

Bacterial RNA-directed Cas9 endonuclease is a versatile tool for site-specific genome modification in eukaryotes. Co-microinjection of mouse embryos with Cas9 mRNA and single guide RNAs induces on-target and off-target mutations that are transmissible to offspring. However, Cas9 nickase can be used to efficiently mutate genes without detectable damage at known off-target sites. This method is applicable for genome editing of any model organism and minimizes confounding problems of off-target mutations.