Exploring non-antibiotic treatment options for BRD

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Project Title:

Use of bacteriophage-derived lysins in combatting multi-drug resistant (MDR) pathogens that cause bovine respiratory disease (BRD)

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Background

Antibiotics are effective tools to prevent or treat BRD but concerns about antibiotic resistance and pressure to reduce antibiotic use mean that non-antimicrobial options need to be explored. One possible solution may come from viruses that specifically attack bacteria (these are known as phages). Phages infect bacteria, hijack the bacterial machinery to manufacture more phages, then produce enzymes (called lysins) that cause bacteria to burst. This releases the offspring phages, which that can go on to infect other bacteria. These researchers will examine whether the page lysin enzymes that cause bacteria to burst can be an effective antibiotic alternative to combat three of the main BRD bacteria, Mannheimia, Pasteurella and Histophilus.

Objectives

1. Identify and engineer LYS from lysogenic phages of Mannheimia haemolytica, Pasteurella multocida and Histophilus somni
2. Evaluate antibacterial activities of the engineered LYS against multidrug resistant BRD pathogens including M. haemolytica, P. multocida and H. somni.
3. Optimize anti-BRD activities of LYS by fusion with lipopolysaccharide-destabilizing peptides and bovine tracheal antimicrobial peptide.
4. Determine effectiveness of the optimized LYS for controlling BRD in experimentally challenged calves.

What they will do

The phage genes that produce the enzymes that cause Mannheimia to burst have been identified. They plan to look for similar genes in Pasteurella and Histophilus phages. These lysin genes from all three phages will be cloned, expressed, the enzyme purified, and tested for effectiveness against multidrug resistant BRD bacteria in the lab. They will evaluate if resistance develops to the phage lysins, optimize their anti-BRD activity by fusing them with antimicrobial peptides that destabilize bacterial cell walls. Finally, they'll challenge 12 cattle with BRD bacteria, treat half of them with lysin, and collect samples over four weeks to see whether there are measurable changes in the respiratory microbiome.

Implications

This initial study will determine whether phage lysins have potential as antibiotic alternatives and are worth further development as a potential BRD treatment option to replace or supplement antibiotics.

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