The Role of Antibiotics in Early Onset Colorectal Cancer (EOCRC) in Mouse Models of CRC

Damien George[1], Maria Marjorette Peña[2]
[1]Department of Biology, Claflin University and SC-ADAR Fellow,
[2]Department of Biological Sciences, University of South Carolina, Columbia SC

INTRODUCTION

- Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the US and worldwide
- However, late CRC rate is decreasing due to healthy life choices and early screening
- But, Early Onset Colorectal Cancer (EOCRC) is CRC in patients 45 years and younger is steadily increasing by 11% in the last two decades
- In 2021, 52,300 are expected to die from CRC and 18% of these is due to EOCRC
- The cause of EOCRC increase is unknown
- **Questions:**

1) What substances are these age groups exposed to that increased risk?
2) Can exposure be mitigated to decrease EOCRC risk?

HYPOTHESIS

- Antibiotic use in children has drastically increased in the last four decades
- Is this causing an increased risk for EOCRC?
- Antibiotics can destroy the gut microbiota causing dysbiosis that leads to inflammation that can increase risk of CRC

METHODS

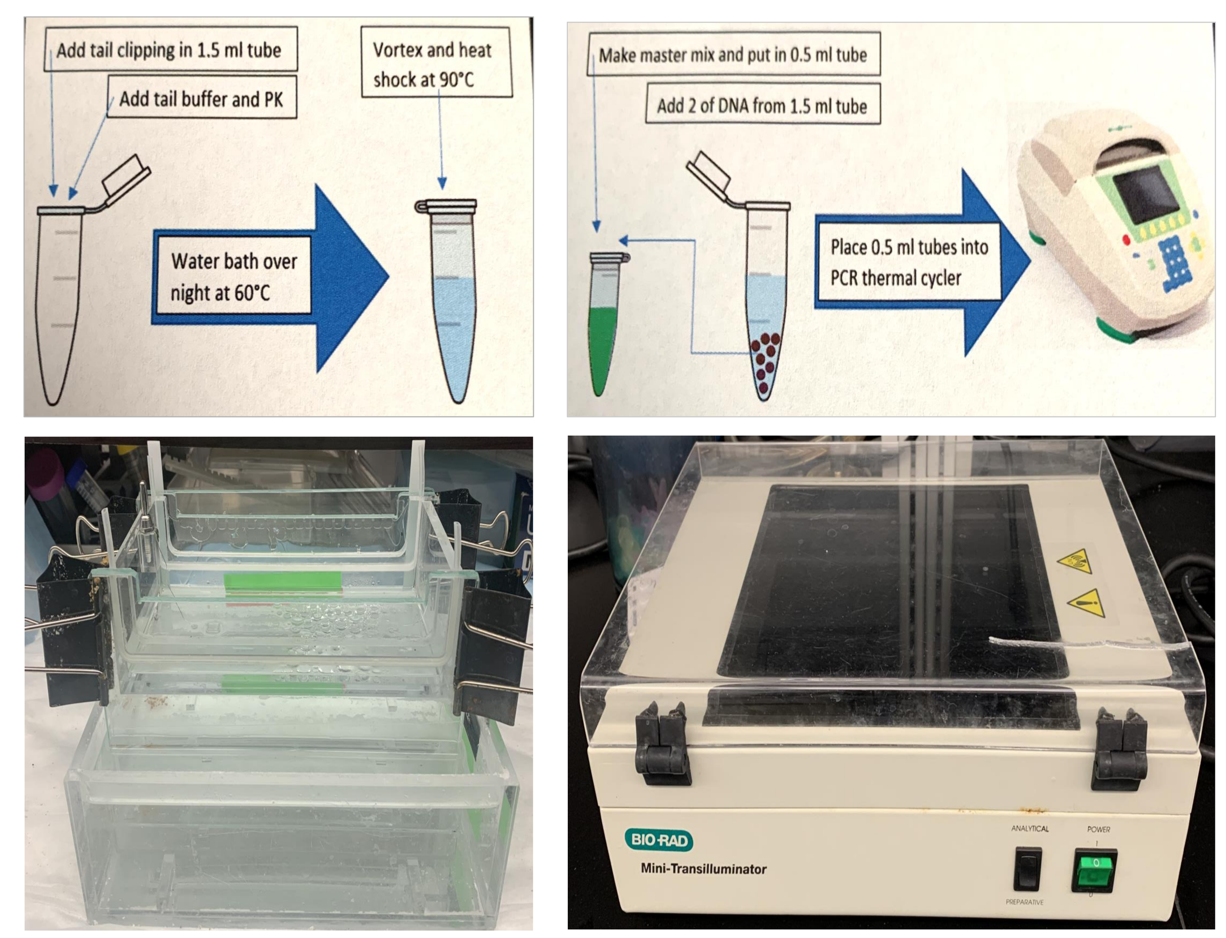
Two mouse models are used to study effects of antibiotic on colon tumor development

A. ***Apc**$^{Min/+}$* **mouse is a genetic model.** It has the same mutation found in inherited and sporadic colon cancer
- We breed these mice as heterozygotes, and they develop tumors in the small intestine and colon

B. AJ mice - mice are induced with the carcinogen Azoxymethane to develop colon tumors

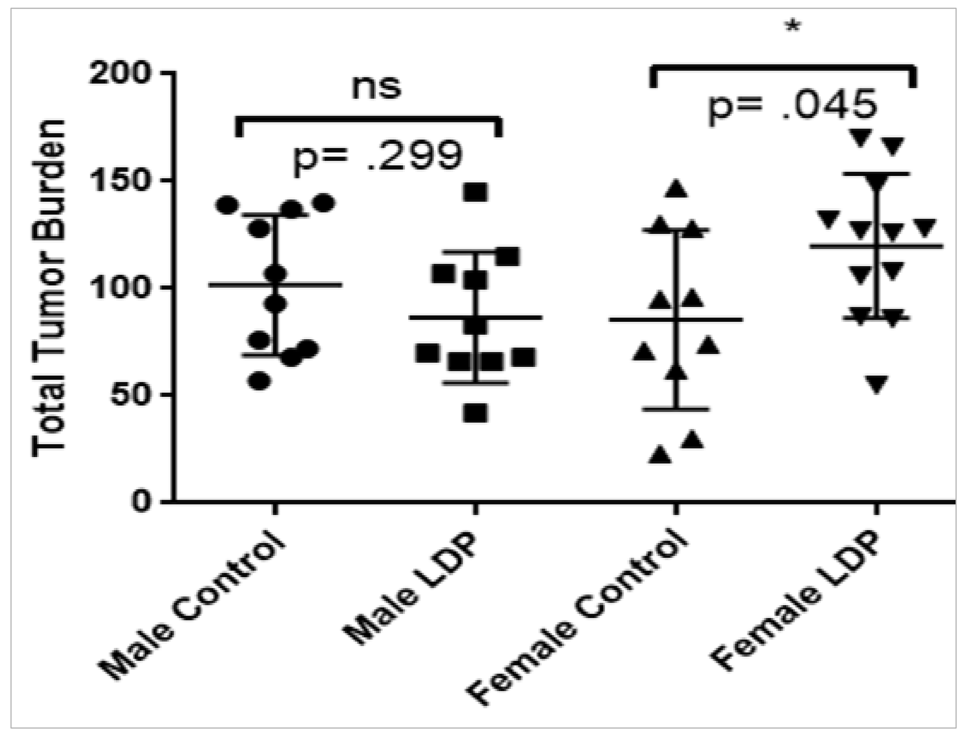
Apc$^{Min/+}$ mice treated with low dose penicillin (LDP, 5 mg/kg)

PCR GENOTYPING FROM TAIL SNIPS



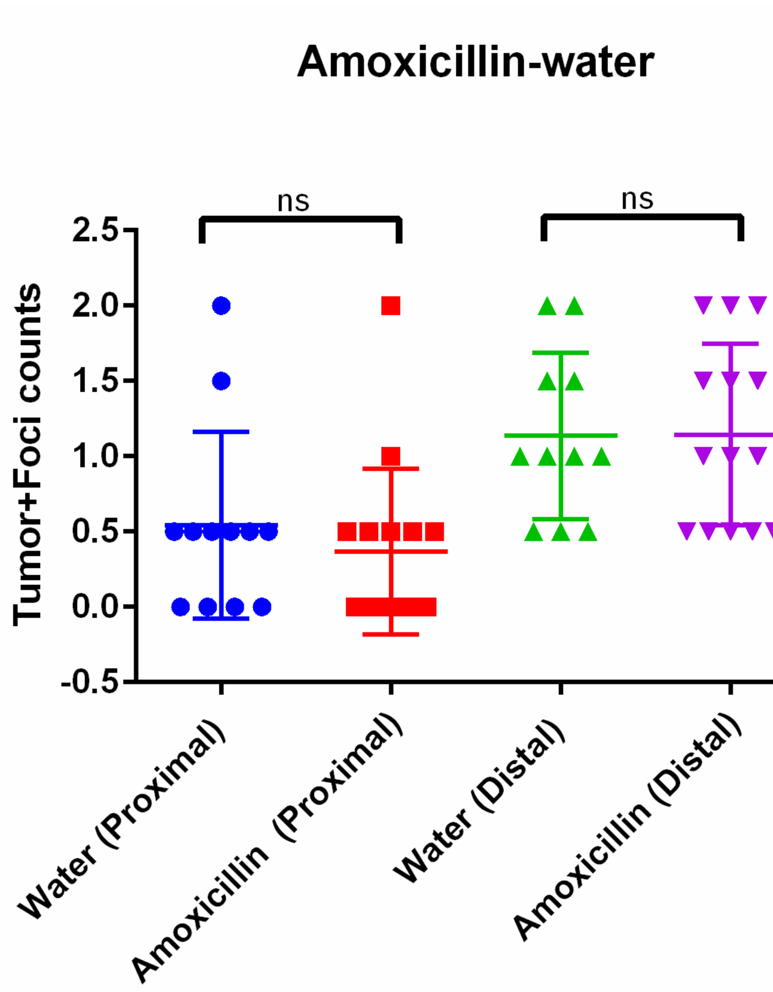
RESULTS

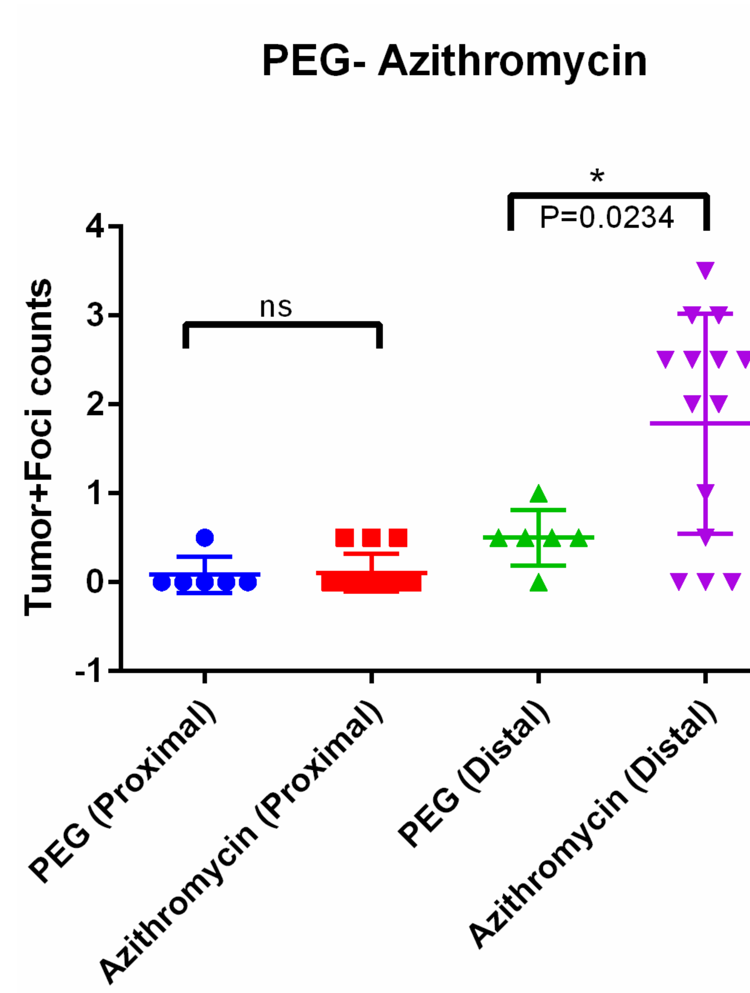
LDP Water at 4 wks for 10 days

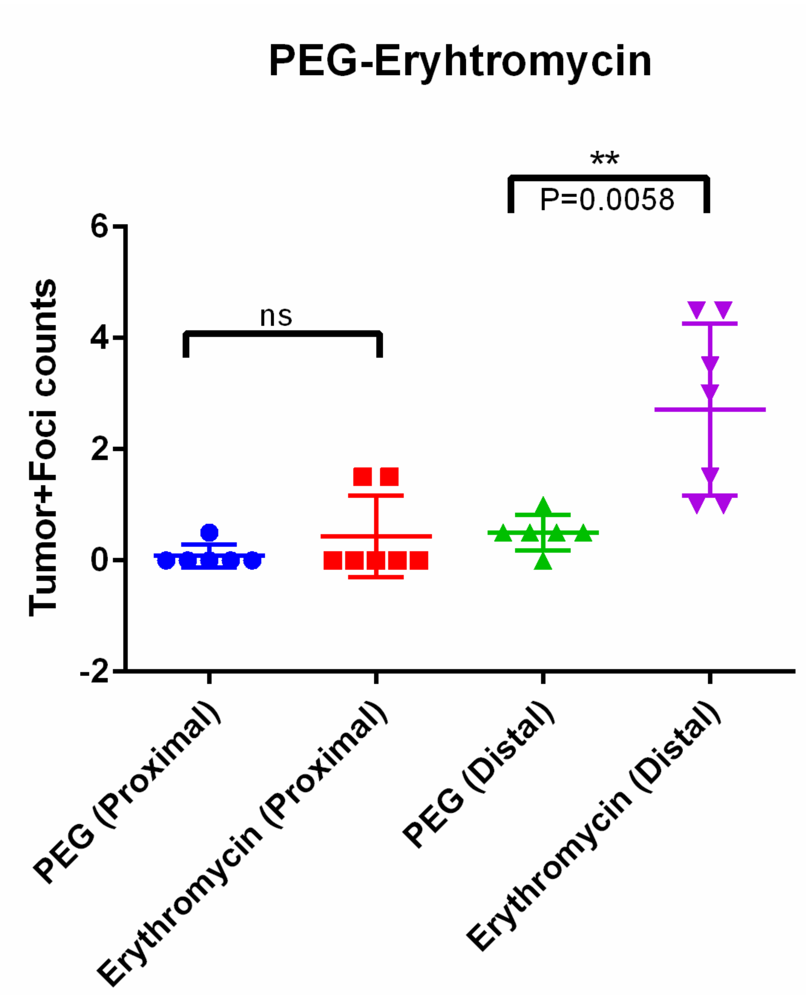


AJ Mice treated with Amoxicillin, Erythromycin, Azithromycin and Azoxymethane

Gavage with AMOX,ERY, and AZI at 4,8,12 weeks for 10 days.







Conclusions and Future Directions

Exposure to antibiotics at early life can lead to increased tumor burden later in life.
We need to determine the status of intestinal inflammation and effect on gut microbiome composition to assess their role in increasing the risk for colon cancer development.

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