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| **Supplementary Table 1 - Primers used in this study to assemble the vectors** |
| nos-pr-CRISPR-F | GCTCGAATTAACCATTGTGGACCGGTGTGAACTTCCATGGAATTACGT |
| nos-pr-CRISPR-R | TCGTGGTCCTTATAGTCCATCTCGAGCTTGCTTTCTAGAACAAAAGGATC |
| nos-ter-CRISPR-F | GCCGGCCAGGCAAAAAAGAAAAAGTAATTAATTAAGACAGAGTCGTTCGTTCATT |
| nos-ter-CRISPR-r | TCAACCCTTCAAGCGCACGCATACAAAGGCGCGCCGTAATTAGTGTTCATTTTAG |
| zpg-pr-CRISPR-F | GCTCGAATTAACCATTGTGGACCGGTCAGCGCTGGCGGTGGGGA |
| zpg-pr-CRISPR-R | TCGTGGTCCTTATAGTCCATCTCGAGCTCGATGCTGTATTTGTTGT |
| zpg-ter-CRISPR-F | AGGCAAAAAAGAAAAAGTAATTAATTAAGAGGACGGCGAGAAGTAATCAT |
| zpg-ter-CRISPR-R | TTCAAGCGCACGCATACAAAGGCGCGCCTCGCATAATGAACGAACCAAAGG |
| exu-pr-CRISPR-F | GCTCGAATTAACCATTGTGGACCGGTGGAAGGTGATTGCGATTCCATGT |
| exu-pr-CRISPR-R | TCGTGGTCCTTATAGTCCATCTCGAGTTTGTACAAGCTACACAAGAGAAGG |
| exu-ter-CRISPR-F | AGGCAAAAAAGAAAAAGTAATTAATTAAGCGTGAGCCGGAGAAAGC |
| exu-ter-CRISPR-R | TTCAAGCGCACGCATACAAAGGCGCGCCACTGCTACTGTGCAACACATC |

Supplementary table 1. Primers used to amplify *nos*, *zpg* and *exu* promoter (pr) and terminator (ter) sequences. Underlined are the Gibson adaptors used to clone promoter and terminator fragments into the CRISPRh vector.

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| **Supplementary Table 2 – Promoter and terminator sequences** |
| Zpg promoter | cagcgctggcggtggggacagctccggctgtggctgttcttgCgagtcCtcttcctgcggcacatccctctcgtcgaccagttcagtttgctgagcgtaagcctgctgctgttcgtcctgcatcatcgggaccatttgtaTgggccatccgccaccaccaccatcaccaccgccgtccatttctaggggcatacccatcagcatctccgcgggcgccattggcggtggtgccaaggtgccattcgtttgttgctgaaagcaaaagaaagcaaattagtgttgtttctgctgcacacgataAttttcgtttcttgccgctagacacaaacaacactgcatctggagggagaaatttgacgcctagctgtataacttacctcaaagttattgtccatcgtggtataatggacctaccgagcccggttacactacacaaagcaagattatgcgacaaaatcacagcgaaaactagtaattttcatctatcgaaagcggccgagcagagagttgtttggtattgcaacttgacattctgctgCgggataaaccgcgacgggctaccatggcgcacctgtcagatggctgtcaaatttggcccggtttgcgatatggagtgggtgaaattatatcccactcgctgatcgtgaaaatagacacctgaaaacaataattgttgtgttaattttacattttgaagaacagcacaagttttgctgacaatatttaattacgtttcgttatcaacggcacggaaagattatctcgctgattatccctctcgctctctctgtctatcatgtcctggtcgttctcgcgtcaccccggataatcgagagacgccatttttaatttgaactactacaccgacaagcatgccgtgagctctttcaagttcttctgtccgaccaaagaaacagagaataccgcccggacagtgcccggagtgatcgatccatagaaaatcgcccatcatgtgccactgaGgcgaaccggcgtagcttgttccgaatttccaagtgcttccccgtaacatccgcatataacaaAcagcccaacaacaaatacagcatcgag |
| Zpg terminator | Gaggacggcgagaagtaatcatatgtccgcattttgcgcaaaccaggcgcttagacaatttgcgcgtaagcacattcgaaatgtgaaaagctgaaagcagtggtttcgccagcccgagttcagcgaaacggattccttccaagtgtttgcattcctggcggagtgttcctcccaaaatgcactcaccctgcgtgcagtgccaaatcgtgagtttcctaattttttcatattgtttattacctaccaactaaagttgttgttatatattgcgttttacgtacgacaaataagttcgtattcagaaatatttgcgataagagagaactcatttgcgatgaatctcattgtatttagctaagtgccttgataagtaagcggaacagcaggaatatgacactccttgggaaatacatgtaagcgtctgtaattagatatatatacacgcaaccaaatggtccatggttgatttaagcactgcctgttgtcgaacattgctataagcaaaataaagaagcattcattaatctaaaatttcttcaaagtgacttcaatgatgatctctaggctatagtgaaagctgaaagcttatttgacaatgcaagggaaagtgacgcacgtgcgtcgtatgggaccgcgcgcatctattctctcagctaattcccctaatcattagtaattgacggcacgatttctgcttcttacttccttttactttggagcttttcatcaataaaaccagtaccatggccgtacgctcaacggaaaagcattcaaaaaaacccgcgttcctcgtgtgatttgtgggtgagtggcgccatctattagagaatagctgtactacatctcgtggacgaaggggtcagagaagttgaaagagagcttgatcgactgctatccaagctaggcgaggaagggagatcgctagagcaaaagaaaaaaaataagcaaatatctttttttataacaaatcgacgttagcgaaatatgtttgaatcgatttaacggttagaattccctttggttcgttcattatgcga |
| Nos promoter | gtgaacttccatggaattacgtgctttttcggaatggagttgggctggtgaaaaacacctatcagcaccgcacttttcccccggcatttcaggttatacgcagagacagagactaaatattcacccattcatcacgcactaacttcgcaatagattgatattccaaaactttcttcacctttgccgagttggattctggattctgagactgtaaaaagtcgtacgagctatcatagggtgtaaaacggaaaacaaacaaacgtttaatggactgctccaactgtaatcgcttcacgcaaacaaacacacacgcgctgggagcgttcctggcgtcacctttgcacgatgaaaactgtagcaaaactcgcacgaccgaaggctctccgtccctgctggtgtgtgtttttttcttttctgcagcaaaattagaaaacatcatcatttgacgaaaacgtcaactgcgcgagcagagtgaccagaaataccgatgtatctgtatagtagaacgtcggttatccgggggcggattaaccgtgcgcacaaccagttttttgtgcagctttgtagtgtctagtggtattttcgaaattcatttttgttcattaacagttgttaaacctatagttattgattaaaataatattctactaacgattaaccgatggattcaaagtgaataaattatgaaactagtgatttttttaaatttttatatgaatttgacatttcttggaccattatcatcttggtctcgagctgcccgaataatcgacgttctactgtattcctaccgattttttatatgcctaccgacacacaggtgggccccctaaaactaccgatttttaatttatcctaccgaaaatcacagattgtttcataatacagaccaaaaagtcatgtaaccatttcccaaatcacttaatgtattaaactccatatggaaatcgctagcaaccagaaccagaagttcaacagagacaaccaatttccgtgtatgtacttcatgagatgagattggacgcgctggtaaaattttatatgggatttgacagataatgtaaggcgtgcgatttttttcatacgatggaatcaattcaagagtcaattgtgcaggatttatagaaacaatctcttatttatgttttgttatcgttacagttacagccctgtcctaagcggccgcgtgaaggcccaaaaaaaagggagtccccaacgctcagtagcaaatgtgcttctctatcattcgttgggttagaaaagcctcatgtgacttctatgaacaaaatctaaactatctcctttaaatagagaatggatgtattttttcgtgccactgaactttcgttgggaagattagatacctctccctccccccccctccctttcaacacttcaaaacctaccgaaaactaccgatacaatttgatgtacctaccgaagaccgccaaaataatctggccacactggctagatctgatgttttgaaacatcgccaaattttactaaataatgcacttgcgcgttggtgaagctgcacttaaacagattagttgaattacgctttctgaaatgtttttattaaacacttgttttttttaatacttcaatttaaagctacttcttggaatgataattctacccaaaaccaaaaccactttacaaagagtgtgtggttggtgatcgcgccggctactgcgacctgtggtcatcgctcatctcacgcacacatacgcacacatctgtcatttgaaaagctgcacacaatcgtgtgttgtgcaaaaaaccgttcgcgcacaaacagttcgcacatgtttgcaagccgtgcagcaaagggcttttgatggtgatccgcagtgtttggtcagctttttaatgtgttttcgcttaatcgcttttgtttgtgtaatgttttgtcggaataatttttatgcgtcgttacaaatgaaatgtacaatcctgcgatgctagtgtaaaacattgctaattcccggtaagaacgttcattacgctcggatatcatcttacgaagcgTGTGTATGTGCGCTAGTACATTGACCTTTAAAGTgatccttttgttctagaaagcaag |
| Nos terminator | gacagagtcgttcgttcattccttttttattactttacaacacatccaaagctctgtgagcttcaagcaacaggtagtagctgacatcggaactggtgggcaagaaaggcttTcagcaaatatgtttCAggctgctcggagaatgttgaagatatatttatttaggaaaagtggaactttatgcaggatgaataattttgccatcgaatcaaatagcgtaagtaggtagagtgaaaaatTgatcttaaaaggatgatttccacgttcgaacattacacattaaggatggtatccatacatacgaatgcggtttaaattcaatatttaccttgaagcagGtgttcgtatcatttcctccttagcatctttatgtctaAacttctttCaaTgacaacatttatCgattttttgatacaacgaatcattttctatgaatcaatcaCttgatgcCttgattaaataaattgcgaagaaatatttaacaacaatcgattctaaatgtgttgttagaagAtacaaccaaaaaacctttaatAtcttggagcgaatgttcaaagatattgTttagcctctctcttcggctaaaatgaacactaattac |
| Exu promoter | ggaaggtgattgcgattccatgttgatgccaatatatgatgattttgttgcatattaatagttgttgttatgttttattcaaatttcaaagataatttactttacattacagttagtgagcatattatctactacataaacacatagatCaaactggtttacataaattcaaaaagtttgGattaaAatcgcagcaattggttatgaaaaaatatgtgCAtaacgtaaatatcaagtaaatttttgcattgcatatttatagaCtcctgttacaatttcggaaaaatgaaaaatgttaattaatcaaagaagaaaaaacaaagAaattaaatcattaggtAgcacaaccacaagtacatatttttatggcatgaatattccTctacactaacatattttatagcaattctattgatcgccttaGtatagcGgaattaccagaacggcactatagttgtctctgtttggcacacgcaatcatttttcatcccagggttgccatagcagtttggcgacggtcacgtagcatgcgaaggatttcgTtcgcacaggatcacttttattctaacgtttgaagaagGcacatctcagtgcaagcgctctggaagctgcttttaccgaacgaactaacttttcaagtaacctcaaaaacttgtctctaacgacaccacgtgctatccgcgagttTcatttcccgtgcaaagttccccgatttagctatcattcgtgaacatttcgtagtgcctctaccctcaggtaagaccattcgaGgtttaccaagttttgtgcaaagaaCGTGCacagtaattttCgttctggtgaaaccttctcttgtgtagcttgtacaaa |
| Exu terminator | gcgtgagccggagaaagcttgcgggacattttaacggtagatgtctgatgattgttgcatagatgcagtagatgcaggaacatacccgattcaaagaacatctttttacggataatggcaaggaatacgaaacatttttaaacacgctcaaatagatttaaggatcatcacgatagaagtagccaactcattcggtatagttgtcctcgtattttagaatcaggtagaagcgctgcttcagcagcaaaatgtcttagctcaggatcatagggaaggatggccgttgaacccgttgaaagtatgcgcgcactttctggggtaatttccaaggcgtcatccggcccacttttagtcacccagaagctaggaccgtttgcttgcatttgtgtggtgcagaaccccattttaatattgtgtaaattattttcactacgtagcaatcaataccaatgtgaggctgcaaaacgtctcttttagctgtggtgggttgtagcagctcagaaatgaaatcaacgatttatgttatgattgtaattgatggaaggtgtacaacacggaagggccagacctctggaaggcgatggcggttccatgttgatgccaatatatgatgattttgttgcattgaatatttgtttgcttgttctatttgattagtgggttgaatttggaaagaaatgtacgatattcggatggagttatgggtgtacaacagtagtgtctgtagttagtgtactaattgtgattaagattttgaattttatttccctttttgagacagaacatttatcgcaggctggacctggctatccagctaccctcgcgtgtcttttgtaccaattgggcattaactatcctgtctagaatgagcttgcttgtgtgtctgtggctcaatgtacgcgctttggggaggaagaaaactgttggtacaattatactactcatgcatctagtatcatgtaaatacactcaaaacatcaatcaatccatcaatagtagttactccttcattagtgcctaggaacgcactgcactaccgatgcagcgccggagaaaacatgtatccttgcgtttgtgtcactagtcctatatatacccaaaactgcccccaacaatcgtgctcaaagtacggttaatacggggcagcggggagatgtgttgcacagtagcagt |

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**Supplementary Figure 1.** Cleavage by *CRISPRh* can generate resistant mutations as a by-product of error-prone end-joining.After cleavage by the nuclease, the majority of target sites will be repaired by homology-directed repair (HDR), leading to a copying over of the *CRISPRh* allele called homing. A small fraction of targets may remain unmodified or may repair perfectly, resulting in a target that can be cleaved upon re-exposure by the nuclease. Chromosomes that are repaired by end-joining may generate a mutant target site that can no longer be cleaved by the nuclease. If the target site is essential (i.e. a female fertility gene), then a mutation that disrupts the function of the target gene, called an R2 mutation, will be selected out of the population. Mutations that re-code a functional target gene, called an R1 mutation, are resistant to the gene drive and will come under strong selection in presence of the drive.