Comparative Effects of Combustible Cigarette versus Electronic Cigarette Exposures on KRAS Mutant Lung Cancer Promotion

**INTRODUCTION**

- Combustible cigarette smoking (CCS) is linked to approximately 90% of all lung cancer cases by inducing a multitude of tumor-initiating effects, including inflammation. Inflammation has been shown to persist even after smoking cessation.
- The use of non-combustible smoking vectors, such as electronic cigarette vapors (ECV), has recently seen increasing popularity among younger generations. Despite this alarming trend, the long-term health effects of ECV are yet poorly understood.
- Our lab aimed to compare the effects of CCS and ECV on lung immune response and tumor growth using a specific mouse model of lung adenocarcinoma with a K-ras mutation in the airway epithelium (CC-LR).

**METHODS**

**CC-LR**

3R4F Research Cigarettes

**Combustible Cigarette Smoke (CCS)**

3mg/ml liquid nicotine in 50%/50% PGVG solution

**Electronic Cigarette Vapors (ECV)**

72mg/mL liquid nicotine in 50%/50% PGVG solution

Figure 1. Exposure regimen for three cohorts of CC-LR mice (Naive, CCS, & ECV) occurring 5 days per week for 2 hours each day.

**RESULTS**

**Figure 2. Validation of exposure regimen.** To ensure exposure regimen was representative of human smoker population, we measured the serum cotinine levels, an oxidative stress marker, and the percent inhibition of superoxide dismutase. Significance was determined at a p-value greater than 0.05.

**Figure 3. Quantification of surface tumors, percent tumor area, total Ki67+ or ERG+ nuclei for determination of tumor burden.** Significance was determined at a p-value greater than 0.05. Scale Bar = 100 μm for H&E images and 50 μm for Ki67 and ERG images.

**Figure 4. Quantification of Myeloid Cells in Bronchoalveolar Lavage Fluid (BALF) and Whole Lung Tissue.** Significance was determined at a p-value greater than 0.05.

**Figure 5. Quantification and Immunophenotyping of Lymphoid Cells in Whole Lung Tissue.** Significance was determined at a p-value greater than 0.05.

**Figure 6. Immunophenotyping of Whole Lung Microenvironment at RNA and Protein Level.** Significance was determined at a p-value greater than 0.05.

**CONCLUSION**

Although both CCS and ECV promoted inflammation with CCS inducing a more immunosuppressive phenotype than ECV, only CCS significantly modulated tumorigenesis. Future studies probing the cell-to-cell crosstalk within CCS and ECV-exposed CC-LR mice are needed for the development of a precise therapeutic strategy targeting K-ras mutant lung cancer.

**ACKNOWLEDGEMENT**

Funded by: The Carl B. & Florence E. King Foundation Summer Program in Biomedical Sciences, The University Cancer Foundation via the IRG program, the University of Texas MD Anderson Cancer Center, and RO1 grant from NIH/NCI (R01CA225977) both to S.J.M.