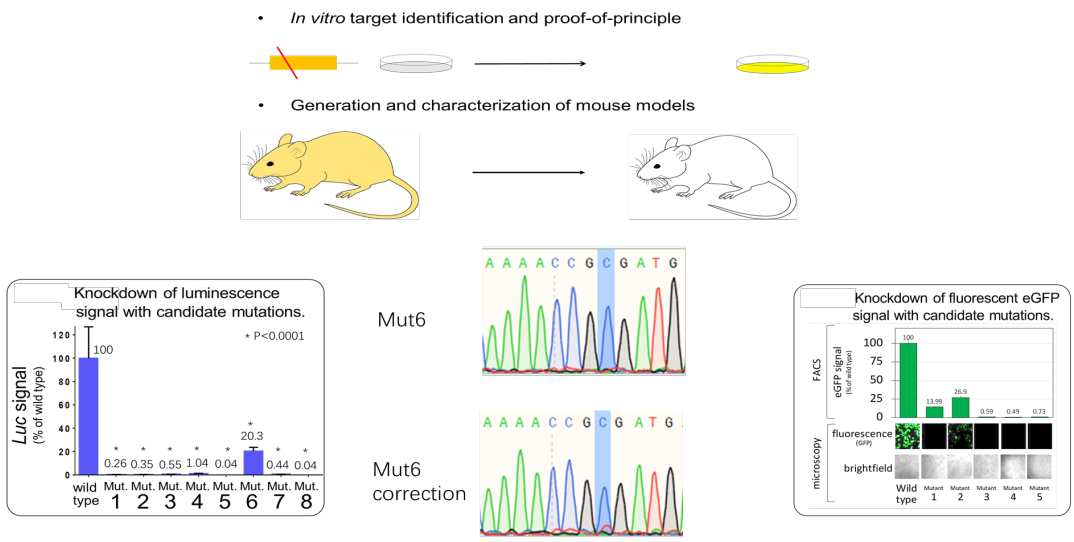

DEVELOPMENT OF I*N VIVO* MUTANT REPORTER MOUSE MODELS TO OPTIMIZE AND EVALUATE CRISPR/CAS9 THERAPEUTIC BASE EDITING

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Of the over 6,250 known monogenic genetic diseases, <5% have effective treatments[1]. New advances in genome engineering, such as CRISPR/Cas9, have provided a new therapeutic opportunity to directly repair disease-causing mutations in patients. We are especially interested in the use of CRISPR/Cas9 base editors to precisely and accurately repair specific nucleotides in the DNA. It has been shown the base editors can achieve up to 15-75% editing efficiency *in vitro*[2,3]. However, there is still a great need to fully understand base editing *in vivo* in order to optimize and evaluate this approach before therapeutic applications. **We aim to develop two mutant reporter mouse models which allow us to easily and precisely quantify gene editing efficiency and analyze off-target effects.**

The point mutations identified in both reporter genes abolish up to 99.96% of the activity *in vitro*. Upon base editing, ~27% mutant nucleotides were corrected to wildtype restoring luminescence/fluorescence which could be quantified. Currently, desired mutations are successfully installed in the founder mice which carry the non-functional reporter genes. Live animal whole body imaging has also confirmed the loss of reporter gene signals in the mice.

We have generated two mutant reporter mouse models. These animal models can be used to monitor *in vivo* genome editing, to optimize delivery of genome-editing components into a variety of target tissues to aid many gene therapy applications, and to compare new generations of base editors.

References

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