTGTTTCCAGGGTCCTAAACCTTGTCACTAGATGCAAA
GACGCCCTTAAAAACAGCTGGATCTATGTCACAGTGTGTTGCTACTATGCACTGAAGATTTCTTATTTAGTACAAGTAGAGGTAATAATAGAAATATAGATAAATTTCTGGCAACTACATATTTAGAACAGGCCAAAGTTAAATGCTATGCT
ATAAATGCAACCAATTTAAATCTGAGCTGGGACATCTGGCAAGTACTGACTTATAAGTTTATAAGGAGAGACTTGTTCACCTTGGCTTAAAGTAGGTAATGATAAATTTTGGCAAAATAGACTTGGAGAAACCCCAAGCA
AAGGAATGTAATAGTTTATGAAAAAAAATTAACCTCAGAGATTTTATGCAAGCATGTTGATGTCOCCAAATAGGTCACCCAGTGTTTTACACATAAATGCAATAAAAAATGAAAAAAAACATTCATGCTCTACTGCTCTCTAGCAAT
CAATAAATGACTCTAGAGATTTTAAACAATATCAAGTTAAACAAAAGATATAGGATAGGTTAAATTTGGCTAATGGAACATACATGATGAACATTTCTCTATGTAACATACAGACATAATATAGTATCTGCTGGAGGCTCTGCTGGAG
TACTGCAACATAATTTGGGAGGTTGCTTCTCCACTGCAAGCAGGCTGAGCCTGCAATAGAAGAGAGTCTCCAAACAGGGGAAATGTTATTTGAGCAGATGCAATAAAGAGGAAATTTGGCTTTAGTGGGAGAAATGTCATACT
TACTCTGCACTATGTTGCAAAACCTAGCTCTCAAGTCAGTACCTAACTCTGTCTTATGCTGTTCTTCAACAACTTTCTGCACTGAACTATCAACCTGGCTCTGCTCTTATTTTAAATGTTTCTGAAAAAATAGGACACAG
GGCAGTTTAACTTTTAGCCAAAAGTGAAGCAACATTAATTAATAAAAAATGTTCACTAATGAATGCAATGTCGAGCTTTCTCAGCAGCACTTAAAGTTGATCTATAGTCTCTACACCTTACTTAAAGCAGAGTCCAAATG
TCTGACCAAGCATATGTCOCCAAAGTTTATAACAGATGATAATAACTGAGTATGATGACTAATTTAAACAGCTGAAAACTCAAAAAGAACCCCAATCAATGCAAGATTCTAGCACAATAGGTTTTCTGTTAAGAAAGAAAAATGAAAAAGC
TAGCTTGTATATCTAAACATTTTAAAAATAATAGGCTTTAGATTTTAAATTAAGTAAATTTAAATACAATTTCTGCACTCTCTTTCCCTCTACTGTTTTCTATATTTCCGATGTGGCCATAAAGGCTCAGCTGATATGCT
TACTTCTTATTTTGGGTTTGTAGACTAGATGACTGACTATGACTTCTTTTATGAAATTACTTACATCTGCTTCTTTGGGTTATAACACAGCAAAAAATGAGTAAAGCTGCTAATAATGAGTTTAAATGTTGTGTGACAGATACTC
GACTAAGGCAAACTTTATGAAACAAATTTAAATGGGGCTGCTCAGAGTTCAGAGTTCATGCTTCTCAATGAGTGAAGTAACTCAAGTGGAAAACTGGCAGTATCCAGGCGGGCAGAGTAGAGTTACTATCTCATCOCAAAAGCTGCTAGGAGAA
GACTGACTTCCAGGCAACTAGGGGTGAGGCAATTAAGCTCCACCCACAGTGCACACACTCTCCAAACATGTCACACTTATCCAAACAGGCCCACTTCCAGAGTGGTCCACTCTGCTGGTCCAAAGAAATTCCAAACCATCACAAGAC
AAACGATTTTTATGCCAGCATTCACTACAGATGATGTTCTGAGGACACATCTGAGTGTCTCACAACATGTGGCAAAAAGATGCTATATAAAAAATAGGTGTGACAGAGCTCAATGATCAAGGGGATACAAAATGAAGAGGGGAAGTCA
AAATATCACTTTGCGAGATGATATGATATATATAAGGACCCCTAAAAATCCACCAAGAGACTCTCAACCTGCAACAGCTTGGTGAAGTGGTGAAGTACTGGAATGAGTGGCAATAAAATTAAGTCAACCAAGTCAATGGCCCTTTCTCACAAAAGAAATA
ACAGCTGGAAGAAATAGGAAATCAACCCCTTCTCAATAGTCCAAATAATATAAATATCTCTTATGACTTAACTAAGAAAGTGGTATGATATAAATCACTCAAGTCTGTAATATAAATCACTCAAGTCTGTAAGAAAGAAATTAAGAAAGATCTCAGAAGA
TGGGACGATCCATGCTAGTGGGATGGGAGGATCAACTTGTAAAAAATGTCATTTGCCAAAAGAACTCAGACTCAATGCAAGCAACCCAAATCCAAATCCAACTCAATTTCTCAAATGAAATAGAGAGGAGAAATTTGCAAAATCTACTA
TGTAGAAATCAAAAACCTAGGATAGCAAAAAAAAACCTTCTCAAGTATAAAGAAACCTCTGGGAAATCAACCTGCTGCAAGTCAACCTGCAAGGAGCAAGCACTTTCAACAATGGTGTGGCAGCAACTGTTTATGATAGAAAG
TAGAACATGAAATGAAATGAAAGCCAGAAATGAACCTAATACTATGCTCAGTCAAGCAAGGAGCAATAAACCTCAATGGAAGAAAGACAGCACTTTCAACAATGGTGTGGCAGCAACTGTTTATGATAGAAAG
AATGGGATGATCACTTATCTGTTACTAAGTCAAATTAATGGATCAAAAGAACTTCACATAAACCAGAGCACTGAACTGAGTGGGGCGGCTGGGGGAAAAAGCCCTGAAGATAGGGGACATCATGTTCTCAGCACTCT
CTCAGGTAACATACTTGGGACTTAAAAACATAATCATAACTTTTCTTAAAAACGATCAAGACTGATAACCATTTGACAAGAGCCATACAGACAGCACCAGCTGGCCTCTTAGGCTTCCAGTATGTCATCAGTTTGGGTCCATTT
TGTAGATAAGAAACTAGGTCOCGC

Figure S13. (B) The representative read sequences display the insertion of LINE-1 and genomic DNA fragments at Alb.

Read #16 **Alb-L1-BB-Alb** @1716251b-f892-4f78-a6d6-bac4f37df9f3_R

GCACCTGATATGCGTTAGTAAGTGAAGGACAGTACGTTTACTTGGCTCATGGCTAAGTGGCTATGAAGTGCATAAATCCCAAGTCTCTGTAACACTTTTCTAACTCCATCACTTTCTTGTTCAGGTCACAACTTGTCACTAGATGC
AAAGACGGTACGCACACAGAGGTTTCTTTCCTGAGAGGAGCTATCCCTGGTTTTTGGTTATTCGACAGGATTTGCAAAATGTCCTTCTAATTCGTTGGAAGAAATGAGTGGAAATTAATGGAGGATGCAATGAACTGTAGATGG
CTTCGGGAAATGCGGCGAAACCCCTATTTTATTTTCTTAAATCAATCAATATGATTCGCTCATGAGACAATAAGTCAATGCTTCAATATATGGAAAGGAAAGATGAGTATCAACATTTTCGAGTTTTCGCTCCATTTTC
CTTTTTTGGGCGCATTTTGCCTCTGTTCTTGTCTCACCAGAAAGCGCTGGGAAAGTAAAGATGCTCGAAGATCAGTTGGGTGATCAGTGGGTACATCGAATGGATTTTAAACAGCGGTAAGATCTTTGAGAGTTTTCGCCCCAAG
AACGTTTCAAAATGATGAGCACTTTAAAGTCTGCTATATGTTGGGCGGTTATATCCGATTTGACGCGGCGGCAAGGCAACTCGGTGCGGATTTGATCGAGTTTCAGAACTGCTGAGTACTACCAGTACAGAAAAGGCACTACGAGATGG
CATGACAGTAAGCAAAATATGCGAGTGTGCCATAAACCATGAGTGAATAACCTGCGGCCAATCTCTGCAACAGTTCGGAGGACCCGAAAGGACTAACCGCTTTTTGCAACAACATGGGATCATGTCGCTTATGTTGGGAGATG
GCTGAATGAGGCATACCAAACGACGAGGCTGACACCAAGTGTGCTGACAAATGTGGCAACAACCTGGCCGCAACTTAATCTGAGGAACACTTACTCTAGCTTCCGCGCAACAATTAAGCTGGATGGGCGGATGTTGGCGGAC
CTCTCTGGCTGGTCTTCGCGTGGCTGTGTTATGCTGATAAATCTTGGACCGGTGTGCGGTGCTCGGTATCATTTGACAGTCTGGGGCCAGATGGTAAAGCGCTCTGCAGTATGTTACTACGAGGGGATGACGCAACTATG
GATGAACGAAATAGACAGATCGCTGAGATAGGCGCTTACTGATTAAGCATTTGCAACTGTCAAAACAAGTTTACTCAGCGGTATACCTTAAATGATTTAAACACTCATTTTTAAATTAAGAGTATGAGTGAAGATCTTTTGATAATCTCA
GGACCAAAATCCCTTAACGTGAGTTTTCGCTCAGCTGAGCGTCAAGCCCTTGTAGAAAAGATCAAAAGGATCTCTTGAAGATCTTTTTTCGCGGTAAATCTGCTGTCGCAAAAACCAACCGCTACCGAGCGGTGTTTGTGGCG
CATCAAGAGAGTCAACACTTTCCGAAAGTCACTGGCTTCAAGCAGAAAGTAGATAACCAAACTACTGTTTCTCTAGTGTCCGCGGTAGTTAGGACCACTTCAAGAACTTACAGAGCTTACCACTGCTTACCACTGCTTACCACTG
GCTGAGATGCGCATAAAGTCTGGCCCTACAGGGCTGGAOCTCGAACAGATAGTTACCGGATAAGGCGAGCGGTGCGGTGGAACGGGTTGCTGCACACCGCAAGCTTGGGACGCAAGCACTTACCAACCTGGAGATACCCACAGC
GTGCTATGAGAAAAGCGCACTTCCGAAAGTCCGGAAGGCGAAGGTCAGGTAATCGGTAAGCGGCGGTGCGAAAGAGAGGCGACGAGAGCTTCCAGGGGAAACCTGCTGATGTTTAAAGTCCAGCGCTTTGCGCACTGTGAC
TTGAGCGTGAATTTTGTGATGCTGTCAGGCGGCGGCTATGAAAAGCGGCAACCGCGCTTTTTCGGTTCCTGGCTTTGTGCTGCTTTGCTCAGATGTCTTTCTCGGTTATCCCGCTGATTTGCGGATAACCGTATTAACCG
CCTTTGAGTGAAGTGAACCGCTGCTGACGCGGAAAGCGAGCGGCGCACTGCTGAGCGGAGGAAGAGCGGCGCAATACGCAAAACCGCTCTCCCTCCGCGCGCTTCAATTAAGTCCAGCTGCGGACGAGGTTTCCCTG
GACTGGAAAGCGCGGAGTGAAGCGCAACGCAACCGCAAGCTGCTCAACACGAGCCCGAGCTTTACACTTATGCTTTCGGTTCCGTTATGTTGTTGGAATTTGAGAGCGGATTAACAAATTTTCAATACCGAGCTGCGAGTGTCAAACA
CATCAACAACCAACTCTTCAAGTAACTATACTTGGGACTTAAAAACATAATCATATAATCAATTTTCTCAAAACGATCAAGACTGATAAACCATTGCAACAGGCAATACAGACAAGCAACAGCTGGCACTTATAGTCTTCAAGTATGGTCAAT
CAGTTTGGCCATTTGATAGAAGAACTGAGGTC

Read #17 **Alb-BB-L1-Alb** @f17a093d-ed82-46f9-95e2-ffbfd705893a

GTTCCTATCTCAAAATGGAACCCAGGCGGTGACCATCGTGAAGACCTAAAAATTTAGCTGGTCTTTACTGTATGGCTTGTGCAAAATGGTTATCAGCTTGATCGTTTGGAGAAAATGATATGATATGTTTTAAGTCCCAAGT
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GGTTGGCTCACTGCGCCGCTTCCGAGTCAGGGAACCTGTGTGCGAGCTGCATTAATGAATCGGCAACCGCGGGAGGCGGTTTGGCTATTGAGCGCTTCCGCTTCCGCTCAGCTCGCTCGCTGCGTCTGGCTGCGAG
CGAGCGCATGGCTCTCAAGCGGTAATCGGTTTCCACAGAAATCAAGCGGATAAACGCGGAAAGAACATGTGACCAAAAGCGGCAAAAAAGGCGGAGCACTTAAAGGCGGCGCTGGGTTTTTCCATAGGCTCCGCGCCCTGCA
CAGCATCAACAAAATCCAGCTCCAAAGTCAAAATTTGGCGAAATTTGGCAAAACCGCAGACTATAAAGATACAGGCGTTCCCTCGCAGACTCCCTGCTGCGCTTCCGCTTCCGAGTACTCGGCTCTTCCCTCT
GGGAAGCGTGGGCTTCTCAGCTCAGCTGTAGTATCTCAGTTCGGTGTAGTGGTGTGCTCAGCTGGGCTGTGCAACGACCCCACTGTCAGCGCGGCGCTGGCCCTATTCGGTAACTATGCTGCGCAGCTCAACCCG
TAAGCAGCACTTATGCGCACTGTAGCAACACTGTGAACAGGATAGCAGAGCGAGTATGAGGCGGTTGTACAGAGTCTTGAAGTGGTGGCTAACTACCGCTGCATTTGAAGAACAGTATTTGATATCGGCTGCTGCGAAAGCAG
TTACTTCCCGGAAAGTATGAGCAGTCTGGTACTTGTACCGGCAAAACCAACCGCTGTGATGAACATTTGGTTTTTTTTCGCTGACTGGTGTGCTCAACCAAGTCACTTGAAGAACAGTATGAGTATCTGATCTTCTACAGGCTG
AGTGTGGAAGCAGCAACTCAGTAAAGGATTTTGGTACGAGATTTCAAAAGGATCTCCACTGATGCTTTTTAAATTAAGAACAGTATTTGAAATAAATCAATCTGATATATGAAGTAACTGGTGTGACAGTAACTAACTAACT
ACTGAGCACTACTCAGGACTGCTGTTTGGTGTGCTGCTGACTCCCGTACTCCGCTGAATCACTAGATAAATCAGTACGGAAGGCTTACCACTGCGCCCACTGTGCAATGATACCGCAGACCCAGCTCAGGCTCAGATTTAT
CAGCAATAAACCGGCGGCGGAGGCGGAAAGCGCAAGTGGTCTGCAACTTTATCCGCTCCATCCAGTCTATTGGTATTTGCGGGAAGCTAGAGTAAGTGTGCGCAGTAAATAGTTTGGCGCACTGTGTGCGATGCTACAGG
CATGCTGGTGTGCAOCTGCTGTTTTGGTATGCTTCATCAGCTCGGTTCCCAAGATCAAGGCGAGTTACATGATCCCGCACTGTGTGCAAAAAAGCGGTTAGCTCCTTGGCTCGATCGTGTGTCAGAAAGTGGCGCGTATGTTT
TATCACTCATAGTTATGGCAGCACTGCATAATCTCTTACTGCTATGCCATCCGTAAGATGCTTTTTCTGTGACTGGTGTGCTCAACCAAGTCACTTGAAGAACAGTATGAGTATGCGGCTATCGGCTTCTGCGCGGCTCAATACCGGA
TAATACCGGCCACATAGCAAGCACTTAAAGTGTCTATCAATGAAAAGCTTCTGCGGCGGAAAAAATCTCAAGGATCTTACCGCTTGTTCAGTTCGATGTAACCCACTGGCTGACCCAACTGATCTCAGCATTTTCTTCCACCA
ACGTTCTGGGTCAGCAAAAAGCAGAAAGCAAAATTTGGCAAAAGGAAAGTGAAGGCGCAGCGAAATTTGAAATCACTACTTCCCTTTCAATATATGACATTTTCAATGATGATGAGCGGATACATATTAAGATCAAT
AGAAAAATTAACAAATAGGCTTCCGATTTTCCCGGAAAGTGGCCACTGGTGGTGCAGATTACTGGTGTAGTATATATGTTCTCTCTCAGGGGATGTCATACACTCAGCTCCTGGGACTTCTCTAGCTCTTCAATGGGCACTA
TGCTCCATTAATGATGACTGTGAGCATCACTTCTGATATAGTCAGGAACTGTCAGAACTCAGAGGACTGATTAAGTCTGCGCAACAGCTAAATGTCGATCAACAGTGTCTGGGTTGGTAAATTTTTTTTGGG
ATGGTCCCGAGTGGGCGAGTTTTCGATGTTATTTTCAGCTGCTGCTCAACTTCTTCCATGACTTCTCCATGACTTTTGGTCCCGCTTCTATGAAAGGCTCAAAAGTCCACTTGGCTTCTCTTCCGATTTTCTGAGTTTCATG
TGTTTGTAATGATCAAGGATTTTAACTTCTGGGCTAAATCCACTTACAGTGTGTCAGATATGATGAGTATTTTGGTACTGGGTTACCTACTCATAAGTATTTATAGTTCATCCATGTTGTCTAAATTTTATGATGAACT
TCATGCTTTTAAATGACTCCGTTTCTGATATACCACTTTCTGATCACTTCTGCTTCTTCAATATAAATAGGCTTCTGCTTCTTATAAATAGGCTTATGAACTATGAGGATATGCTTACGCCAAGT
GGAGCATCTTGGGTAATGTCGAGAGGTTATCCCTGGACCTCAGTGAAGATATGAACAAATTTTCTGAGAAATAACAAACTGATTTCCACAGTGGTGTGCCAGCTTACAATCCACTAGCAATGGAGAGTGTCTCTTTCTCCAC
CTCTTACCAACTCTGCTGCTCACTGAATTTTGTATGAGCACTTGCATGCTGTGAGGTAATCGGGTGTGTTTTTGGATTTCAATCCCTGAAGATTAAGGATGTGAAACATTTTGTAGGTTCTTCAATAGTCAATATTCATA
AGCAAACTTTTGTAGCTGTGACCCCAATTTTAAATAGTGTACTTGGTTTTTCAACCAACTCTGACTTCTTATAATCTGAGTGTGAGCGCCCTACTGAGATGGGATGGTAAAGATTTCCCGCACTGTTGGTGGTGTGAGTT
TTGCTTTGACAATGCTTCTTGTGCGCACAGATGCTTGAATTTTATGAGTCCCACTTTGTCATCTCTCAGCAGCAAGGAAATTTTCCTCCCTCAGTCACTTCTGAGCTTCCCGCACTTCCCTCTAATAGTTCAGGTT
CTCTAATTTATGTCAGTTTAACTAGACTTAGACTTTGTCAGGGGAGATGATGATGATCTGATCTCTTCACTCATTAACCTGTCAGCACTTTTGAATAATGCTGTCTTTTAACTACTGATGTTTATACAGGCTGTAGTTGTCACTT
TTGTAACCACTCAATGACCACTGTGTTGGGATCATCTAAGGCGTCTTTGCTACTGATGCAAGGTTTGGACCTGAAAACAAAGAAATGATGATGTTAGAAAAGTATTAGCAGGCTGTAGTTGTCACTTATGGCATGAGCAATGACA
TAGTAAACGACTGGCTGCTGAT

Read #18 **Alb-BB-L1-Alb** @3e9c16a4-5357-40ab-a0e4-94b9550244a9

ACTCCTGAAAGTGAAGGACAGTACGTTTACTATGTCAATGCTATGGCTATGAGTGCATAAATCCCAAGTCTCTGTAACACTTTTCTAACTCCATCACTTTCTTGTGTTTCAGGTCACAACTTGTCACTAGATGCAAGCGCTTGG
ATTCATCTGCCACAGGTGGCACTTTTGGGAAACTGTGGCGGGAACCCCTATTTGTTTATTTTCTAAATACATCAAAATGATGATTCGCTCATGAGACAATAAAGTAAATGCTTCAATATATGAAAAGGAAAGTATGAGTATGCA
ACATTTTCGCTGTGCGCTTATTCCTTTTTTGGCGCATTTTGGCTTCCGTTTTACTCACCGAAGAAAGCGTGGTGAAGAAAGAGCAAGATCAGTTGGGTGCAAGGATGATTTTATGAACTGGATCTCAACCGGCTAAGATCTTGAGA
GTTTTTTCGCGCGGAAAGCGTTTCCAAATGATGAGCACTTTAAAGTCTGCTATATGTTGGGCGGTTATATCCGATTTGACGCGGCGGAAAGGCAACTCGGTCGCGCATACACTATTCTCAGAAATGACTGGTGGTACTCAOCCAGT
GAGAAAGGATCTTACGATGGCAGTACAGAAATTTTAAATGAGTAACTTACAGCTGTGCCATAAACCATGAGTGAATAACACTGCGGCCAATCTACTCTGACAACGATCGGAGGACCGAAGGACTAACCGCTTTTTGCAACAACATGGG
GATCAGCCACTGCTGTTGGAAACCGGAGTGAATGAGGCACTACCAAACGACGCGTGCACCAAGATGCTGTGAGCAATGCAACAGCTTGCAGCAATATAAATCGGCACTTCACTTACTTACCTTCCGCGCAACAATTAATAGACTG
GATGGAGCGGATAAAGTTCGAGGCACTTCTGCGCTCGGCCCTTCGCGTGGCTGTTTATGTGCTGATAAATCTGGAGCGGTGAGCGTGGGCTCGCGGTTACATGCAAGCACTGGGGCCAGATGGTAAAGCGCTCCGCTATGTAGTTA
TCTACACGAGCGGAAATCCGAGCAACTATGATGAAACAAAAATAGACAGATCGCTGAGATAGTGGCTCACTGATTAAGCAATGTAACCTGTCAGACCAAGTTTACTCATATACTTTAGATGATTTAAACTTCAATTTAAATAAAAA
GGATCTAGGTGAAGATCGCTTTTGAATATCATGACCAAAATCCCTTAAOOGGTGAGTTTGTGCTCAGCTGGGCGTGCAGACCGGTAAGAAAAGATCAAAAGGATCTTCCCGAGATCCCTTTTTCTAGTGGCGATACTGCTGCTG
TTGCAACAAAAACCGCTACCGCTACCGCGGTGGTGGTTTACCAGATCCAAAACTACCACTTTTTTCCGAAGTACGCTGGCTTCAAGCAGCGCAGATAACCAATAGTGTCTTCTAGTGTAGCGGTAGTTGGCCACCGCTTCAA
AACTCTGTAGCACCGCTACATACCTGCTCTGCTAATCTGTTACCAGTGGCTGCTGCGAGTGGGTAAGTGGTCTTCAOCCGTTGACTCAAGACGATAGTTACCGGATAAAGCGCACGGGTGGCGTGAACGCGGTTGTGTCACA
CAGCCAGCTTGGAGCGAAGCACTACACGAACTGAATACCAACGCGTGGCTATGAGAAGCGCACCGCTCCGAGGGGAGGAGGAGAGAGAAAAGGCGGACGGTTATCCGTAAGCGGCGGCTGGCAACAGGAGGCGCACAGG
GACTTCCAGGGGAAAGCGCTGGTATCTTATAGTCTGTGGGTTTTGCGCACTCTGACTTGAOGTGGTTTTTGTGATGCTGTCAGGGCGGAGCCTATGAAAACCGCAGCAOOGCGCTTTTACAGTTCTGGCTTTTGTCT
GGCTTTTGTGCATGTTCTTCTGCGTTATCCCTGATTTCTGTGATAACGATTAACCGCTTTGAGTGAAGTATACCGCTTGGAGTGAAGTACCGCTGTCAGCGCTGATACCGCTGCGCGCAGCGCAACGACCGGCGCGGAGT
TACGCAACCGGCTTCCCGCGGCTGGCGGATCAATTAATGAGTGGCAGCGCAGGTTTCCCGGCTGGAAGGGCGGAGTGGCGCAACCGGTTAAAGTGGTGTAGTCTACTTATAGGCCCGGCTTACACTTATGCTTCCG
CTGATGTTGTGGAATTTGAGCGGATAACAAATTTCAACATAAGGACTAAGGCAAAAATCTCTAATTAACAAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAAT
GCTACTACTCAAAAATCTTAAACAACTCACCAACCAAACTTTCTAGTAACTATACTTGGGACTTAAAAACATAATCATATAATCAATTTTCTCAAAACGATCAAGACTGATAAACCATTGCAACAGGCAATACAGACAAGCAGGCT
GGCATCTTAACTGCTACGATGATCAGTGGTGGTCTGATAGA

Figure S13. (C) The representative read sequences illustrate the insertion of both the plasmid backbone and LINE-1 fragment at Alb.

pD-sgDocut-LA190-E2A-BDDF8-Wpre-PolyA-RA130-sgDocut-Backbone (sgBB)

GGTGGTGCAGATGAACCTCAATGGGTCAGAGAGCCTGCTTTAGGAATCTAAGTAGAACTGTAATTAAGCAATGCAAGGCACGTACGTTTACTATGTCATTGCCATGGCT
ATGAAGTGCAAATCTTAACAGTCTGCTAATACTTTTCTAACATCCATCATTCTTTGTTTCAGGGTCCAAACCTTGCTACTAGATGCAAAAGCGCCTTAGCCAGTGT
ACTAATTATGCTCTCTTGAATTGGCTGGAGATGTTGAGAGCAACCCAGGTCCCATGCAATAGAGCTCTCCACTGCTTCTTTCTGTCCTTTTGGCATTCTGCTTTAG
TGCCACCAGAAAGTACTACTGGGTGCAGTGGAACTGTCATGGGACTATGCAAAAGTGATCTCGGTGAGCTGCCTGTGGACCGCAAGATTCTCCCTAGAGTGCCAA
AATCTTTTCACTCAACAACCTCAGTCGTTGATACAAAAGACTCTGTTTGAATACTCAGGATCACCTTTTCAACATCTAGCCAAAGCCACCTGGATGGGTCTGCT
AGGTCTACCATCCAGGCTGAGGTTTATGATACAGTGGCTTACACTTAAGAACATGGCTTCCCCTCTGTCAGTCTTCTGCTGTTGGTGTATCTACTGAAAAGCT
TCTGAGGGAGCTGAATGATGATCAGCAGACTCAAAAGGAGAAAGAGATGATTAAGTCTTCCCTGGTGGAAAGCCATACATGTCGGCAGTCTGAAAAGAGAA
TGTTCCAATTGGCTCTGACCCTGTCCTTACTCATATCTTTGATGTCAGTGGCACTTAACATAGATCACCTTTTCAACATCTGAACTCAGGCTCATTGGAGCCTACTAGTATGTA
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CGAAGCAGCGCAGCGAGTCACTGAGCGAGGAAAGCGGAAGAGCGCCAATACGCAAAACCCGCTTCCCGCGGCTTGGCCGATTCAATATGCTCAGCTGGGAC
GACAGGTTTTCCGACTGGAAGCGGGCAGTGAGCCCAAGCAGCAATATGTAGTTACTACTTATGGCACCCAGGCTTTACTCTTATGCTCCGCTGCTGATG
TTGTGGAATGTGAGCGGATAACAATTTACACAGGA

Figure S14. The sequence of pD-BDDF8-sg vectors with HA190-130. The backbone used for the plasmids in our study is derived from pBR322, a well-known bacterial cloning vector.

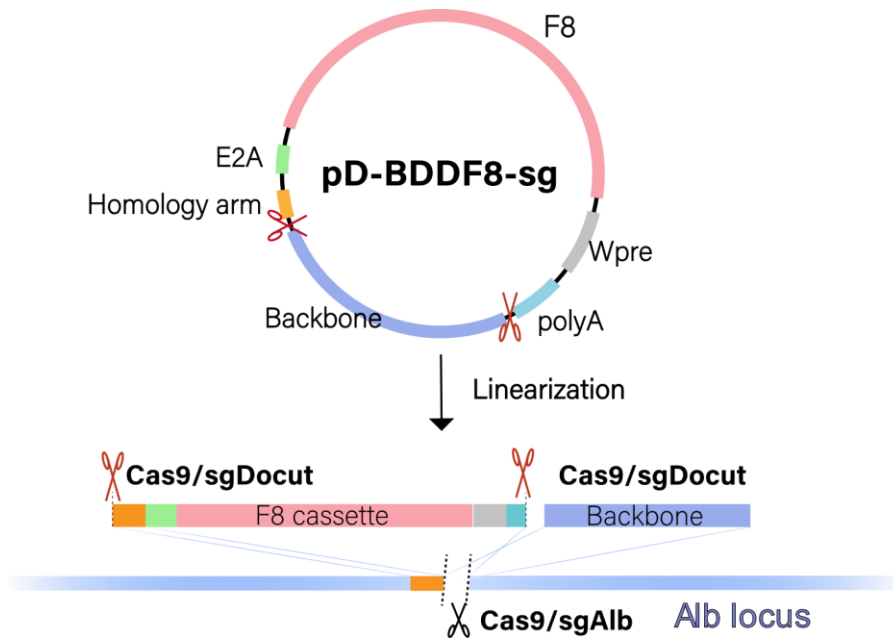


Figure S15. Linearization and Integration of Double-Cut Donor Plasmid: This schematic illustrates the process where a double-cut donor plasmid is linearized into two distinct fragments within hepatocytes. Subsequently, these fragments integrate at the genomic site cleaved by sgAlb. The diagram provides a visual representation of the linearization and integration steps, highlighting the two resulting fragments and their integration at the targeted genomic location.

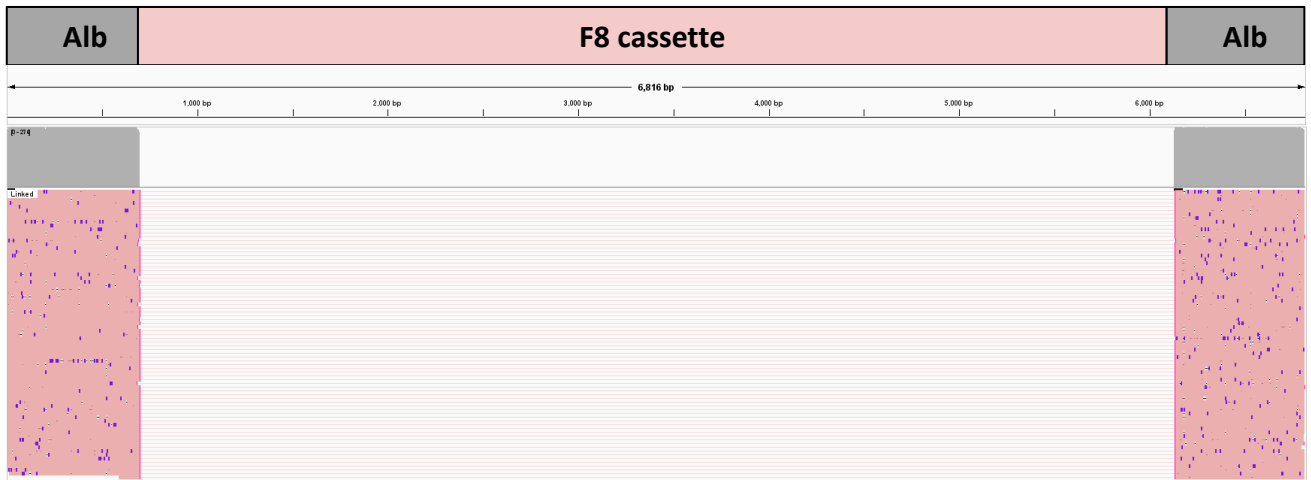


Figure S16. Analysis of Circular Donor Plasmid Integration: This figure analyzes the integration of a circular donor plasmid with HA600-600 homology arms, which lacks the sgDocut, into the target genomic site. The reference sequence used for alignment is based on the expected outcome of homology-directed repair (HDR) editing. This panel shows random 200 reads out of over 6000 aligned with the reference sequence. Nanopore sequencing of over 6,000 reads failed to reveal any F8 insertions. This lack of detection likely resulted from the preferential amplification of shorter background sequences (1.3 kb) without insertions, overshadowing potential longer insertions.

Target site	sgRNA Sequence
sgAlb-E14	GTTGTGATGTGTTTAGGCTA
sgDocut	GGTGGTGCAGATGAACTCCA
sgBB	AATAAACCCAGCCAGCCGGAA

Table S1. The target sequences of sgRNAs utilized in this study.

Primer	Sequence	Length
Alb-PE150-F-BC1	aacaaggtATTGCCTATGGCTATGAAGTGC	242 bp
Alb-PE150-F-BC2	aacattccATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC3	aaccgtaaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC4	aacgagaaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC5	aacttggaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC6	aagaccaaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC7	aaggtcatATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC8	aatagtggATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC9	aatgccttATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC10	acaatagcATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC11	acaggattATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC12	accgacctATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC13	acgagtccATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC14	acgcataaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC15	acggacgaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC16	acgtatggATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC17	actaaccaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC18	actcaggtATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC19	acttggtgATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC20	agaagtacATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC21	agccactcATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC22	agctctaaATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC23	aggtgtctATTGCCTATGGCTATGAAGTGC	
Alb-PE150-F-BC24	agtccgttATTGCCTATGGCTATGAAGTGC	
Alb-PE150-R	TGCTTGCTGTATGGCTCTTGT	

Table S2. The primers employed to determine the cleavage efficiencies of Cas9-sgRNA that targets Alb.

Primer	Sequence	Length
Alb-4.9kb-F-BC1	gccggttgaaTGAGACCTTCACCTTCCACTCTG	4886 bp
Alb-4.9kb-F-BC2	ggtatagatggTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC3	gtacttgtagTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC4	taagctcaagTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC5	tcgctccatcTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC6	ttagaatcacgTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC7	ttcaggtgtcTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC8	ttctgcaccgcTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC9	caatcttacagTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC10	ccaggagggtgTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC11	cgagactattcTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC12	gacctgacatcTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC13	aacaacaacacTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC14	aacattgagccTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC15	aagaccataggTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC16	aatagtgtcggTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC17	acaatgcgaatTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC18	accgctatgccTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC19	acgtaggataaTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC20	actattactccTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC21	agctcggacctTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC22	agtctagcgttTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC23	atggaggacggTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-F-BC24	attggtgcataTGAGACCTTCACCTTCCACTCTG	
Alb-4.9kb-R	TGGCTCGTTATTAGCCCAGTTGATAGC	

Table S3. The primers utilized to detect large deletions in Figure 1C.

Primer	Sequence	Length
Alb-4.7kb-F-BC1	aacaccttcttTGTGGGCAAAAACCACAGTA	4727 bp
Alb-4.7kb-F-BC2	aaccgtccaccTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC3	aagcggttataTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC4	aattccgcgctTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC5	acctcctgtaaTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC6	acggaaccagcTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC7	agaagaagagaTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-F-BC8	aggtgagtcttTGTGGGCAAAAACCACAGTA	
Alb-4.7kb-R	ACCTGGCTCGTTATTAGCCCAGTTGATAG	

Table S4. The primers utilized for long-range PCR amplification in Figure 2A.

Primer	Sequence	Length
Alb-HA600-1.5kb-F1	GGAGCAACTGAAGACTGTCATGGA	1586 bp
Alb-HA600-1.5kb-R1	AGTGTCAAAGTCAGGGGTCTCACC	
Alb-HA600-1.4kb-F2-BC1	aaacactttctcCGGAGCAACTGAAGACTGTCA	1380 bp
Alb-HA600-1.4kb-F2-BC2	ttaacgaaaccgCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC3	aaactctgagaaCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC4	tgtatcaaagacCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC5	aacgtctccataCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC6	tcgattaactgaCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC7	acaaagtaaccCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC8	tagcgaacaaccCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC9	acagcagtttgCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC10	gtagagacatgtCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC11	accatagctaagCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC12	gcactaacctttCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC13	atgcacgaacagCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC14	gatatgatgttgCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC15	caaacactccaCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-F2-BC16	cgttccaatacCGGAGCAACTGAAGACTGTCA	
Alb-HA600-1.4kb-R2	AGCCTTCATTATTGCCCTATT	

Table S5. The primers employed for nested PCR amplification of long genomic flanking regions in Supplementary Figure S2.

Primer	Sequence	Length
Alb-HA85-0.5kb-F1	Acaacagatgtcagagagcctgc	499 bp
Alb-HA85-0.5kb-R1	Cagggctaactcctttgctctgg	
Alb-HA85-332bp-F2-BC1	acgccacgttAGCAATGCAAGGCACGTACG	332 bp
Alb-HA85-332bp-F2-BC2	cgactagaccAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC3	cagtgaccagAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC4	ccaggctcttAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC5	tcgcgacactAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC6	agccgtcacaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC7	gtgcatatccAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC8	accgagccatAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC9	cactctcaggAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC10	gtagtcaatgAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC11	ccgtgtggttaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC12	gaatcgagacAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC13	gacgcggtaaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC14	gaacaccacaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC15	caactcctgaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC16	cgattacctcAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC17	gaccactatcAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC18	gagacacggtAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC19	gatatgcttAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC20	gcaacagaggAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC21	gccagacaagAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC22	gctaggatctAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC23	ggagttaccgAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC24	ggtacgtgcaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC25	gtactgacaaAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC26	taacatgaggAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-F2-BC27	tacaacggatAGCAATGCAAGGCACGTACG	
Alb-HA85-332bp-R2	TATCTACAAATGGAACCCAACTGATGACC	

Table S6. The primers utilized for nested PCR amplification of short genomic flanking regions in Figure 3.

Primer	Sequence	Length
qPCR-BDDF8-FL-F	CACGTACGTTTACTATGTCA	261bp
qPCR-BDDF8-FL-R	AGTATCTTCTGGTGGCACTA	
qPCR-BDDF8-FR-F	CTGTAAGCGGATGCCGGGAG	249bp
qPCR-BDDF8-FR-R	GCTGGTGCTTGTCTGTATGG	
qPCR-BDDF8-RL-F	GCACGTACGTTTACTATGTC	283bp
qPCR-BDDF8-RL-R	AAACCTCTGACACATGCAGC	
qPCR-BDDF8-RR-F	CCCAGGTAGTATCTTCTGGT	281bp
qPCR-BDDF8-RR-R	CCAGCTGGTGCTTGTCTGTA	
qPCR-BB-FL-F	CCTATGGCTATGAAGTGCAA	248bp
qPCR-BB-FL-R	GTTGAATACTCATACTCTTC	
qPCR-BB-FR-F	AAGCGGGCAGTGAGCGCAAC	248bp
qPCR-BB-FR-R	GGCTCTTGTCAAATGGTTAT	
qPCR-BB-RL-F	CACGTACGTTTACTATGTCA	277bp
qPCR-BB-RL-R	ACGACAGGTTTCCCGACTGG	
qPCR-BB-RR-F	CGCACATTTCCCGAAAAGT	285bp
qPCR-BB-RR-R	TCTCCCTGGTTTGGTCTCCT	
qPCR-F8fBBr-junction-F	GCTTGTCTGTAAGCGGATGC	203bp
qPCR-F8fBBr-junction-R	CACTCATTAGGCACCCCAGG	
qPCR-F8rBBf-junction-F	GCACAGAAAGAAGCAGGTGGA	227bp
qPCR-F8rBBf-junction-R	CATTTCCCGAAAAGTGCCA	

Table S7. The primers employed for qPCR to correlate with the proportion of different insertion outcomes analyzed based on Nanopore sequencing data in Figure 5.

Primer	Sequence	Length
Forward left junction		
Alb-S516-FL-F-BC1	aacattgagccCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC2	aagttcattccCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC3	accacagattaCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC4	aacaccgattagCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC5	aaccactctaagCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC6	aaccgtatccgtCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC7	aaccttggatggCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC8	aacttctctccCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC9	aagaaggttacgCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC10	aagagtggaagtCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC11	aaggatactctcCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-F-BC12	aagtcacacgccCGTCATGGGTGTGACTTTTG	
Alb-S516-FL-HA85-190-R	AAACTCATCAATGTATCTTATCATGTCTG	5.3kb
Alb-S516-FL-HA600-R	CCCAGGCTTTGCAGTCAAAC	4.9kb
Forward right junction		
Alb-S516-FR-F-BC1	acgtaggataaCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC2	attaacatgccCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC3	catacagaccgcCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC4	aatagcaatcggCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC5	aattacgagaggCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC6	acaaccttcagcCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC7	acaatgacaaggCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC8	acagtaataggCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC9	accacaatgatgCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC10	accgaacgccatCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC11	acctctcgaaCCTTGAAATCTCGCCAATA	
Alb-S516-FR-F-BC12	acgccatacataCCTTGAAATCTCGCCAATA	
Alb-S516-FR-HA85-190-R	actcgtcatgtgtatataagttgtg	
Alb-S516-FR-HA600-F-BC1	aagaggaggttggactgcaaagcctggg	
Alb-S516-FR-HA600-F-BC2	ctggaaatgttggactgcaaagcctggg	
Alb-S516-FR-HA600-F-BC3	cttgttgggttggactgcaaagcctggg	
Alb-S516-FR-HA600-F-BC4	tatgcgttgggttggactgcaaagcctggg	
Alb-S516-FR-HA600-R	GTGGGCAGATGACACACTGA	4.1kb
Reverse left junction		
Alb-S516-RL-F-BC1	ccagagcacacCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC2	cgagactattcCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC3	cttgacgttaaCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC4	acggttctaatacCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC5	actcagccggtacCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC6	actgaggtgagcCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC7	agagcataaggaCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC8	aggaagagagagCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC9	agtaagcgtccCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC10	agtatctggtgaCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC11	agtcttctatcCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-F-BC12	ataagactcaccCGTCATGGGTGTGACTTTTG	
Alb-S516-RL-R	ACACAGACCTTGCACAAATTTATACTACT	6.1kb
Reverse right junction		
Alb-S516-RR-F-BC1	gagtcgtggtAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC2	ggacaccgtaaAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC3	gtcgtcatgtcAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC4	atctcaaggtaAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC5	atggagattggtAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC6	attgagtcttccAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC7	caacgtagtaagAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC8	cacattcattggaAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC9	cacttccgagctAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC10	cagagcaaccatAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC11	caggttgatccgAATCACAGCCCATCAACTCC	
Alb-S516-RR-F-BC12	catcaagaacggAATCACAGCCCATCAACTCC	
Alb-S516-RR-R	ATTGAGAATTCTCGTAATGTTGAAGTATT	

Table S8. The primers utilized to distinguish NHEJ and HDR in Figure 6.

Primer	Sequence	Length
Alb-HA600-1.8kb-F1	CCTTAAACTGTGGCCTCACATTCC	1832 bp
Alb-HA600-1.8kb-R1	TACTTGGTGGGCAGATGACACACT	
Alb-HA600-1.4kb-F2	GGAGCAACTGAAGACTGTCATGG	1384bp
Alb-HA600-1.4kb-R2	AAGCCTCCATTATTGCCCTATTTT	

Table S9. The primers utilized to detect the insertion of donor plasmid at a circular stage (with no sgDocut) .