

Differential virulence of enterohemorrhagic *E. coli* O157:H7 genotypes

Smriti Shringi and Tom Besser

Department of Veterinary Microbiology and Pathology, Washington State University, Pullman, WA 99164

Enterohemorrhagic *E. coli* O157:H7 (EHEC) is a major cause of food and water borne illness characterized by diarrhea, hemorrhagic colitis and life threatening hemolytic uremic syndrome. Cattle are the major reservoir host of EHEC. Production of Shiga toxins (Stx) is an important pathogenicity trait of EHEC and the insertion sites of the Stx-encoding bacteriophages differentiate EHEC isolates into groups commonly isolated from cattle but rarely from sick humans (bovine-biased genotypes, BBG) and commonly isolated from both cattle and human patients (clinical genotypes, CG). Even though BBG and CG share all known cardinal virulence factors of EHEC, their differential representation in human disease suggests that BBG may be less pathogenic. Therefore, we are testing the hypothesis that **the bacteriophage-mediated inactivation of virulence associated gene/s is responsible for the reduced virulence of bovine-biased EHEC genotypes.** Challenge studies show significant difference in virulence potential of CG and BBG EHEC O157 with CG resulting in more severe disease accompanied by earlier and higher mortality when compared with BBG, using a modified conventional neonatal pig model. Bacteriophage-mediated genetic changes were identified by comparing the optical maps of BBG and CG strains with *in silico* maps of the sequenced strain (Sakai) using optical scanning technology (OpGen, USA). Two of the divergent loci show significant association among the BBG and CG strains. These studies may identify new EHEC virulence genes or mechanisms, which can be exploited for developing improved diagnostic tools for differentiating strains based on virulence potential, and may lead to new approaches for prevention and control of this important food-borne pathogen.