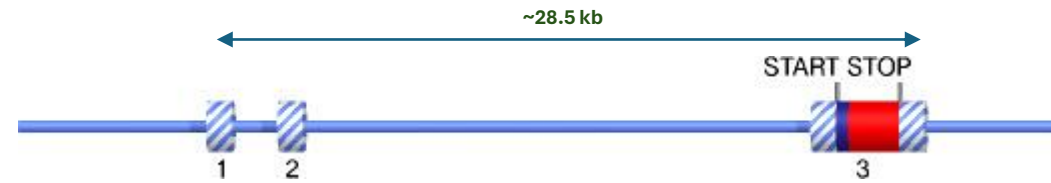
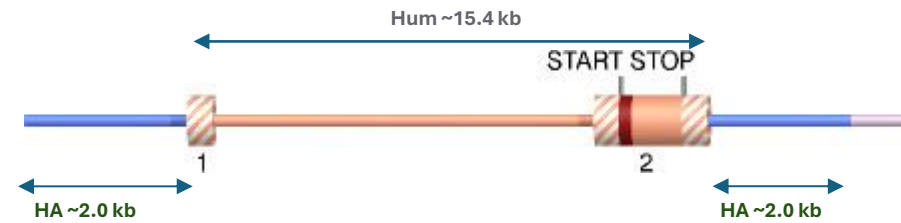


(not drawn to scale)

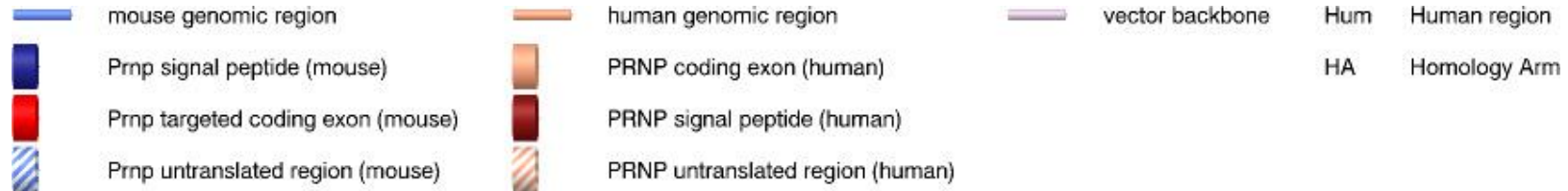
Mouse genomic locus



Targeting vector



Humanized allele (after CRISPR/Cas9-mediated gene editing)



Proximal guide RNA (gRNA1)

```
ACTCATTCCC CCACCCCCCA CCCCCCGCG AGAGACGCGG CGCGGCCATT GGTGAGCATC ACGCCCCGCC CCTCGCCCAG CCTAGCTCCC GCCTGCCCCG
TGAGTAAGGG GGTGGGGGGT GGGGGGGCGC TCTCTGCGCC GCGCCGGTAA CCACTCGTAG TCGGGGGCGG GGAGCGGGTC GGATCGAGGG CGGACGGGGC
```

```
exon_1
CCCCCTTCCA CTCCCGGCTC CCCCAGCTTG TCGGATCAGC AGACCGATTG TGGGCGCTGC GTCGCATCGG TGGCAGGTAA GCGGGCTGCT GAAGCCAGGC
GGGGAAAGGT GAGGGCCGAG GGGGCGCAAC AGCCTAGTCG TCTGGCTAAG ACCCGCGACG CAGCGTAGCC ACCGTCATT CGCCCGACGA CTCGGTCCG
```

gRNA1

Distal guide RNA (gRNA2)

```
exon_3
GTCATATAAA AAGTTTATAA ATGTTTGCTA TCAGACTGAC ATTAAATAGA AGCTATGATG AACACCTGGC GGGGTTTGTT CTCTCTCCAA TGCTCCGAGT
CAGTATATTT TTCAAATATT TACAAACGAT AGTCTGACTG TAATTTATCT TCGATACTAC TTGTGGACCG CCCCAAACAA GAGAGAGGTT ACGAGGCTCA
```

gRNA2