One Health Research Project Abstract

Sri Harsha Vishwanath

Principal Investigator: Dr. Fiona McCarthy, Professor, School of Animal and Comparative Biomedical Sciences & BIO5 Institute

Research Abstract:
Clostridioides difficile is a Gram-positive, anaerobic, spore-forming bacillus which is a pathogen for both humans and animals. *C. difficile* infection is a One Health problem because the pathogen infects diverse mammalian species, and contaminates food, water, and the environment. In swine operations, *C. difficile* is routinely recovered from suckling piglets inside the farrowing barn where >75% of neonates may harbor *C. difficile*. Animals that survive infection remain colonized, shed *C. difficile*, and further contaminate the environment. *C. difficile* is seen in healthcare settings, placing a severe burden on the US healthcare system due to high transmission rates and in recent years has increasingly been associated with community transmission. While *C. difficile* is well studied with a plethora of genetic and phenotypic data published and in database archives, this published information is not readily accessible to researchers and datasets require significant effort to integrate and normalize. We will integrate this data and provide additional information about host-pathogen interactions using prediction methods established in our research group. This data will be combined with recently published preliminary data from our collaborator's laboratory indicating that veterinary strains of *C. difficile* have significantly different biology compared to other, humanprevalent, *C. difficile* lineages. Our integrated resources will be publicly available as a resource to support further *C. difficile* research, including hypothesis generation. We will demonstrate the utility of this resource by investigating genetic differences between *C. difficile* strains which are human-prevalent and those that infect both humans and animals. We hypothesize that veterinary-dominant *C. difficile* strains express a unique virulence. We will test this hypothesis by (1) employing newly developed modeling approaches to identify host (porcine) factors engaged by *C. difficile*; (2) using multiomics to identify *C. difficile* RT078 factors important for disease; and (3) performing functional studies in vitro and in neonatal piglets to interrogate *C. difficile* RT078 virulence.