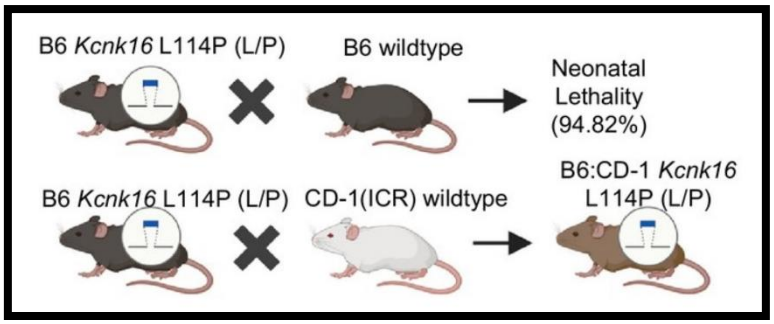
Vanderbilt Genome Editing Resource

SUMMER 2024 NEWSLETTER



Mouse Highlight. VGER helped David Jacobson (Professor in MPB) to derive a mouse model mouse for a MODY-associated *KCNK16* L114P mutation. In humans, this mutation causes an increase in islet glucagon secretion and limits insulin secretion resulting in transient neonatal diabetes and glucose dysregulation in adults. The mutation was frequently lethal in a C57BL/6J background, but this was overcome by breeding into the CD-1 strain, allowing in-depth analysis.

Nakhe AY, Dadi PK, Kim J, Dickerson MT, Behera S, Dobson JR, Shrestha S, Cartailler JP, Sampson L, Magnuson MA, Jacobson DA. *Elife*. 2024 May 3; PMID: 38700926

Safe-Harbor Loci. The CRISPR-READI strategy, which achieves high genome editing efficiency by combining AAV-mediated introduction of donor DNA into mouse embryos with electroporation of CRISPR/Cas9 ribonucleoproteins, is leading us to recommend the routine utilization of safe harbor loci for integrating transgenes into the genome. Insertions into these loci assure consistent transgene expression levels and patterns over time. Using CRISPR-READI we've obtained an average 42% integration efficiency for 14 relevant projects, and we now have strategies using it that will insert 4 kb of DNA into either the Igs1/Hipp11/H11 or Gt(ROSA)26Sor sites.

Guide RNA Arrays for CRISPR Mutagenesis and Inhibition. We welcome new projects to implement small scale *in vivo* CRISPR screens as described in Large-scale multiplexed mosaic CRISPR perturbation in the whole organism. We've successfully produced our first so-called iMAP mouse that contains an expression array of six guide RNAs and will soon see how well it works. This is a promising technology that can be used in a wide variety of ways.

Vanderbilt Cryopreserved Mouse Repository. Cryopreserving your mouse strains safeguards the integrity of your colony, keeps cage costs down, and facilitates distribution of your lines to other investigators. We encourage you to submit your unique mouse strains to be securely held in monitored liquid nitrogen tanks and curated in our online repository database. Accepted strains do not accrue storage fees and we can hold your strain privately for up to one year, at which point we make the strain available to the wider scientific community.

Thank you, Ron. We are pleased that Dr. Ron Emeson, Professor of Pharmacology, has agreed to chair the Faculty Advisory Committee for VGER. Dr. Emeson is a long-term VGER user, former VGER Scientific Director, and chair of the Vanderbilt IACUC. He will help us comply with new VBS oversight guidelines that seek to improve shared resource management.

Make a new mouse! It has never been easier to reliably derive new mouse models. Our CRISPR-based technologies have significantly improved the efficiency, precision, and versatility of generating mouse models. Please see our website for an overview of the currently available technologies. We're always happy to discuss potential new projects.

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Contact VGER. As always, please contact Leesa Sampson at leesa.sampson@vanderbilt.edu or Jennifer Skelton at jennifer.skelton@vanderbilt.edu to discuss or initiate a project. Also, please email Jennifer Skelton to let us know about your recent publications describing new VGER strains.

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Linda Gower
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Mark A. Magnuson

Years in existence	30
Investigators served	369
Unique lines produced since 1993	>3500
CRISPR-edited lines since 2013	165
Lines cryopreserved	>1000
Lines shared in VCMR	57

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