Small molecule targeting outer membrane lipopolysaccharide transporter complex (LptD/E) reduces avian pathogenic E. coli (APEC) infection in poultry

Dipak Kathayat, Yosra A. Helmy, Loic Deblais, Vishal Srivastava, Gary Closs Jr, and Gireesh Rajashekar

Food Animal Health Research Program, Department of Veterinary Preventive Medicine, The Ohio State University, kathayat.1@osu.edu, rajashekar.2@osu.edu

INTRODUCTION

- Avian pathogenic E. coli (APEC), a most common bacterial pathogen of poultry, causes colibacillosis in chickens.
- Colibacillosis results in high morbidity and mortality in chickens, decreased meat and eggs production, and increased condemnation of carcasses at slaughter.
- APEC has been also reported as a foodborne human uropathogen transmitted through consumption of contaminated poultry products.
- Antibiotics are routinely used to treat APEC infections; however, the emergence of antibiotic resistant APEC strains and increased restrictions placed on the use of antibiotics in food-producing animals necessitate the development of newer therapies.

HYPOTHESIS

- High throughput screening of bioactive small molecule (SM) library can identify new antimicrobial(s) effective in treating APEC infection in poultry.

OBJECTIVE

- To identify, evaluate, and develop anti-APEC SM antimicrobial(s) with novel antibacterial target(s) as an alternative to antibiotics.

METHODS

1. Bioactive SM library (ChenBridge) was screened, which identified 40 small molecules inhibitory to APEC growth at 100 µM.
2. Eleven SMs, which were bactericidal to APEC, were selected and evaluated for efficacy and toxicity in vitro in cultured epithelial and macrophage cells and in wax moth larva model.
3. Eight SMs, that are non-toxic and effective in vitro and in larva model, were evaluated in commercial broiler chickens by administering orally in non-natural subcutaneous (i/o) APEC infection model (Fig. 1).

RESULTS

- GI-7 most effectively reduced the mortality, APEC load, and APEC lesions in chickens when administered at 60 mg/L in drinking water (Fig. 2).
- GI-7 administration resulted in effective anti-APEC effect in chickens (Fig. 3).
- GI-7 when administered at 60 mg/L in drinking water resulted in effective anti-APEC effect in chickens (Fig. 4).

CONCLUSION AND FUTURE DIRECTIONS

- GI-7 can represent a novel anti-APEC therapeutic; thereby, can be developed as an alternative to currently used antibiotics.
- Our future studies will be focused on validating the antibacterial target of GI-7 and developing formulations to advance GI-7 into field applications.

ACKNOWLEDGEMENTS

- This work is funded by USDA NIFA Agriculture and Food Research Initiative Competitive Grant no. 2015-88004-23131, Technology Commercialization Office (TCO)/The Ohio State University, and Ohio State Innovation Foundation.