Innovative Alternatives to Antibiotics to Prevent and Treat Avian Colibacillosis

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Impact on California Agriculture: Colibacillosis, caused by avian pathogenic *Escherichia coli* (APEC), can affect birds of all types and ages in various poultry production systems. California's poultry industry, a key player in the state's agricultural landscape, generates over $2.5 billion in sales annually and supports over 25,000 direct jobs, with many more in related industries. However, the economic impact of colibacillosis-related factors such as mortality, treatment costs, reduced egg production, and decreased feed efficiency amounts to over $100 million in losses each year in California.

Rationale/Introduction: Traditionally, colibacillosis has been managed with antibiotics. However, in response to growing concerns about antibiotic resistance, California implemented a ban, effective January 1, 2018, on the use of antibiotics in livestock without a veterinary prescription or veterinary feed directive. This shift to a "no antibiotics ever" system, coupled with the rapid expansion of free-range production systems and backyard poultry, presents a mounting challenge for the California poultry industry. While alternatives to antibiotics such as prebiotics, probiotics, vitamins, immune enhancers, and anti-inflammatory drugs have been proposed, their therapeutic efficacy is limited, and their widespread use remains largely unexplored.

Bacteriophages, or phages for short, are viruses that target bacteria. Lytic phages work by lysing bacteria and have been employed in combating bacterial infections for some time. While phages hold promise as a therapy, they come with certain drawbacks and concerns, such as challenges in formulating and stabilizing phage preparations, limited host range, potential gene transmission between bacteria, and the risk of transmission to humans via the food chain.

Experimental Approach: To address the challenge of avian colibacillosis in an era where antibiotic use is restricted in poultry, we have been developing a recombinant endolysin to target APEC. Endolysins are enzymes naturally produced by phages, which are capable of disrupting bacterial cell walls. To date, there have been no reports of using endolysins to prevent or treat APEC infections. While endolysins are typically effective against Gram-positive bacteria, APECs present a unique challenge as Gram-negative bacteria with an outer membrane that may impede the access of endolysins to the cell wall. To solve this problem, we incorporated a membrane-permeating peptide into the recombinant endolysin to enhance its efficacy in lysing APEC.

Major Conclusions: The recombinant endolysins have been successfully expressed and purified from bacteria. Although we have made some progress in bacterial lysis, we are currently engaged in refining the activity of the recombinant endolysin. Our long-term goal is to establish biotechnology-driven alternatives to antibiotics for the prevention and treatment of avian colibacillosis, thereby safeguarding the health of California's poultry and consumers alike.

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