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

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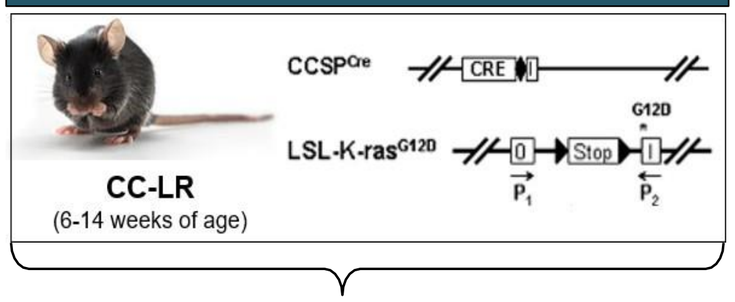
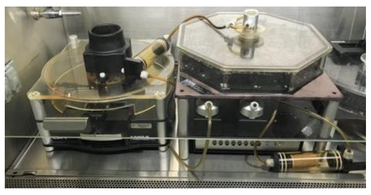
INTRODUCTION

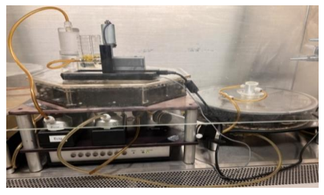
- Combustible cigarette smoking (**CCS**) is linked to approximately 90% of all lung cancer cases by inducing a multitude of tumor-initiating effects, including inflammation. Inflammation has been shown to persist even after smoking cessation.
- The use of non-combustible smoking vectors, such as electronic 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





Combustible Cigarette Smoke (CCS)
3R4F Research Cigarettes



Electronic Cigarette Vapors (ECV)
72mg/mL liquid nicotine in 50%/50% PGVG solution

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

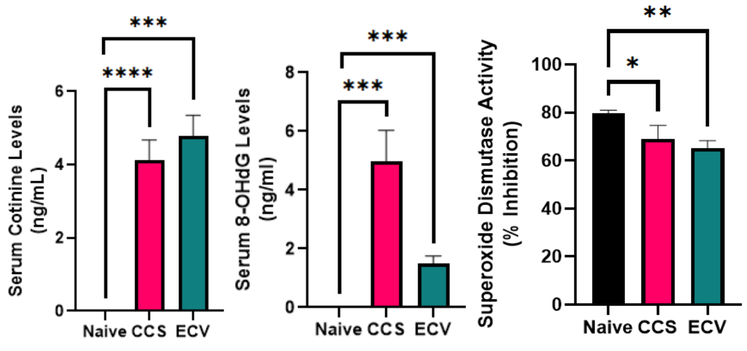


Figure 2. Validation of exposure regimen. To ensure exposure regimen was representative of human smoker population, we measured the serum cotinine levels, an oxidative stress marker, and the percent inhibition of superoxide dismutase. Significance was determined at a p-value greater than 0.05.

RESULTS

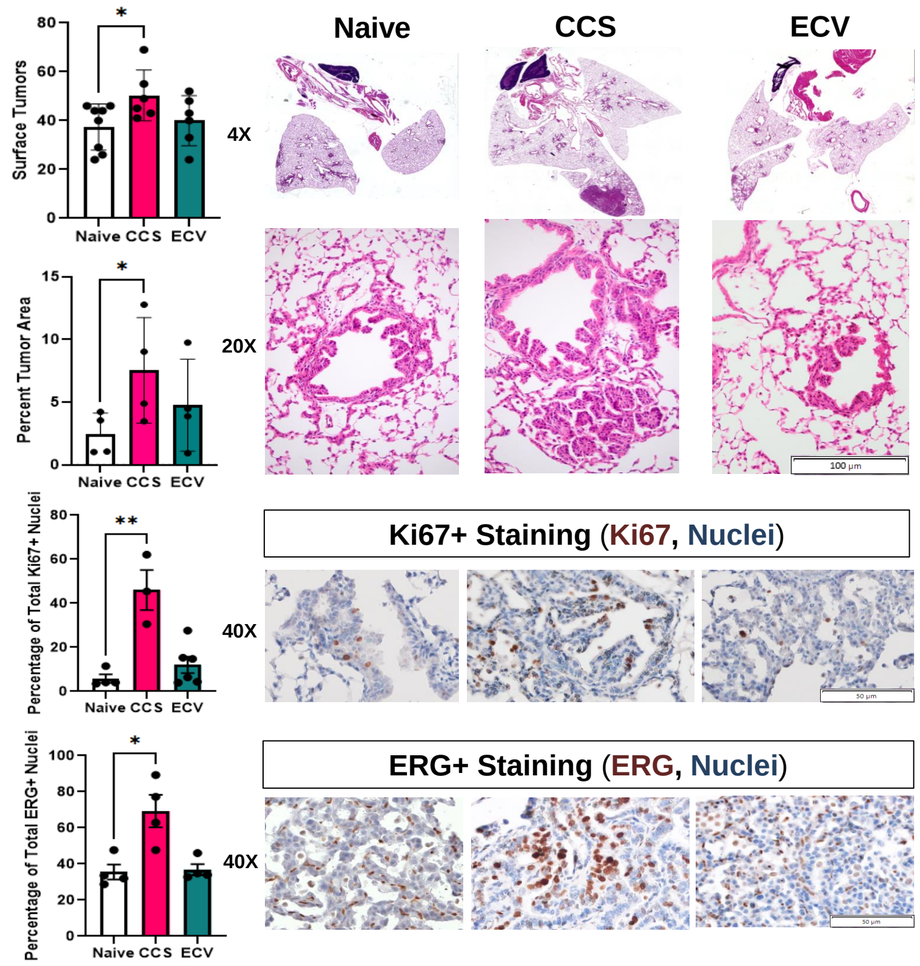


Figure 3. Quantification of surface tumors, percent tumor area, total Ki67+ or ERG+ nuclei for determination of tumor burden. Significance was determined at a p-value greater than 0.05. Scale Bar = 100 μm for H&E images and 50 μm for Ki67 and ERG images.

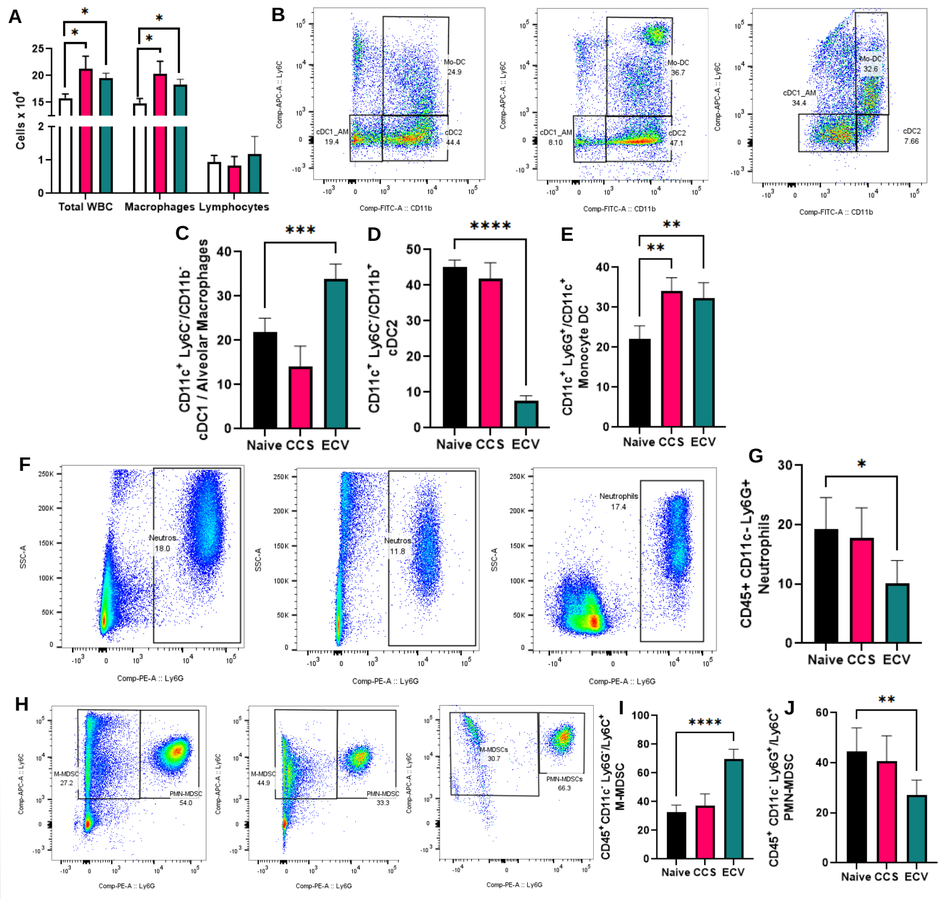


Figure 4. Quantification of Myeloid Cells in Bronchoalveolar Lavage Fluid (BALF) and Whole Lung Tissue. Significance was determined at a p-value greater than 0.05.

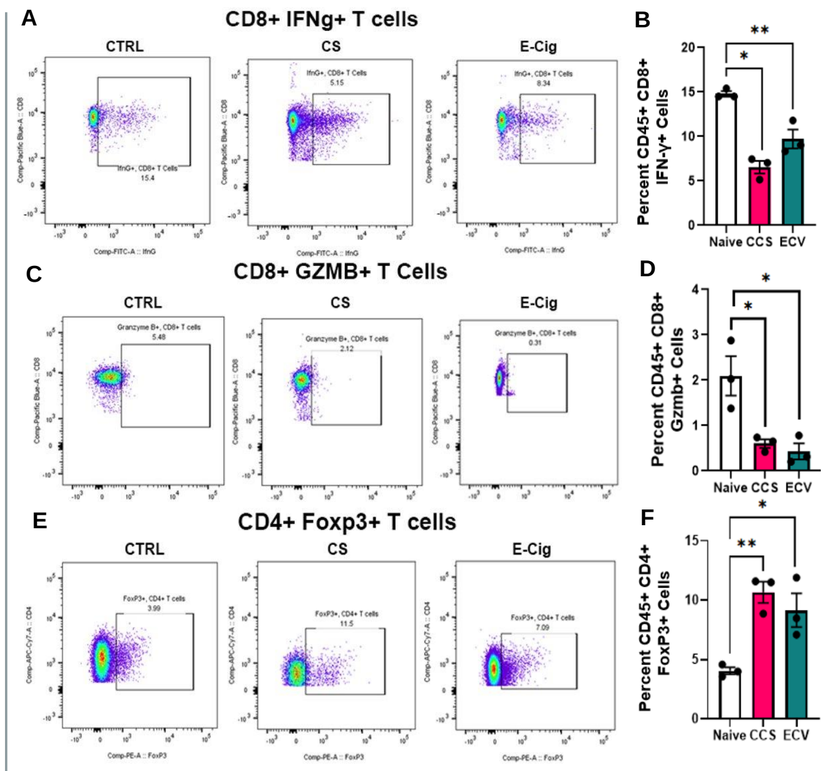


Figure 5. Quantification and Immunophenotyping of Lymphoid Cells in Whole Lung Tissue. Significance was determined at a p-value greater than 0.05.

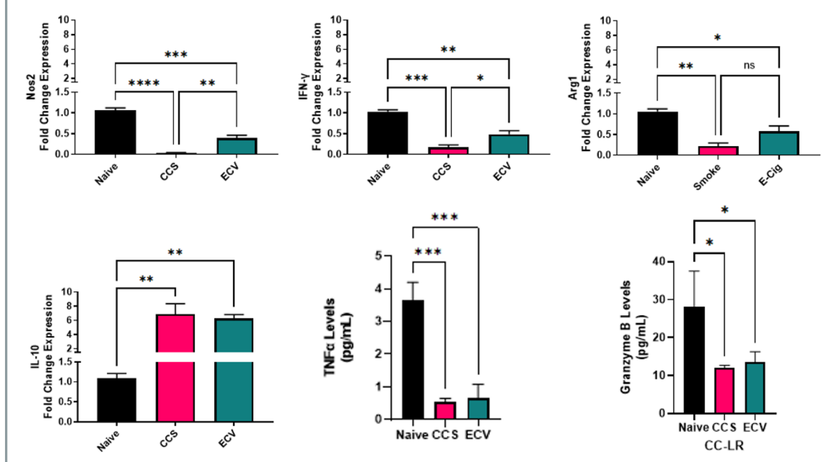


Figure 6. Immunophenotyping of Whole Lung Microenvironment at RNA and Protein Level. Significance was determined at a p-value greater than 0.05.

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.

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