Lung adenocarcinoma (LUAD) is an aggressive form of non-small cell lung cancer.

30% of LUAD patients have mutations in the Kirsten rat sarcoma viral oncogene (K-ras).

K-ras mutations are challenging to directly treat due to drug resistance.

Transcription factor STAT3 is a major component of tumor associated inflammation in K-ras mutant tumors.

STAT3 upregulates immune checkpoint molecules PD-1/PD-L1.

Based on preliminary data, single treatment of TTI-101 reduces tumor number and area in CC-LR mice.

The aim is to investigate the significance of targeting downstream or co-occurring pathways of K-ras.

The methodology involves CC-LR lung cancer mice treated with TT1-101 (a STAT3 inhibitor) and/or anti-PD-1 to investigate the significance of targeting downstream/co-occurring pathways of K-ras.

Results:

- **Figure 1:** Injection of TTI-101 reduces tumor number and area in CC-LR mice. Figures produced by Marco A. Ramos-Castaneda and Stephen Peng.

- **Figure 2:** Injection of TTI-101 reduces tumor number and area in CC-LR mice. Figures produced by Michael J. Clowers and Cody Chou.

- **Figure 3:** TTI-101 +/- anti-PD1 treatment trends toward reduced surface tumor number, but not tumor area in CC-LR mice. Figures produced by Michael J. Clowers and Cody Chou.

- **Figure 4:** Immune cell composition of different treatments in CC-LR mice. Figures produced by Michael J. Clowers.

- **Figure 5:** TTI-101 oral gavage causes modest weight loss in CC-LR mice. Figures produced by Michael J. Clowers and Cody Chou.

Conclusion:

- Based on preliminary data, single treatment of TTI-101 trends toward reduced tumor number.

- Combination treatment of TTI-101 and anti-PD-1 trends toward reduced tumor number and area.

- Combination treatment, when compared to single treatment, is not significant.

- Personalized treatment with TT1-101 and anti-PD-1 may serve as an alternative approach in the future.

Future Work:

- We plan to perform immunohistochemistry staining to detect pSTAT3.

- We also plan to perform qPCR to detect inflammatory markers in the tumor environment.

References:


**Background**

- Lung adenocarcinoma (LUAD) is an aggressive form of non-small cell lung cancer.
- 30% of LUAD patients have mutations in the Kirsten rat sarcoma viral oncogene (K-ras).
- K-ras mutations are challenging to directly treat due to drug resistance.
- Transcription factor STAT3 is a major component of tumor associated inflammation in K-ras mutant tumors.

**Aim**

We treated a K-ras mutant lung cancer mouse model, CC-LR, with TTI-101 (a STAT3 inhibitor) and/or anti-PD-1 to investigate the significance of targeting downstream/co-occurring pathways of K-ras.

**Methodology**

- CC-LR lung cancer mice were treated with TT1-101 (provided by Tweardy and Eckols) and/or anti-PD-1 from 10 to 14 weeks of age.
- Lung samples were extracted and stained with Hematoxylin and Eosin (H&E) staining to determine tumor area percentage.