B6-*p53*$^{LSL-R172H}$

Stain Name：B6/JGpt-*Trp53*$^{em1Cin(LSL-R172H)}$/Gpt

Strain Type：Targeted Mutation

Strain Number：T007671

Background：C57BL/6JGpt

Description

The tumor suppressor *p53* exerts its biological function by regulating transcription of numerous downstream target genes involved in cell cycle arrest, apoptosis, DNA repair, senescence, and metabolism as a transcription factor[1,2]. P53 is also directly recruited to the mitochondria and induces apoptosis independent of its function as a transcription factor[3]. Under unstressed physiological conditions, P53 expression is maintained at a low level. Once cells are exposed to genotoxic stresses, P53 is posttranslationally modified through phosphorylation and acetylation, becomes stabilized, and induces cell cycle arrest and/or cell death. P53 act as the guardian of the genome. When P53 activity is lost by gene deletion or mutations, normal cells lose the abilities to control their growth and death, leading to immortalization and ultimately cancer[4]. The observation that over 50% of human cancers have mutations in the *p53* gene. *p53*^{R172H} mutations not only lose the transcriptional activity, but also have the dominant-negative (DN) activity by hetero-oligomerizing with wild-type P53. Moreover, mutant *p53* shows oncogenic gain-of-function (GOF) activities, such as enhanced tumor progression, metastatic potential, and drug resistance, when overexpressed even in cells lacking wildtype *p53*[5].

GemPharmatech use gene editing technology to develop *p53*$^{LSL-R172H}$ mouse on C57BL/6 background(B6-*p53*$^{LSL-R172H}$). Floxed Stop cassette will be deleted in genome when Cre recombinase exists, and then P53^{R172H} protein express, which allows to control of the timing, location, and multiplicity of tumor initiation. When B6-*p53*$^{LSL-R172H}$ mice cross with B6-*Pdx1* Cre (expressing Cre recombinase in pancreas) mice, the mRNA in pancreas would express *p53* R172H in offspring mice. B6-*p53*$^{LSL-R172H}$ mice can be use for the study of cancer and development.

Strategy

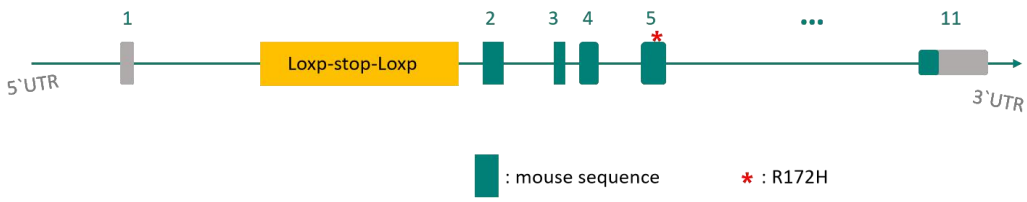

Fig.1 Schematic diagram of B6-*p53*$^{LSL-R172H}$ model Stratery.

Application

1. Pancreatic cancer, colorectal cancer, breast cancer and non-small cell lung cancer study
2. Screen of small-molecule antitumor drugs

Data support

1. mRNA analysis of B6-*p53*$^{LSL-R172H}$ mice

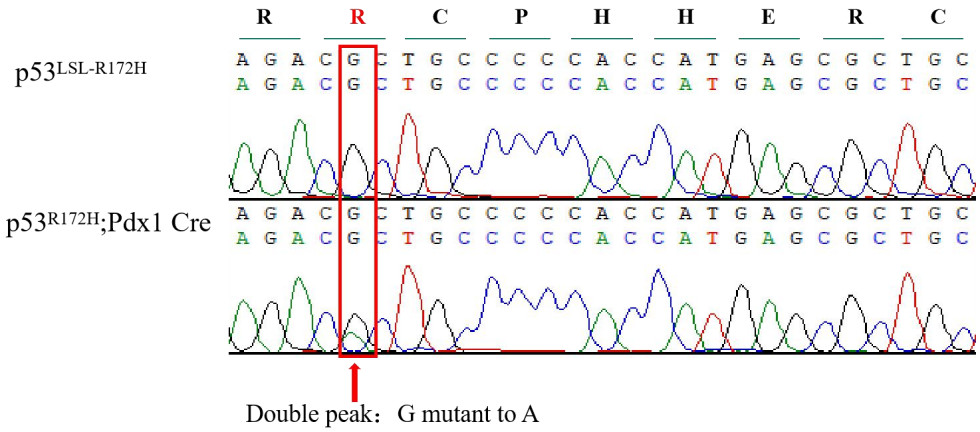

Fig 2. mRNA analysis in pancreas of B6-*p53*$^{LSL-R172H}$ mice. B6-*p53*$^{LSL-R172H}$ mice crossed with B6-*Pdx1* Cre mice, the pancreas of offspring mice (B6-*p53*^{R172H}*;Pdx1* Cre, 5 weeks) were extracted total mRNA for sequencing. The double peak suggests that *p53* codons 172 mutate from CGC to CAC,and the amino acid change from R to H. **The results showed that：** B6-*p53*$^{LSL-R172H}$ mice could express R172H when the Stop sequences deleted. B6-*p53*$^{LSL-R172H}$ mice can be use for the study of cancer and development.

References

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4. Muller, Patricia AJ, and Karen H. Vousden. "p53 mutations in cancer." *Nature cell biology* 15.1 (2013): 2.

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