



Evaluation of impacts from exposure to antimicrobial residues in the environment on the gut microbiome and resistome using a mouse model

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INTRODUCTION

Antimicrobial resistance poses a serious public health threat, with antimicrobial resistant bacteria (ARB) and their genes (ARGs) distributed in diverse environments such as farms and water systems. These bacteria can reach humans through contaminated food, water, or direct contact, colonizing our gut upon ingestion. We hypothesize that exposure to clinical antimicrobials and environmental residues of antimicrobials, such as ampicillin and tetracycline, exacerbates ARB colonization, leading to microbial dysbiosis and enhanced ARG spread. Ampicillin is clinically relevant, while tetracycline is widely used in agriculture and animal husbandry and is extensively distributed in the environment.

AIM

The aim of this study is to investigate the persistence of *Salmonella Heidelberg* carrying ARGs on an IncA/C plasmid within the gut microbiota, and to examine the horizontal transfer of these ARGs among Enterobacteriaceae under varying levels of antimicrobial exposure, including sub-inhibitory and clinically relevant concentrations using a mouse model

METHOD

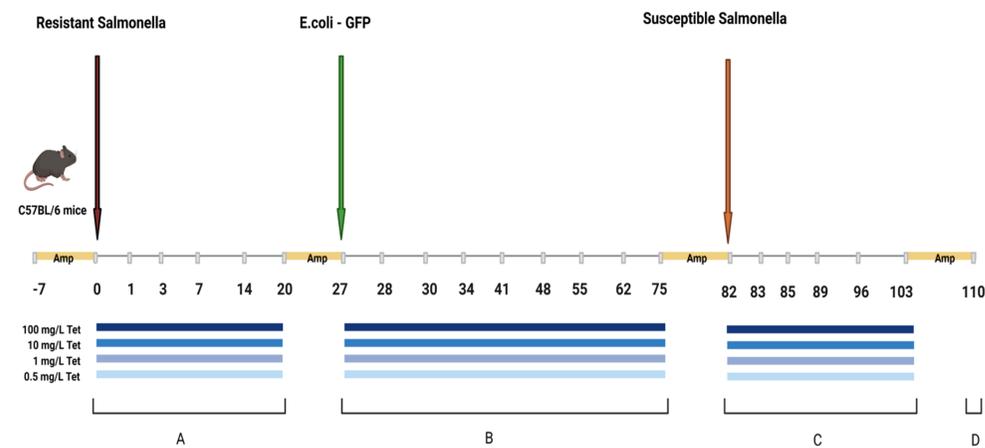


Fig.1 Shows the experiment design of the mouse experiment, including antimicrobial exposure and inoculations at different time points

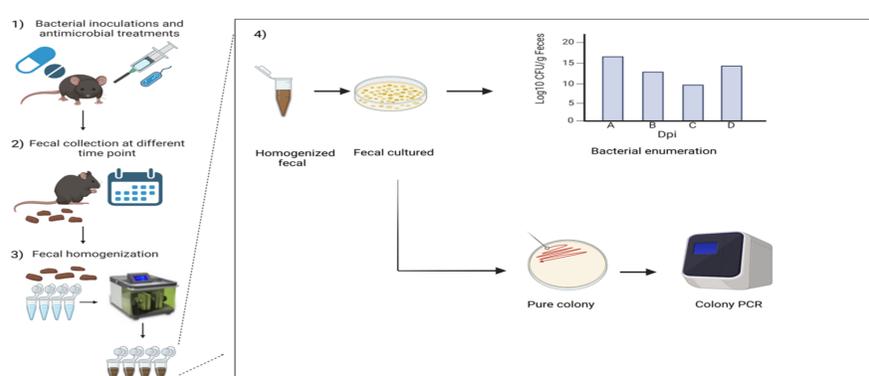


Fig.2 The schematic summaries all experiments in the mouse model study

RESULTS

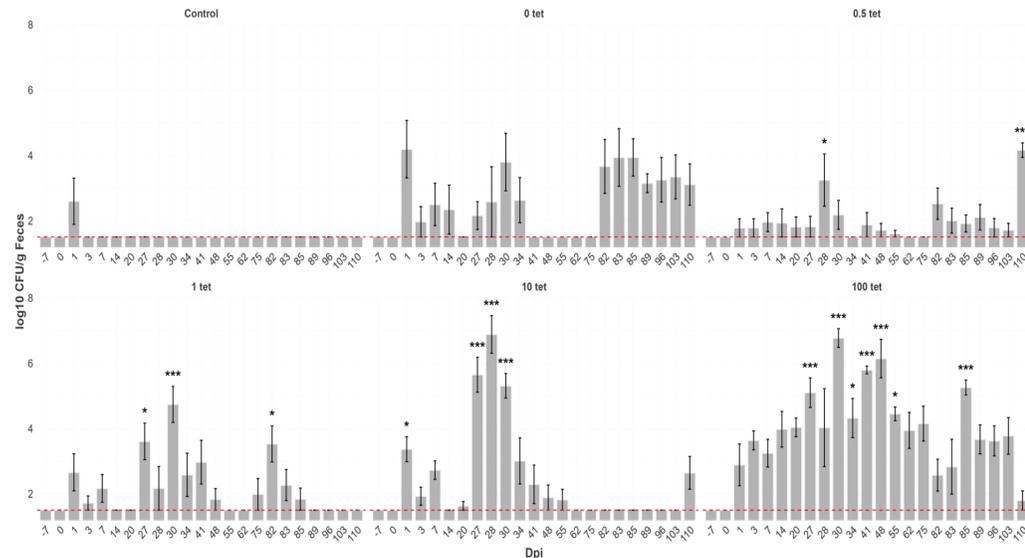


Fig.3 Persistence of donor *Salmonella Heidelberg* in all treatment groups over time in the mouse experiment. The Bar group represents the mean of log₁₀ CFU/g feces. The dashed line is the detection limit. DPI: days post-inoculation.

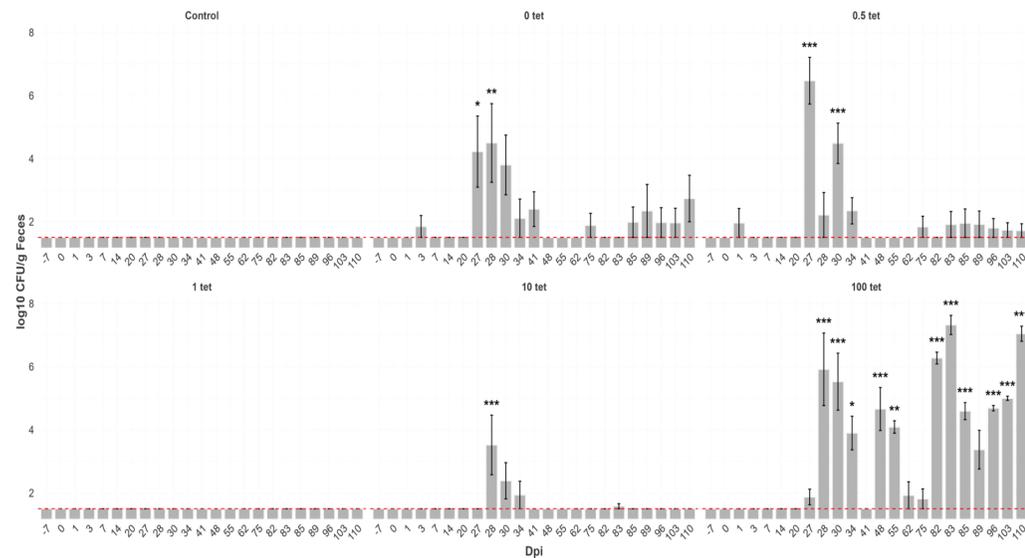


Fig.4 Transconjugant commensal *E. coli* in all groups in the mouse experiment. The Bar group represents the mean of log₁₀ CFU/g feces. The dashed line is the detection limit.

DISCUSSION

- The donor *Salmonella Heidelberg* persisted in the gut microbiome and thrived in a cyclic pattern following each clinical dosage of ampicillin treatment. The tetracycline significantly increased the persistence in concentration depended pattern.
- Commensal *E. coli* received the AMR plasmid from SH and persisted in the gut microbiome after intermittent clinical dosage of ampicillin treatment. The tetracycline increased the persistence at higher subclinical doses.

CONCLUSION

Our This study demonstrated that *Salmonella Heidelberg* harboring ARGs on an IncA/C plasmid can persist in the gut microbiota and transfer resistance genes to other Enterobacteriaceae under various tetracycline exposure levels, with no transfer observed at the MIC. These findings underscore the influence of antimicrobial concentration on horizontal gene transfer dynamics.