Novel Anti-virulence Compound to control Avian Pathogenic Escherichia coli (APEC) Infections in Poultry

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Introduction

- Colibacillosis is an endemic disease of poultry caused by avian pathogenic E. coli (APEC).
- Colibacillosis is associated with a wide range of symptoms including, airsacculitis, peritonitis, colisepticemia, etc.
- The most prevalent APEC sero-groups causing colibacillosis are O1, K1, O2, and K88.
- The disease is widely prevalent (up to 36.7%) in all age groups of chickens and characterized by high morbidity and mortality. In addition, the disease results in egg and meat production losses.
- Therefore, the control of APEC is crucial for sustainable poultry farming and food security.
- Current control methods (vaccines and antibiotics) have limited effect, therefore there is a need for novel therapeutic approaches.
- Inhibition of quorum sensing (QS) and virulence mechanisms are important strategies to tackle APEC infection.
- QS is implicated in several physiological state changes including virulence factor production.
- These quorum sensing inhibitors (QSIs) do not affect APEC growth, making them good candidates to limit the development of bacterial resistance.
- QSI characterize by:
  1. have small size allows them to diffuse readily into cells.
  2. stable and suitable for mass application.
  3. their novel mode-of-action reduces the risk of the development of resistance.

Aims

1. Identify novel approaches to control APEC in poultry.
2. Test and evaluate the efficacy of the identified QSIs in APEC-infected chickens.

Methods

Activity 1: Testing the best QSIs in infected chickens

- We previously screened a library 4,182 SMs and identified 10 SMs inhibited QS of APEC O78. These 10 QSIs possessed no toxicity to chicken RBCC, Caco-2 and HD-11 cells and were effective against APEC in Caco-2, HD11 and THP-1 cells and wax moth infected larvae.
- Seven QSIs (QSI-1, 2, 5, 8, and QSI-10) were tested in one-week-old broiler chickens infected with APEC O78 (Fig. 1).

Activity 2: Optimizing the dose of QSI-5

- The efficacy of the best QSIs (QSI-5, QSI-8, QSI-10) on the gut microbiota of chickens was analyzed by 16S RNA sequencing using Qiime 2 by comparing the relative abundance of gut microbiota community (Fig. 5).
- QSIs-5, QSI-8 and QSI-10 significantly reduced chicken’s mortality, APEC load and lesions severity in the internal organs.
- QSI-5 reduced mortality by 100%; while QSI-10 and QSI-8 reduced the mortality by 75% and 50%, respectively compared to PC.
- The average reduction of APEC load in internal organs ranged between (5.2-8.1), (3.4-4.3) and (2.2-3.1) log CFU of tissue in QSI-5, QSI-8 and QSI-10 treated chickens, respectively (Fig 4A).
- QSI-5, QSI-8 and QSI-10 reduced the pathological lesions severity in internal organs by (82%-93%), (85%-100%) and (77%-83%), respectively compared to PC (P<0.05; Fig 4B).

Activity 3: Showing better efficacy of QSI-5 compared to antibiotic sulfadimethoxine in field simulated conditions

- QSI-5 at 1 mg/mL reduced chicken’s mortality by 58%, APEC load in internal organs up to 3.1 logs and lesions severity up to 66.3% compared to PC group (Fig. 5).
- QSI-5 showed better efficacy than currently used antibiotic sulfadimethoxine in field simulated conditions.

Conclusion

1. QSI-5 possessed the highest efficacy in APEC infected chickens compared to other QSIs.
2. The optimal dose of QSI-5 to treat infected chickens was 1 mg/mL.
3. QSI-5 showed no impact on body weight gain, feed conversion ratio and gut microbiota;
4. QSI-5 was detected in 0.5 in blood and no residues in muscle liver and kidney of treated chickens at xx days post treatment.
5. QSI-5 showed better efficacy than currently used antibiotic sulfadimethoxine in field simulated conditions.

Future directions

- Identifying the antibacterial target of QSI-5

Bibliography


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