Objective
Conditional knockout of the IL-1R receptor in KM-LUAD mouse models will allow for a greater understanding of the involvement of the IL-1 cytokine family in tumor promotion and potentially support the idea of a new target for treatment.

Introduction
As of last year, 23% of cancer-related deaths have been attributed to lung cancer. It is the third most common cause of cancer in males and females and its low survival rate has also been an area of concern with only 25% of diagnosed patients surviving up to 5 years.

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer, in which mutations of the K-ras oncogene are the driving factor leading to the progression of lung adenocarcinoma (LUAD), a histological subtype of NSCLC.

Mutations of the K-ras oncogene have been shown to cause increased activation of the NF-κB pathway and inflammatory response, promoting a pro-tumor microenvironment.

The pro-inflammatory cytokine IL-1β plays a major role in the activation of the NF-κB pathway and has been found in abundance in tumor sites.

Methods
Animals:

Step 1 (H&E and IHC):
H&E staining was used to calculate tumor area. IHC staining for Ki-67 and ERG markers were performed to measure proliferation and angiogenesis, respectively.

Step 2 (qPCR):
Used to find the concentration of desired DNA in our samples of interest. Fold changes between test groups and controls were calculated using the 2−ΔΔCt method.

Results

Conditional Knockout of the IL-1 receptor leads to a significant decrease in tumor area. (A) Representative photomicrographs of the H&E stained whole lung sections from 14 week old CC-LR mice as well as LR/IL-1RΔΔ mice (4X). Representative photomicrographs of the stained IHC sections (20X) and corresponding quantification of (B) proliferation marker Ki-67 and (C) angiogenesis marker ERG. Data represent mean±SEM; unpaired t-test, *p<0.05.

Conclusion
- IL-1R conditional knockout results in a significant decrease in tumor burden as shown by the H&E staining.
- IHC staining indicated a negative trend in the expression of Ki67 along with ERGs, which could mean the IL-1R conditional knockout suppressed tumor proliferation and angiogenesis.
- qRT-PCR analysis of RNA extracted from the lung revealed an increase in Cds expression along with a significant decrease in Ym1 expression, which supports the notion of increased antitumor cytotoxic activity.

Future Directions
- Repeat qPCR analysis to confirm results and add additional markers to gain a more complete understanding of the tumor microenvironment.
- Stain samples with p65 marker to evaluate the effects of conditional knock-out of IL-1R will have on the NF-κB pathway.

References
3. https://doi.org/10.1016/j.lungcan.2019.05.015

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