KPS

Strain Name： B6/JGpt-*Kras*$^{FLEX-G12C}$; *Trp53*$^{em1Cin(LSL-R172H)}$; *Sftpc*$^{em1Cin(IRES-iCre)}$/Gpt

Strain Type： Targeted Mutation

Strain Number： T057165

Background： C57BL/6JGpt

Description

KRAS (Kirsten rat sarcoma virus) is a membrane-associated GTPase signaling protein that participates in the process of cell proliferation and differentiation [1]. Mutations of KRAS are found in a variety of human malignancies, including pancreatic cancer, colorectal cancer, and non-small cell lung cancer at high frequency [2]. KRAS G12C is the most common mutation in lung cancer (about 50%).

The tumor suppressor p53 exerts its biological function by regulating the transcription of numerous downstream target genes involved in cell cycle arrest, apoptosis, DNA repair, senescence, and metabolism as a transcription factor [3,4]. When P53 activity is lost by gene deletion or mutations, normal cells lose the ability to control their growth and death, leading to immortalization and ultimately cancer [5]. The observation is that over 50% of human cancers have mutations in the p53 gene.

Surfactant protein C (SP-C), is one of the pulmonary surfactant proteins, encoded by the SFTPC gene. IRES-iCre was introduced downstream of the 3'UTR of mouse Sftpc gene by CRISPR/Cas9 technology to build the Sftpc-IRES-iCre(T004715) mice [6]. When crossed with a strain with a loxP site flanked sequence in its genome, Cre-mediated recombination will result in the excision of the DNA fragment between the two loxPs in Type II alveolar cells.

To facilitate lung cancer research and promote lung cancer treatment, we established the KPS mouse model. KRAS G12C and P53 R172H protein were expressed at endogenous levels in ATII cells, inducing the occurrence of lung cancer. The KPS mouse model can be used to study the occurrence and development of lung cancer, and screen-related drugs.

Strategy

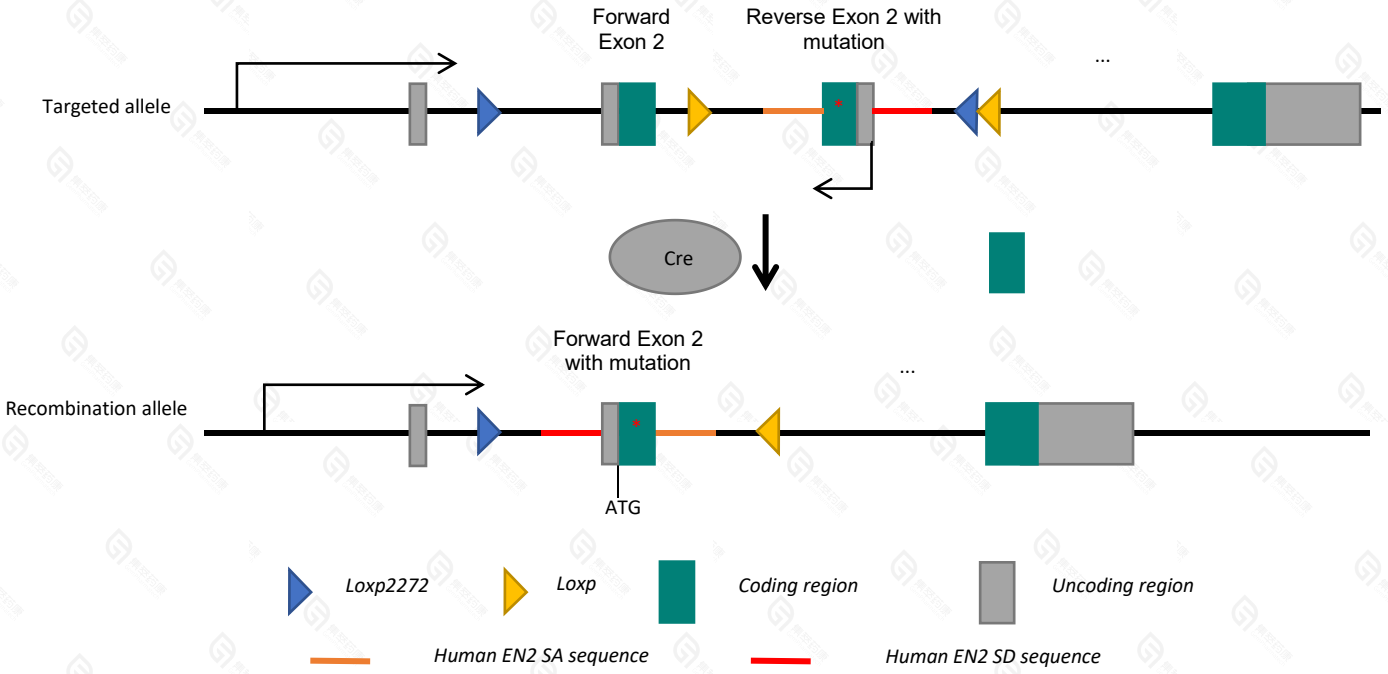

Fig 1. Schematic diagram of Kras$^{FLEX-G12C}$ model stratery

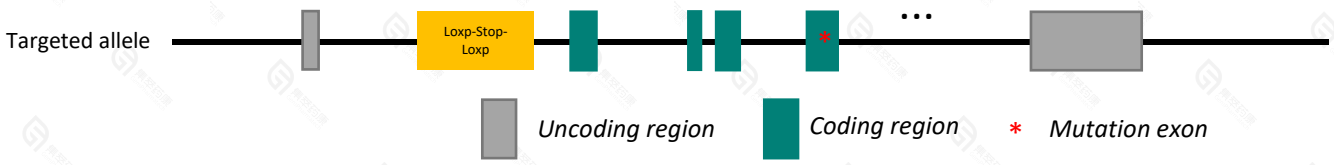

Fig 2. Schematic diagram of B6-p53$^{LSL-R172H}$ model stratery

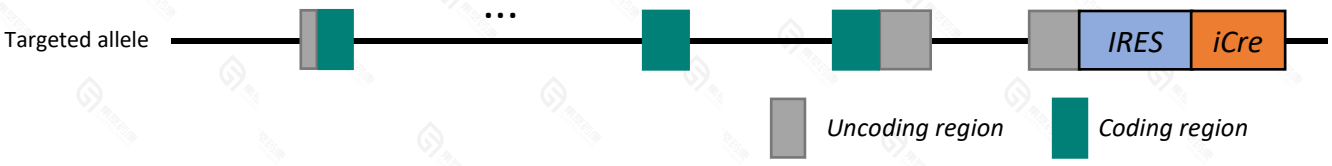

Fig 3. Schematic diagram of Sftpc-IRES-iCre model stratery

Applications

1. Non-small cell lung cancer study
2. Screen of small-molecule antitumor drugs

Supporting data

1. Histopathology data

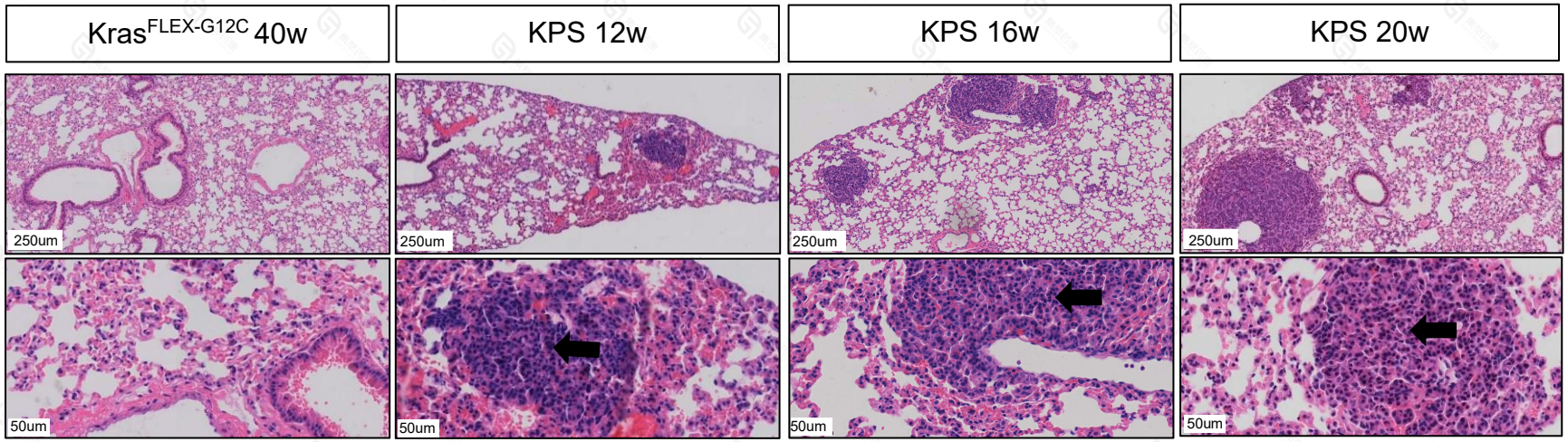

Fig 4. Histopathology of lung tissues from Kras$^{FLEX-G12C}$; p53$^{LSL-R172H}$; Sftpc-IRES-iCre (KPS) mice at different ages.
The lungs were collected from KPS mice between 12-20 weeks of age. All tissue were examined by H&E staining for pathology analysis. The tumors were detected beginning at 12 weeks, and the proportion of tumor cells in the lung increased with age. All KPS mice (16/16) developed lung cancer. These results showed that the TP53^{R172H} mutation accelerated the occurrence and progression of the lung cancer. Black arrow: infiltration of tumor cells.

References

1. Campbell, Sharon L., et al. "Increasing complexity of Ras signaling." Oncogene 17.11 (1998): 1395.
2. Downward, Julian. "Targeting RAS signalling pathways in cancer therapy." Nature Reviews Cancer 3.1 (2003): 11.
3. Levav-Cohen, Yaara, et al. "The p53-Mdm2 loop: a critical juncture of stress response." Mutant p53 and MDM2 in Cancer. Springer, Dordrecht, 2014. 161-186.
4. Vaseva, Angelina V., and Ute M. Moll. "The mitochondrial p53 pathway." Biochimica et Biophysica Acta (BBA)-Bioenergetics1787.5 (2009): 414-420.

5. Muller, Patricia AJ, and Karen H. Vousden. "p53 mutations in cancer." Nature cell biology 15.1(2013): 2.
6. Shimshek D R, Kim J, Hübner M R, et al. "Codon‐improved Cre recombinase (iCre) expression in the mouse." genesis 2002, 32(1): 19-26.