

The Effects of Lung Microbiota on Lung Tumorigenesis

Asim Mohiuddin, Qingsheng Li, Ph.D., Nejat Egilmez, Ph.D.
University of Louisville, School of Medicine

Introduction

- Lung cancer remains as the leading cause of cancer death
- Smoking is a well-known risk factor for lung cancer due to its carcinogenic chemical components
- Emerging studies suggest that multiple additional factors, including systemic inflammatory responses and infections with certain microorganisms might also contribute to lung cancer development
- Research data from murine models demonstrated that the gut microbiota serves as a contributor to colon tumorigenesis
- In the lungs, the microbiome has shown to produce both protective and adverse effects in chronic diseases of the lung
- Epidemiological studies have shown that lung cancer may be influenced by the lung microbiota

Hypothesis

- We hypothesize that antibiotics delivered to the lungs will enhance tumor burden by altering the lung microbiota balance

Methods

- LSL-K-rasG12D (LSLKras) lung cancer model was selected for this study
- Antibiotics (ampicillin, neomycin and vancomycin) were delivered via intubation-mediated intratracheal (IMIT) instillation in order to isolate the local lung microbiota in one treatment arm
- Antibiotics were given in drinking water to deplete the gut microbiota in another treatment arm
- Lung tumor formation was analyzed on histology following treatment using QuPath Software
- An independent samples T-test was used to determine significant difference in tumor burden between the treatment arms and the control group
- All parts of the experiment were conducted under an approved IACUC protocol

Results

Figure 1: Tumor Percentage Based On Treatment

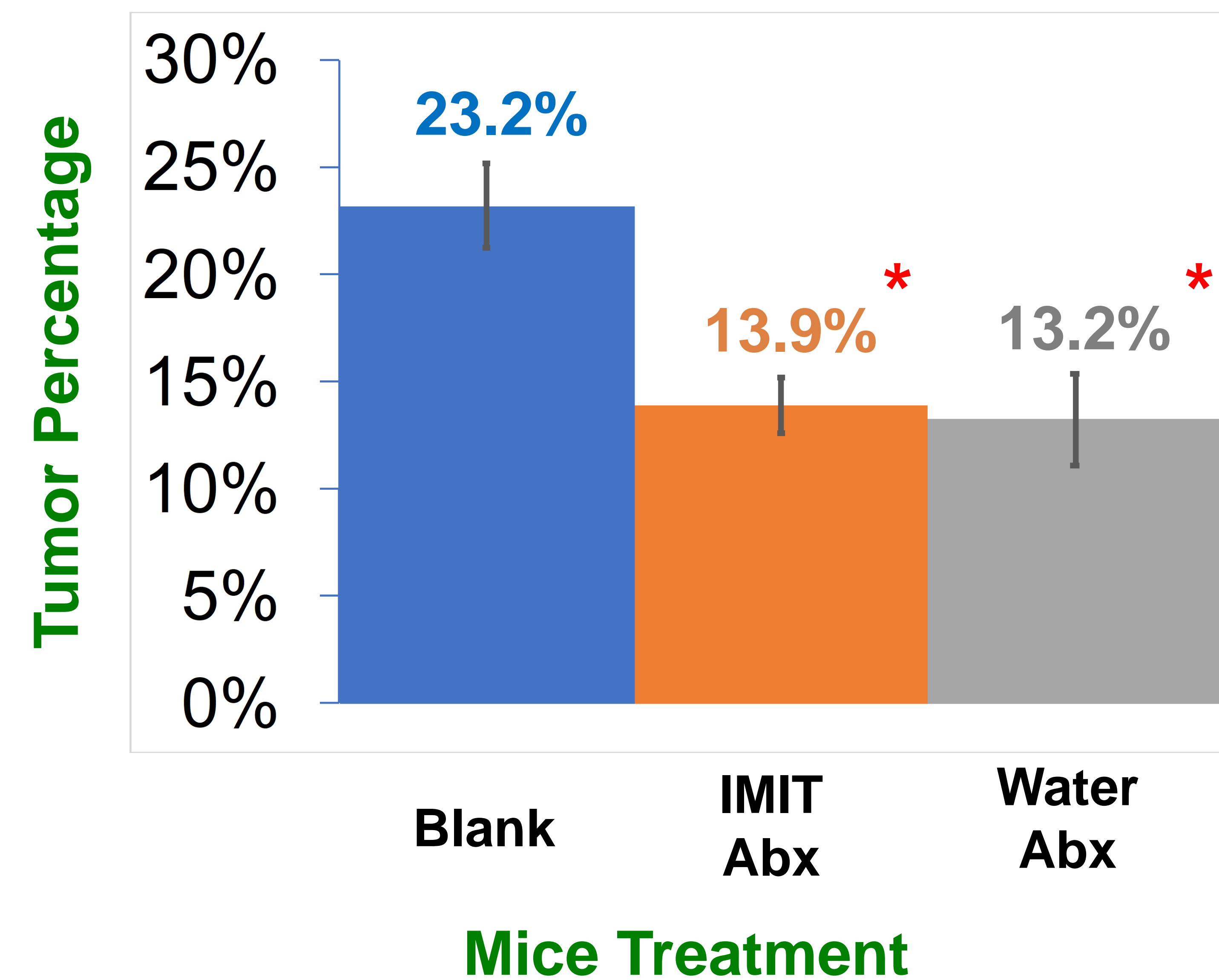


Figure 1: Tumor burden for mice treated with antibiotics was significantly less compared to the control group ($p < 0.05^*$)

Figure 2: Sample

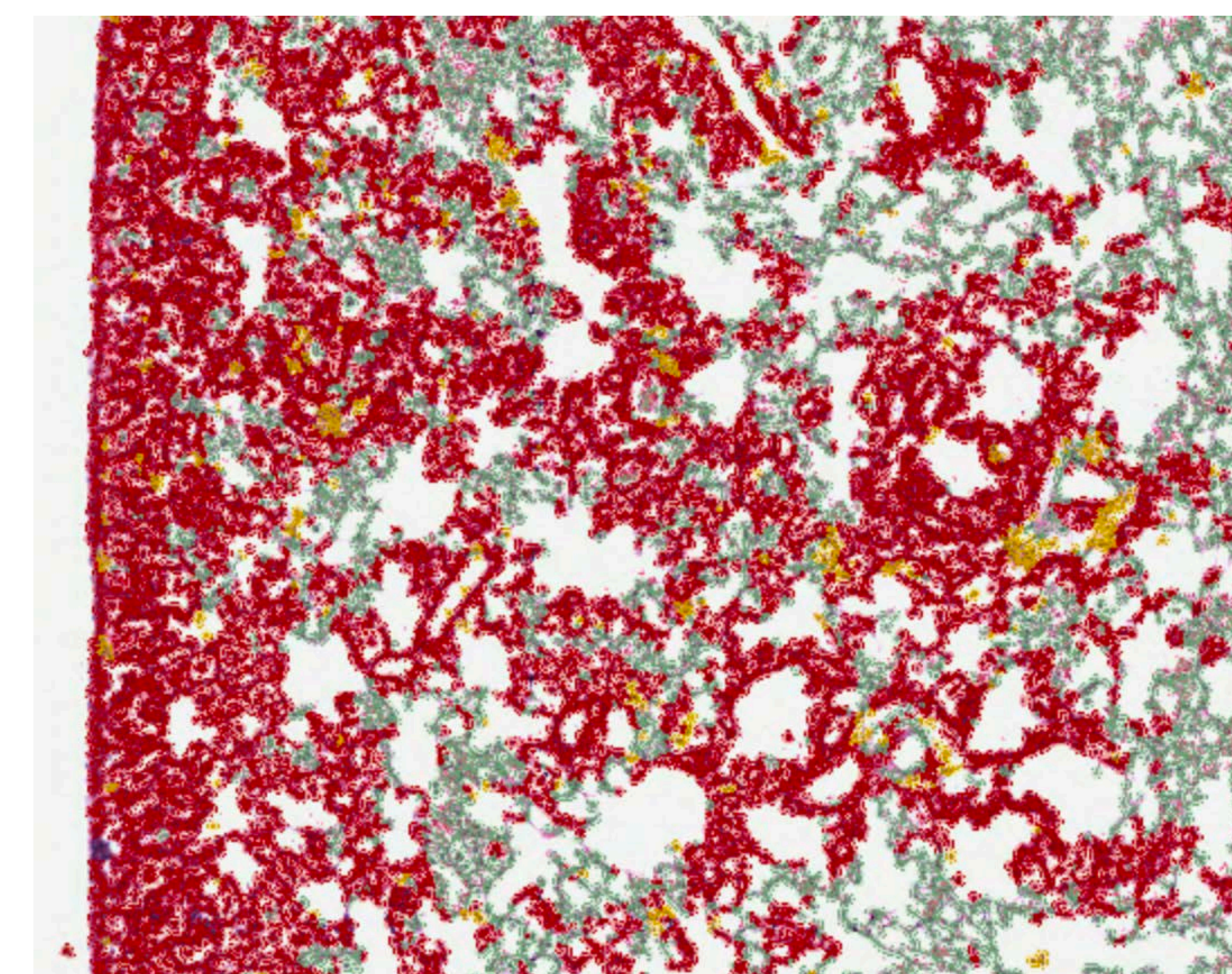
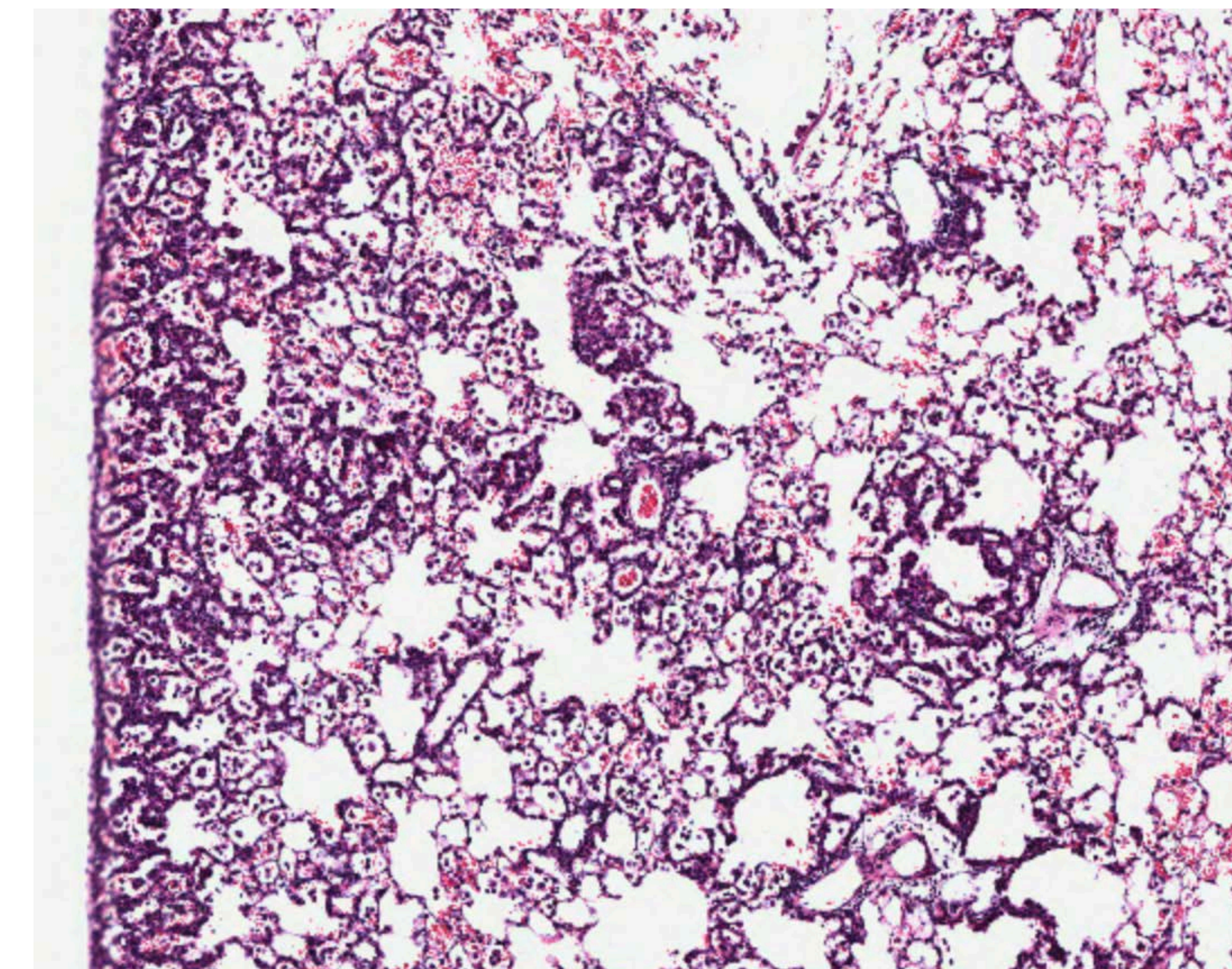


Figure 2: Sample tumor calculation in QuPath Software

Conclusions

- Our data suggests that the normal gut and lung microbiota may play a role in tumorigenesis
- Treating mice with antibiotics significantly lowered their tumor burden after a six-week treatment period
- A direct relationship between the microbiota in the lung and lung tumorigenesis has not been previously established
- This study bridges previous epidemiological data with a prospective trial in a murine model
- Understanding the role of microbiota in lung cancer can pave way to potential treatments that can at least augment current therapy

Future Direction

- Although the mechanism(s) by which antibiotics may improve lung tumor burden cannot be established from this study, future studies should look at what organism present in the normal microbiota promote tumorigenesis
- Specific antibiotics can be targeted towards organisms to isolate tumor-promoting agents
- Another strategy for future studies is to use non-systemic oral antibiotics to isolate gut and lung microbiota

Bibliography

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