Analysis of the Bovine Intracellular Enteric Pathogen Interactome

Each year the beef and dairy industries lose more than $330 million because of enteric diseases that cause the death of more than 650,000 head of cattle. This figure does not include lost revenue attributable to morbidity and reduced cattle weight gain.

Understanding how cattle respond to enteric pathogens during acute infection is crucial for developing new vaccines, chemotherapeutics, multiplexed diagnostic tests, and new strategies for preventing clinical disease. To this end, researchers at the College of Veterinary Medicine at Texas A&M University have developed an in vivo bovine ligated ileal loop model to study bovine response to enteric pathogens and the pathogens’ response to the hosts—that is, the interactomes. This model has been used to study the interactomes of three enteric pathogens: *Salmonella enterica* Serotype Typhimurium, *Brucella melitensis*, and *Mycobacterium avium* subsp. paratuberculosis. The hosts and pathogen responses have been investigated over seven time points during the early phases of infection to develop comprehensive profiles of the genome, transcriptome, and proteome for both host and the three pathogens. Bayesian mechanistic analyses have been developed to compare and contrast the bovine interactomes of these pathogens for unique targets for diagnostics, for common pathways for therapeutic targets, and new in vivo expressed immunogens. These investigations provide a new platform, interactome analysis, for Texas AgriLife Research and development of improved animal health for the Texas and U.S. cattle industries.

Process
- Gene expression and proteomic data have been and will continue to be collected from bovine ligated ileal loop studies to develop a host response profile for bovine infection with *Salmonella enterica* Serotype Typhimurium, *Brucella melitensis*, and *Mycobacterium avium* subsp. paratuberculosis.
- The animal host and pathogens response profiles will be mapped to molecular pathways and analyzed to identify previously unexplored targets both for potential therapeutic intervention, multiplexed diagnostic tests, and in vivo immunogens for bovine enteric diseases.
- Mutant bacteria will be used to determine which bacterial factors induce specific aspects of host response, with the added benefit of identifying potential bacterial targets for therapy; RNAi technology will be used to confirm phenotypes of critical host genes for controlling the pathogens.

Objectives
- Develop global host and pathogen response profiles of intracellular enteric pathogens via interactome analysis.
- Identify novel targets for the development of new clinical diagnostics, therapeutics, and vaccines.

Outcomes
- Refine new discovery platform of interactome analysis for cattle.
- Identify new targets for clinical diagnostics, therapeutics, and vaccines.
- Develop new rationales and strategies for enteric disease prevention.

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