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TECHNOLOGY ABSTRACT

Mouse Model for Organ-Specific, CRISPR-Based Target Discovery

Description

A multiplexed *in vivo* CRISPR mouse platform enabling rapid, organ-specific discovery of cancer drivers in native tumor microenvironments.

Background

Identifying and validating cancer driver genes remains a major bottleneck in oncology research and drug discovery. While genetically engineered mouse models are considered the gold standard for studying gene function *in vivo*, traditional approaches are slow, costly, and limited to testing only a few genes at a time. At the same time, *in vitro* CRISPR screens often fail to capture the complexity of native tissue architecture, immune interactions, and tumor microenvironments that critically influence cancer initiation and progression. There is a strong unmet need for scalable, physiologically relevant in vivo screening platforms that allow rapid functional interrogation of large numbers of candidate genes across multiple organs.

Technology Overview

This technology is a versatile *in vivo* screening platform that integrates highly multiplexed CRISPR/Cas9 genome editing with autochthonous, organ-specific mouse cancer models. The system enables simultaneous functional interrogation of hundreds of candidate genes directly within native tissues, preserving intact immune systems and physiological microenvironments.

The platform is built on conditional Lox-Stop-Lox (LSL) Cas9-GFP mouse strains, which allow spatially and temporally controlled activation of Cas9. Organ-specific delivery of lentiviral vectors encoding single-guide RNAs (sgRNAs) and Cre recombinase enables precise induction of somatic gene knockouts in targeted tissues. Multiple delivery routes—including *in utero* injections, intraductal injections, inhalation-based lung delivery, and retrograde bile duct injections—allow efficient transduction of diverse organs such as skin, head and neck epithelium, brain, lung, mammary gland, and pancreas.

Careful viral titration generates tens of thousands of discrete Cas9-positive clones per organ, each traceable via fluorescent markers. Knockout efficiencies of approximately 70–85% have been demonstrated across multiple tissues and validated using both reporter genes and endogenous tumor suppressors. Importantly, the system supports combinatorial genetic perturbations,

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enabling direct study of genetic interactions, such as cooperation between oncogenic mutations and tumor suppressor loss.

By enabling rapid, parallel testing of hundreds of genes in a single mouse experiment, this technology dramatically reduces time, cost, and animal usage compared to conventional mouse modeling approaches. It provides a powerful discovery engine for uncovering novel cancer drivers, tumor suppressors, and context-specific genetic dependencies.

Benefits

- Enables high-throughput *in vivo* gene screening in native tissues
- Preserves physiological microenvironment and immune context
- Dramatically reduces cost and time versus traditional mouse models
- Supports multiplexed and combinatorial genetic interactions
- Applicable across multiple cancer-relevant organs

Applications

- Discovery of novel cancer driver and tumor suppressor genes
- Target identification and validation for oncology & immune-oncology drug development
- Functional genomics studies in complex tissues
- Preclinical modeling of genetic interactions, combination targets and resistance mechanisms
- Platform for academic, pharmaceutical, and biotech oncology research

Commercial Opportunity

Available for sponsored research/ partnership

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