

SNP analysis of the *Klebsiella* spp. bacterial genomes yielded no unique identifier for each of our phenotypic classes. This indicates that our heteroresistant phenotype and our resistant phenotype contain the same sequences.

Plasmids contain a variety of AMR genes. The MCR family of genes all confer resistance to colistin. Annotations for MCR genes were made on genomes in all three phenotype groups. These

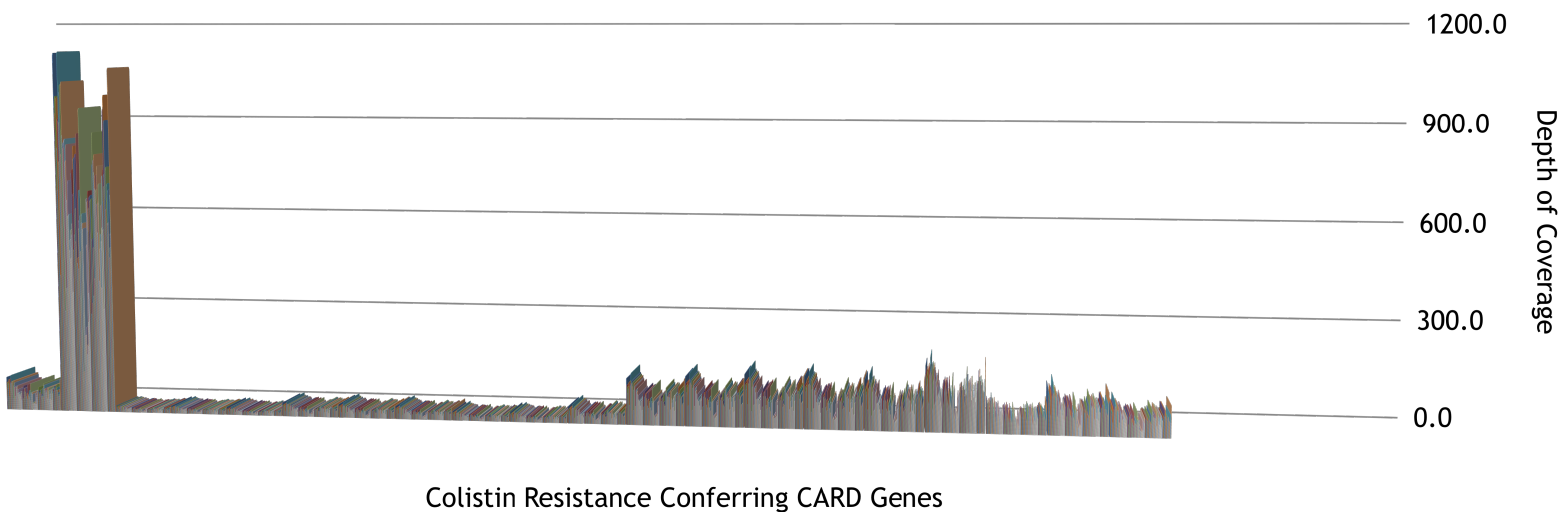
The AMR genes on plasmids of *Klebsiella* have particularly high stability which can be shown by the fact that even years after extended-spectrum cephalosporins stopped being used to treat Extended spectrum β -lactamase producing *Klebsiella* spp., it is still possible to find the genes which confer resistance to this drug on their plasmids.

These facts lead one to believe that the resistant subpopulation may be due to copy number variation of AMR genes.

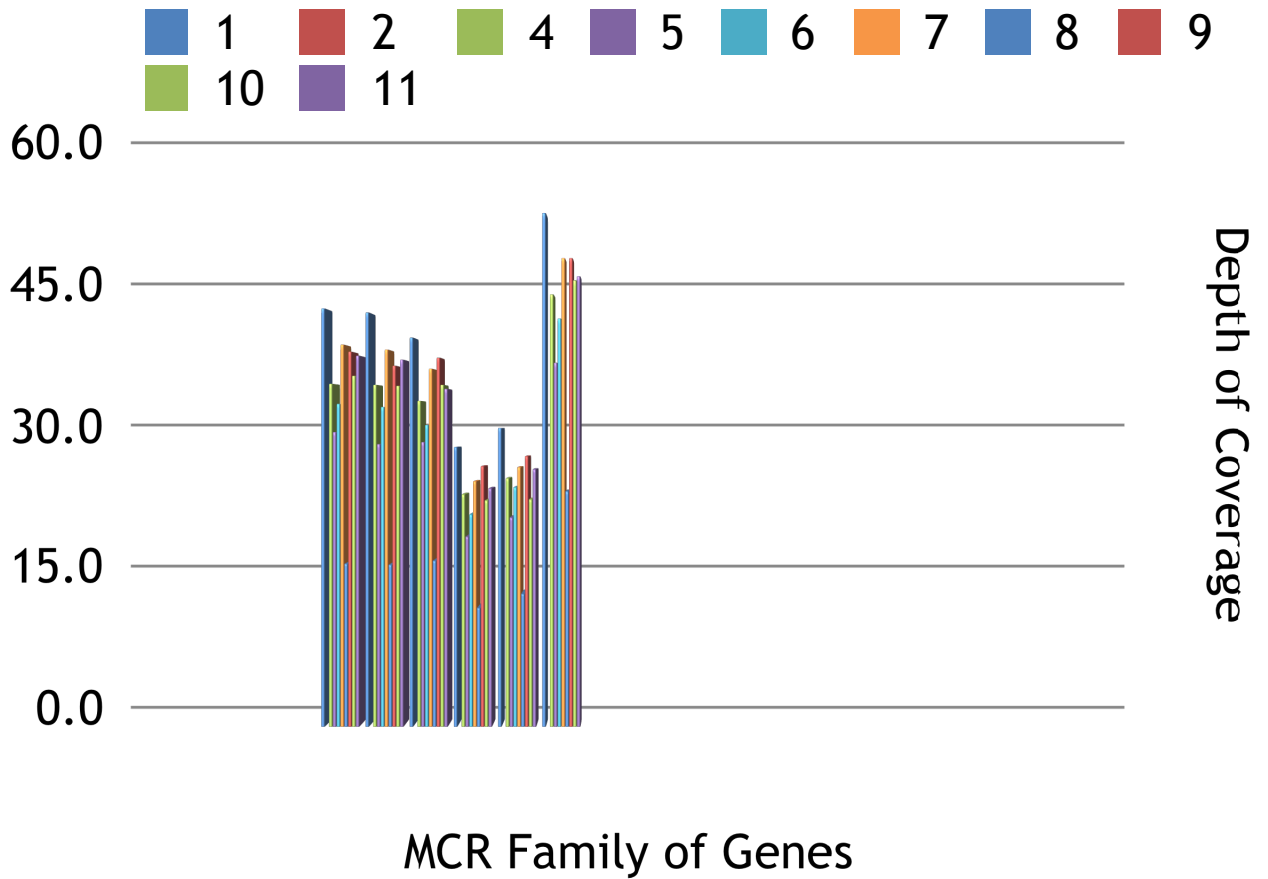
First, the average kmer depths for colistin resistance conferring genes from the CARD database were determined using the program STing in GDETECT mode. The results were visualized for each isolate. The patterns in the plots were consistent across all three phenotype groups.

All Samples:

Mean Kmer Depth for all Colistin Resistance CARD genes

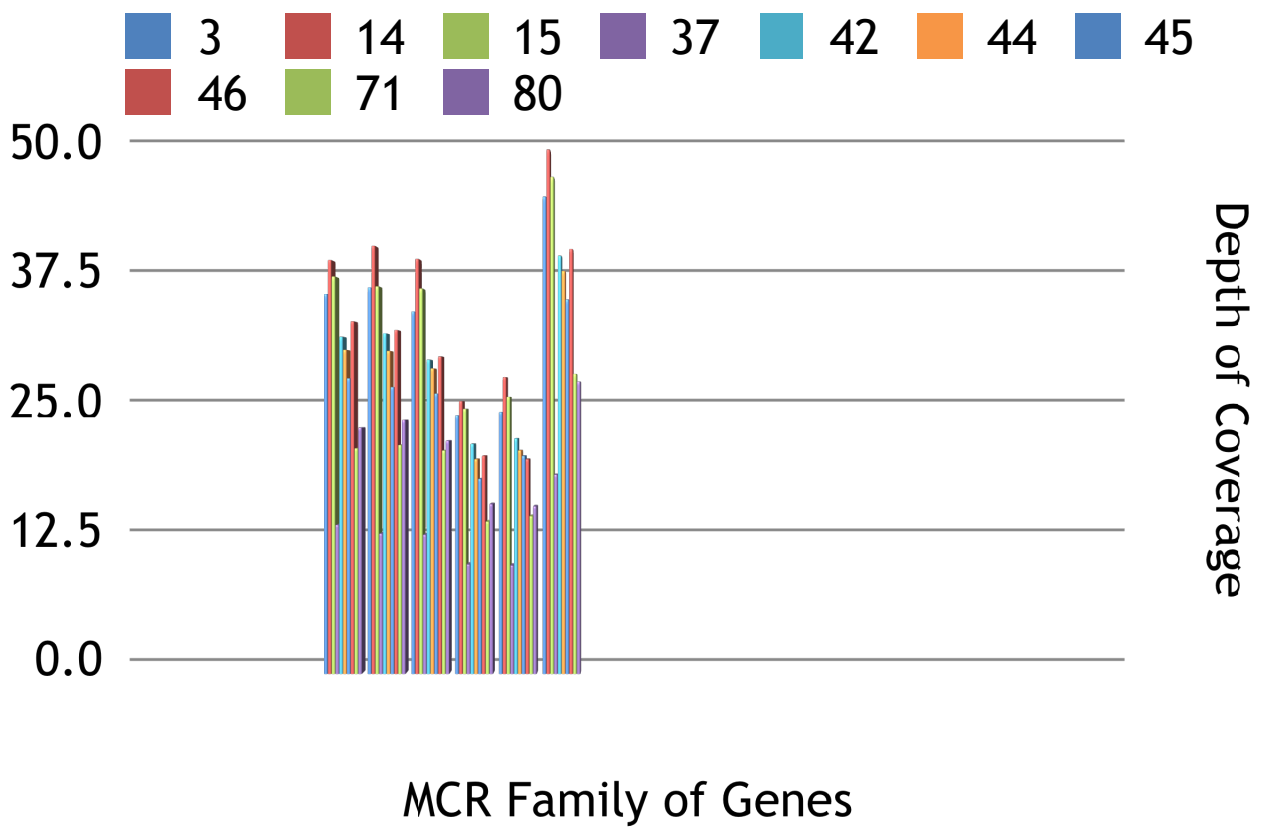


Mean Kmer Depth for MCR Genes: Susceptible

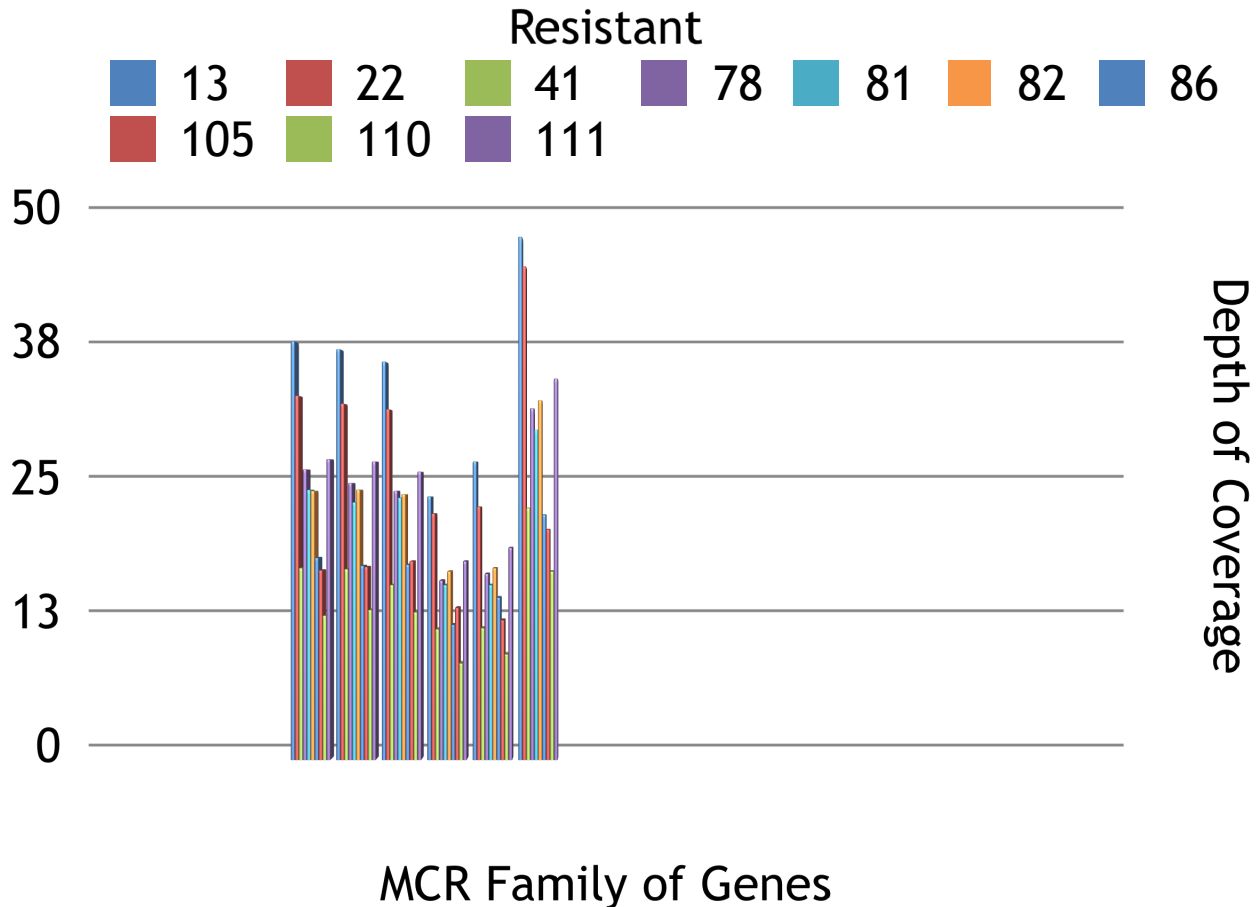


Narrowed focus to MCR family of genes:

Mean Kmer Depth for all Pan-Plasmidome Genes: Heteroresistant



Mean Kmer Depth for all Pan-Plasmidome Genes:



Upon seeing the same patterns in these graphs across phenotype classes it was determined that per nucleotide coverage depth statistics would provide much greater resolution. It may also be possible that copy numbers of other genes on the plasmid may be effecting expression. To investigate this further the plasmids found in the set of isolates were assembled using plasmidSpades and the gene sequences were extracted to form the pan-plasmidome. Using the pan-plasmidome as a reference, the per base nucleotide depths will be determined. We hope to find a clear distinction between phenotype groups based on copy number variation both of the whole plasmid, and copy number variation of genes on individual plasmids.