

Docket #: S15-174

CRISPR/Cas9 Knock-in Mice

Researchers in Prof. Monte Winslow's laboratory have developed two viable, fertile transgenic mouse strains that enable rapid, simple generation of loss-of-function models with CRISPR/Cas9 mediated genome editing in vivo or ex vivo. These mice can be used to inactivate genes of interest without the time and expense needed for traditional knock out mice. Specifically, the H11LSL-Cas9 knock-in mice have Cre recombinase-dependent expression of Cas9 directed by a CAG promoter. There is an additional strain without the LSL cassette that can be used for genome editing with vectors that do not carry Cre. These mice enable the rapid functional investigation of any gene of interest and make loss-of-function experiments in vivo no more difficult than altering those genes in vitro.

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Stage of Research

The inventors have used this mouse strain to study pancreatic cancer by initiating pancreatic neoplasias that progress into invasive and metastatic tumors. They continue to use these strains to generate additional mouse models of human cancer.

Applications

- **Genome editing** in vivo and ex vivo for functional genetic research

Advantages

- **Fast, simple, and low-cost** - does not require generation of new mouse alleles and incorporating them into complex genetically engineered mouse models

- **Controlled expression** - researchers can easily control the spatial and temporal inactivation of genes of interest by targeted delivery of Cre or by using cell- or tissue-specific promoters
- **No packaging size constraints** - unlike viral delivery of Cas9, which is burdened by packaging size limits, researchers using these mice can generate single or multiple simultaneous mutations by selecting a Cre recombinase driven by a promoter of interest and a specific single guide RNA (sgRNA)

Publications

- Chiou, S. H., Winters, I. P., Wang, J., Naranjo, S., Dudgeon, C., Tamburini, F. B., ... & Caswell, D. R. (2015). [Pancreatic cancer modeling using retrograde viral vector delivery and in vivo CRISPR/Cas9-mediated somatic genome editing.](#) *Genes & development*, 29(14), 1576-1585.
- Nature Methods paper: <https://www.nature.com/articles/nmeth.4297>
- Nature Communications paper: <https://www.nature.com/articles/s41467-017-01519-y>

Innovators

- Monte Winslow
- Santiago Naranjo
- Ian Winters

Licensing Contact

Brenda Martino

Biological Materials Specialist

[Email](#)