

In vivo genome engineering with CRISPR-Cas9

These publications demonstrate the application of CRISPR-Cas9 genome engineering techniques for target gene knockout, chromosomal deletions, precise knock-in, or gene correction in a variety of animal models.

Species	Stage/tissue	Reference	Target	Type of editing	Cas9 and guide RNA source	Delivery method	Link
Mouse	Neonatal pups inner ear hair cells	Gal <i>et al. Nature</i> 2018	<i>Tmc1</i>	Single gene knockout	Cas9 protein and sgRNA (IVT)	Cas9 and sgRNA stable integration	http://dx.doi.org/10.1038/nature25164
Mouse	Pre-implantation embryos	Yoon <i>et al. Nat. Commun.</i> 2018	<i>Tyr</i>	Single gene knockout	Cas9 and sgRNA in rAAV vector	IVT Cas9 mRNA and sgRNA	http://dx.doi.org/10.1038/s41467-017-02706-7
Mouse	Brain	Zhou <i>et al. Nat. Neurosci.</i> 2018	<i>Ascl1, Neurog2 and Neurod1; Dkk1 and Hbb</i>	Multiplex transcriptional activation	dCas9 tg-mouse, tandem sgRNAs in rAAV	Cas9 and two sgRNAs in adenoviral vector	http://dx.doi.org/10.1038/s41593-017-0060-6
Mouse	Liver	Jiang <i>et al. Cell Res.</i> 2017	<i>Pcsk9</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Cas9 mRNA and sgRNA (IVT)	http://dx.doi.org/10.1038/cr.2017.16
Mouse	Zygotes	Lei <i>et al. Nat. Commun.</i> 2017	<i>Igf2/H19</i> imprinting region	CpG methylation	dCas9-MQ1 and sgRNA plasmids	Microinjection	http://dx.doi.org/10.1038/ncomms16026
Mouse	Muscle, kidney and liver	Liao <i>et al. Cell</i> 2017	<i>Fst, Kl, Il10, Pdx1, Utrn</i>	Transcriptional activation	Cas9 tg-mouse, truncated gRNA in rAAV vector	Intramuscular, intravenous or intracerebral injection	http://doi.org/10.1016/j.cell.2017.10.025
Mouse	Retina	Latella <i>et al. Mol. Ther. Nucl Acids</i> 2016	Human RHO in tg-mouse	Single gene knockout	Cas9 and sgRNA plasmids	In vivo electroporation	http://dx.doi.org/10.1038/mtna.2016.92
Mouse	Cardiac and skeletal muscle	Long <i>et al. Science</i> 2016	<i>Dmd</i>	Exon skipping	Cas9 and sgRNA AAVs	Intramuscular, intraperitoneal and retro-orbital injection	http://dx.doi.org/10.1126/science.aad5725
Mouse	Brain	Mikuni <i>et al. Cell</i> 2016	<i>Mecp2, Actb, Dcx, Rab11a, Fmr1, Arc, Pkca, Cacna1c, Ywhae, Camk2a, Camk2b</i>	Epitope tag with ssODN	Cas9 and sgRNA plasmids	In utero electroporation	http://dx.doi.org/10.1016/j.cell.2016.04.044
Mouse	Brain	Monteis <i>et al. Mol. Ther.</i> 2016	<i>Human HTT in tg-mouse</i>	Allele-specific single gene knockout	Cas9 and sgRNA plasmids	Stereotactic injection	http://dx.doi.org/10.1016/j.jymthe.2016.11.010
Mouse	Cardiac and skeletal muscle	Nelson <i>et al. Science</i> 2016	<i>Dmd</i>	Exon deletion	Cas9 and sgRNA AAVs	Intramuscular, intraperitoneal and intravenous injection	http://dx.doi.org/10.1126/science.aad5143
Mouse	Cardiac and skeletal muscle	Tabebordbar <i>et al. Science</i> 2016	<i>Dmd</i>	Exon deletion	Cas9 and sgRNA AAVs	Intramuscular, intraperitoneal and intravenous injection	http://dx.doi.org/10.1126/science.aad5177
Mouse	Liver	Yin <i>et al. Nat. Biotechnol.</i> 2016	<i>Fah</i>	Gene correction with rAAV vector	Cas9 mRNA/lipid nanoparticles, sgRNA + HDR template in rAAV vector	IV injection	http://dx.doi.org/10.1038/nbt.3471
Mouse	Zygotes	Aida <i>et al. Genome Biol.</i> 2015	<i>Actb</i>	Reporter knock-in with plasmid donor	Cas9 protein, synthetic crRNA:tracrRNA	Microinjection	http://dx.doi.org/10.1186/s13059-015-0653-x
Mouse	Non-small-cell lung cancer cell line	Chen <i>et al. Cell</i> 2015	Genes driving tumor growth and metastasis	In vivo screening	Cas9 and sgRNA stable integration	Lentiviral particles	http://dx.doi.org/10.1016/j.cell.2015.02.038
Mouse	Zygotes	Han <i>et al. RNA Biol.</i> 2014	<i>Rian</i>	Chromosomal deletion with two sgRNAs	IVT Cas9 mRNA and sgRNA	Microinjection	http://dx.doi.org/10.4161/rna.29624
Mouse	Lungs	Maddalo <i>et al. Nature</i> 2014	<i>Eml4-Alk</i>	Chromosomal rearrangement	Cas9 and two sgRNAs in adenoviral vector	Intratracheal instillation	http://dx.doi.org/10.1038/nature13902
Mouse	Zygotes	Yang <i>et al. Cell</i> 2013	<i>Tet1-loxP + Tet2-loxP, Sox2-V5, Nanog-mCherry, Oct4-GFP</i>	Reporter knock-in, epitope tag with ssODN or dsDNA	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1016/j.cell.2013.08.022

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Rat	Retina	Suzuki <i>et al. Nature</i> 2016	<i>Mertk</i>	Gene correction by NHEJ-mediated targeted integration	Cas9, sgRNA and donor template in rAAV vector	Subretinal injection	http://dx.doi.org/10.1038/nature20565
Rat	Zygotes	Kaneko <i>et al. Sci. Rep.</i> 2014	<i>Il2rg</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Electroporation	http://dx.doi.org/10.1038/srep06382
Rat	Zygotes	Yoshimi <i>et al. Nat. Commun.</i> 2014	<i>Tyr, Asip, Kit</i>	Gene correction with ssODN	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/ncomms5240
Rat	Zygotes	Hu <i>et al. Cell Res.</i> 2013	<i>Dusp6, Gata5</i>	Single gene knockout, chromosomal deletion with 2 sgRNAs	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/cr.2013.141
Cynomolgus monkey	Zygotes	Niu <i>et al. Cell</i> 2014	<i>PPARG + RAG1</i>	Multiple genes knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1016/j.cell.2014.01.027
Dog (beagle)	Zygotes	Zou <i>et al. J. Mol. Cel. Biol.</i> 2015	<i>MSTN</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1093/jmcb/mjv061
Cattle	Fetal fibroblasts	Ikeda <i>et al. Sci. Rep.</i> 2017	<i>IARS</i>	Gene correction with dsDNA fragment	Cas9 and sgRNA plasmids	Cell electroporation, transgenic embryos produced by SCNT	http://dx.doi.org/10.1038/s41598-017-17968-w
Cattle	Fetal fibroblasts	Gao <i>et al. Gen. Biol.</i> 2017	<i>SLC11A1</i>	Gene insertion with Cas9 nickase and plasmid donor	Cas9n and sgRNA plasmid	Cell electroporation, transgenic embryos produced by SCNT	http://dx.doi.org/10.1186/s13059-016-1144-4
Pig	Fetal fibroblasts	Wang <i>et al. Mol. Ther. Nucl. Acids</i> 2016	<i>APP, LRRK2</i>	Gene mutation with ssODN	Cas9 and sgRNA plasmids	Cell electroporation, transgenic pig produced by somatic cell nuclear transfer (SCNT)	http://dx.doi.org/10.1038/mtna.2016.101
Chinese Bama miniature pig	Zygotes	Wang <i>et al. Sci. Rep.</i> 2015	<i>NPC1L1</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/srep08256
Goat	Zygote	Wang <i>et al. Sci. Rep.</i> 2015	<i>MSTN and FGF5</i>	Multiple genes knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/srep13878
Sheep	Zygotes	Wang <i>et al. Sci. Rep.</i> 2016	<i>MSTN, ASIP, BCO2</i>	Single and multiple genes knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/srep32271
Rabbit	Zygotes	Song <i>et al. Cell. Mol. Life Sci.</i> 2016	<i>TYR</i>	Gene deletion with two gRNAs	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1007/s00018-016-2143-z
Rabbit	Zygotes	Jiang <i>et al. Sci. Rep.</i> 2018	<i>ATP7B</i>	Gene mutation with ssODN	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/s41598-018-19774-4
Ferret (<i>Mustela putorius furo</i>)	Zygotes	Kou <i>et al. Cell Res.</i> 2015	<i>DCX, ASPM and DISC1</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/cr.2015.130
Chicken (<i>Gallus gallus</i>)	Embryos	Abu-Bonsrah <i>et al. Sci. Rep.</i> 2016	<i>DGCR8</i>	Single gene knockout	Cas9 and sgRNA plasmid	Microinjection, electroporation	http://dx.doi.org/10.1038/srep34524
Japanese medaka (<i>Oryzias latipes</i>)	Zygotes	Ansai & Kinoshita. <i>Biol. Open</i> 2014	<i>park7</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1242/bio.20148177
Zebrafish (<i>Danio rerio</i>)	Zygotes	Chang <i>et al. Cell Res.</i> 2013	<i>etsrp, gata5, gata4</i>	Single gene knockout, sequence knock-in with ssODN	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/cr.2013.45
Zebrafish (<i>D. rerio</i>)	Zygotes	Hwang <i>et al. Nat. Biotechnol.</i> 2013	<i>fh, th1, apoea, rgs4, tph1a, drd3, grla3a, slc6a3, tial1, gsk3b</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/nbt.2501
Zebrafish (<i>D. rerio</i>)	Zygotes	Jao <i>et al. PNAS</i> 2013	<i>egfp, tyr, gol, mitfa, ddx19</i>	Single and multiple genes knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1073/pnas.1308335110
Frog (<i>Xenopus</i>)	Zygotes	Nakayama <i>et al. Genesis</i> 2013	<i>tyr, six3</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1002/dvg.22720
Silkworm (<i>Bombyx mori</i>)	Preblastoderm embryos	Wang <i>et al. Cell Res</i> 2013	<i>BLOS2</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/cr.2013.146
Silkworm (<i>B. mori</i>)	Eggs	Ma <i>et al. Sci Rep</i> 2014	<i>BmKu70</i>	Single gene knockout	Cas9 and sgRNA plasmids	Microinjection	http://dx.doi.org/10.1038/srep04489
Butterfly (<i>Papilio xhutus</i>)	Eggs	Li <i>et al. Sci Rep</i> 2015	<i>Abd-B, ebony, frizzled</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT)	Microinjection	http://dx.doi.org/10.1038/ncomms9212
Drosophila	Lethal at pupal stage	Lin <i>et al. Genetics</i> 2015	<i>Wg</i>	Transcriptional activation	dCas9-VPR and sgRNA tg-flies	Cross of transgenics flies	http://dx.doi.org/10.1534/genetics.115.181065
Drosophila	Preblastoderm embryos	Bassett <i>et al. Cell Rep.</i> 2013	<i>yellow, white</i>	Single gene knockout	Cas9 mRNA and sgRNA (IVT) ^a	Microinjection	http://dx.doi.org/10.1016/j.celrep.2013.06.020

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Mosquito (<i>Anopheles stephensi</i>)	Zygotes	Gantz <i>et al. PNAS</i> 2015	<i>kh</i>	Gene drive	Cas9 protein + plasmid expressing Cas9, sgRNA and gene drive	Microinjection	http://doi.org/10.1073/pnas.1521077112
Mosquito (<i>A. gambiae</i>)	Zygotes	Hammond <i>et al. Nat Biotechnol</i> 2016	<i>AGAP005958, AGAP007280, AGAP011377</i>	Gene drive	Cas9, sgRNA and gene drive plasmids	Microinjection	http://dx.doi.org/10.1038/nbt.3439
Mosquito (<i>Aedes aegypti</i>)	Preblastoderm embryos	Kistler <i>et al. Cell Rep.</i> 2015	<i>AAELO10779, AAEL004091, AAEL000926, AAEL014228, AAEL002575, AAEL013647, Aaeg-wtrw</i>	Gene knockout with ssODN, chromosomal deletion with two sgRNAs, reporter knock-in with plasmid donor	Cas9 protein or mRNA and sgRNA	Microinjection	http://dx.doi.org/10.1016/j.celrep.2015.03.009
<i>Caenorhabditis elegans</i>	Gonads	Paix <i>et al. Nucl. Acids Res.</i> 2016	<i>dpy-10, gtbp-1, meg-3</i>	Reporter knock-in with ssODN or dsDNA, gene replacement	Cas9 protein, synthetic crRNA:tracrRNA (Dharmacon)	Microinjection	http://dx.doi.org/10.1093/nar/gkw502
<i>C. elegans</i>	Gonads	Friedland <i>et al. Nat. Methods</i> 2013	<i>unc-119, dpy-13, klp-12, Y61A9LA.1</i>	Single gene knockout	Cas9 and sgRNA plasmids	Microinjection	http://dx.doi.org/10.1038/nmeth.2532

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