Kras$^{FLEX-G12C}$

Strain Name： C57BL/6JGpt-*Kras*$^{FLEX-G12C}$ /Gpt
Strain Type： Knock-in
Strain Number： T053603
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]. Somatic mutations in the KRAS gene are involved in the development of several types of cancer, particularly pancreatic, colorectal cancers and lung cancers. The mutation on codon 12, which is particularly prevalent in pancreatic cancers, substitutes glycine for a valine or aspartate [2] and leads to GTPase losing its function and essentially allows GTP to continue to signal cell growth [3], thereby allowing uncontrolled and continuous growth, angiogenesis as well as overriding apoptosis [1]. Although it has long been deemed “undruggable”, with the development of drugs specifically binding the KRAS-G12C mutant protein, clinical trials that directly inhibit oncogenic RAS have recently made promising improvements.

To study the relationship between the mutational activation of KRAS and tumorigenesis, and promote the development of KRAS-G12C inhibitors, we established Kras$^{FLEX-G12C}$ strain. The traditional KRAS-G12C conditional expression mouse model, that inserted the loxp-stop-loxp casset in the intron of Kras gene, has a risk of leakage of KRAS G12C protein expression for the failure of the stop casset. compared in the B6-*Kras*$^{LSL-G12C}$. While Leakage of KRAS G12C protein expression will not occur in the Kras$^{FLEX-G12C}$ without cre recombinase.

Floxed sequences are likely to reverse and delete in the Kras$^{FLEX-G12C}$ mouse genome when cre recombinase exists. And oncogenic KRAS-G12C protein are expressed with endogenous levels, which allows to control of the timing, location, and the multiplicity of tumor initiation. When Kras$^{FLEX-G12C}$ mice crossed with Sftpc-IRES-iCre(T004715) mice (expressing Cre recombinase in type II alveolar cells), the offspring mice were developed the lung tumor. Kras$^{FLEX-G12C}$ mouse model can be used to study the occurrence and development of cancer.

Strategy

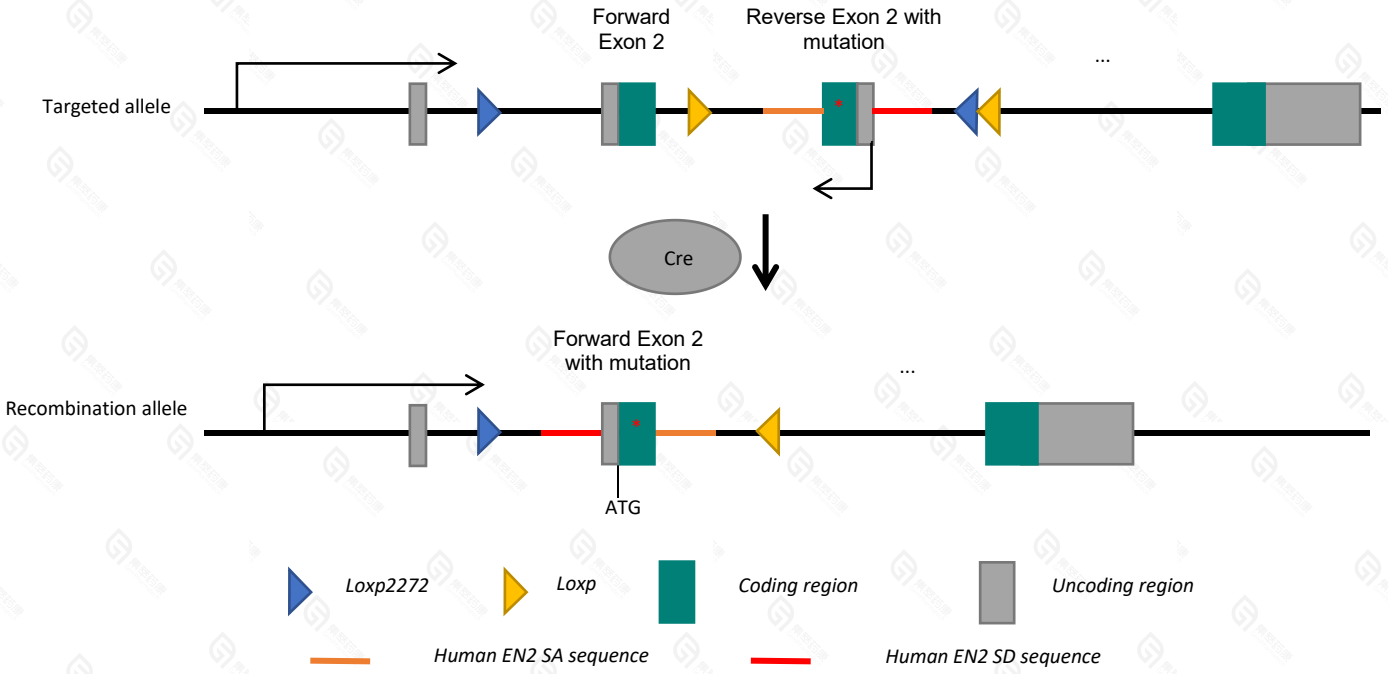

Fig 1. Schematic diagram of Kras$^{FLEX-G12C}$ model stratery

Applications

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

Data support

1. Histopathology datas in the Kras$^{FLEX-G12C}$ crossed with Sftpc-IRES-iCre mouse model

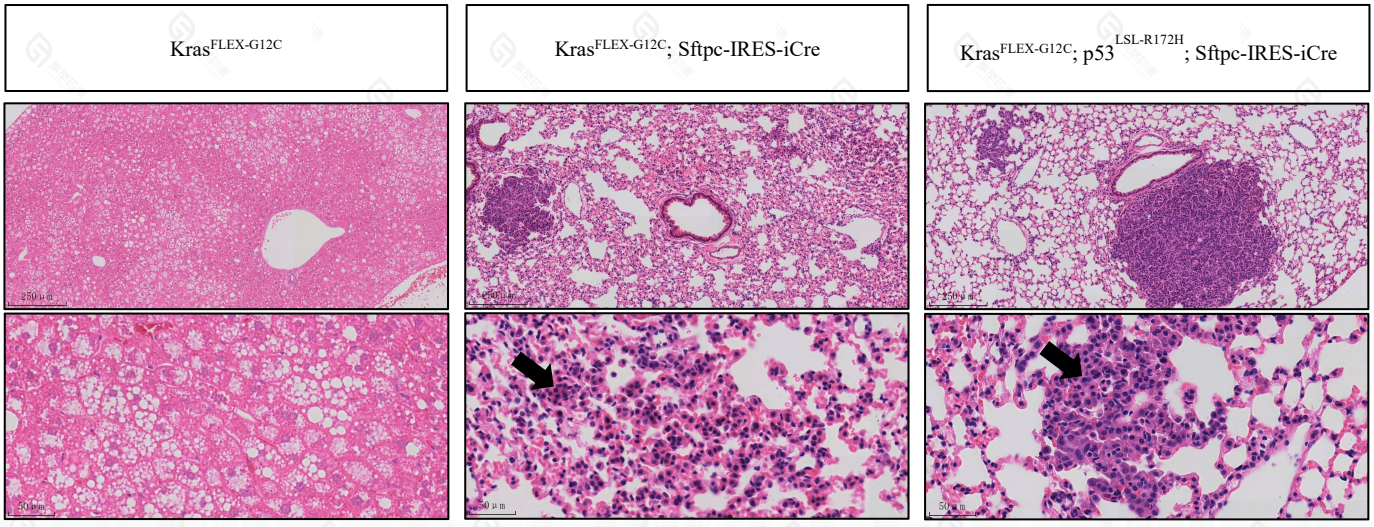

Fig 2. Detection of the lung histopathology in the Kras$^{FLEX-G12C}$ crossed with Sftpc-IRES-iCre mouse model

The lung tissues were collected from the Kras$^{FLEX-G12C}$; Sftpc-IRES-iCre mice at 26 weeks of age and the Kras$^{FLEX-G12C}$; p53$^{LSL-R172H}$; Sftpc-IRES-iCre mice at 18 weeks of age for detecting the occurrence of lung cancer. All mice (6 mice for each strain) have developed lung cancer.

Note: Black arrows indicate the 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.