Dr. Thomas Denagamage

Characterization of ESBL-encoding Salmonella plasmids

Enterobacteriaceae resistant to extended spectrum cephalosporins (ESCs) represents an emerging public health risk for which urgent research is needed to develop new antibiotics for treatment and formulate strategies for control their emergence and dissemination. ESC resistance is conferred predominantly by Ambler class C cephamycinases (CMY), carbapenamases, and Ambler class A extended-spectrum β-lactamases (ESBLs). The ESBLs are plasmid-mediated β-lactamases which hydrolyze ESCs, such as third and fourth generation cephalosporins and monobactams but not cephamycin or carbapenems. They are also generally susceptible to β-lactamase. The ESBLs include TEM and SHV enzymes, which have evolved from narrow spectrum parents (e.g. blaTEM-1, blaTEM-2, or blaSHV1) as well as a new class of ESBL genes called blaCTX-M. ESBLs belonging to CTX-M-type are the most widespread type in Europe but are infrequently detected in the U.S.

Over the last decade, there has been an increasing occurrence of ESBL producing Enterobacteriaceae in food-producing animals. For example, our laboratory detected ESC-resistant nontyphoidal Salmonella (Salmonella Heidelberg, Salmonella Bredeney and Salmonella Senftenberg) serovars in poultry. These ESC-strains of Salmonella harbored blaCTX-M-1-containing IncN (40-kb) or IncI1 (100-kb) plasmids, which were recently sequenced by our laboratory. Notably, ESC-resistant Salmonella are a major concern to both animal and public health due to limited therapeutic options as well as possibility of transfer of these resistant bacteria or their plasmids to bacteria of medical importance. The overall goal of this study is to further characterize these plasmids.

These specific aims are to:

1. Assemble and annotate the available sequences of two ESBL-encoding plasmids - one IncN-type and one IncI1-type plasmids
2. Study the transmissibility rates of these plasmids among bacteria belonging to the same Salmonella serovar, different Salmonella serovars and different species of Enterobacteriaceae family (e.g. from Salmonella to Escherichia coli)

The Student's role:

1. We have already sequenced these plasmids and the student will perform sequencing data assembly, annotation, and submission to National Center for Biotechnology Information (NCBI).(student will be walked through the sequencing workflow to provide the missing genome sequencing experience).
2. Select recipient strains for bacterial mating experiments based on antimicrobial susceptibility testing (Kirby Bauer disc diffusion), plasmid profiling, and polymerase chain reaction
3. Perform bacterial mating experiments.
4. Prepare a publication quality manuscript.