



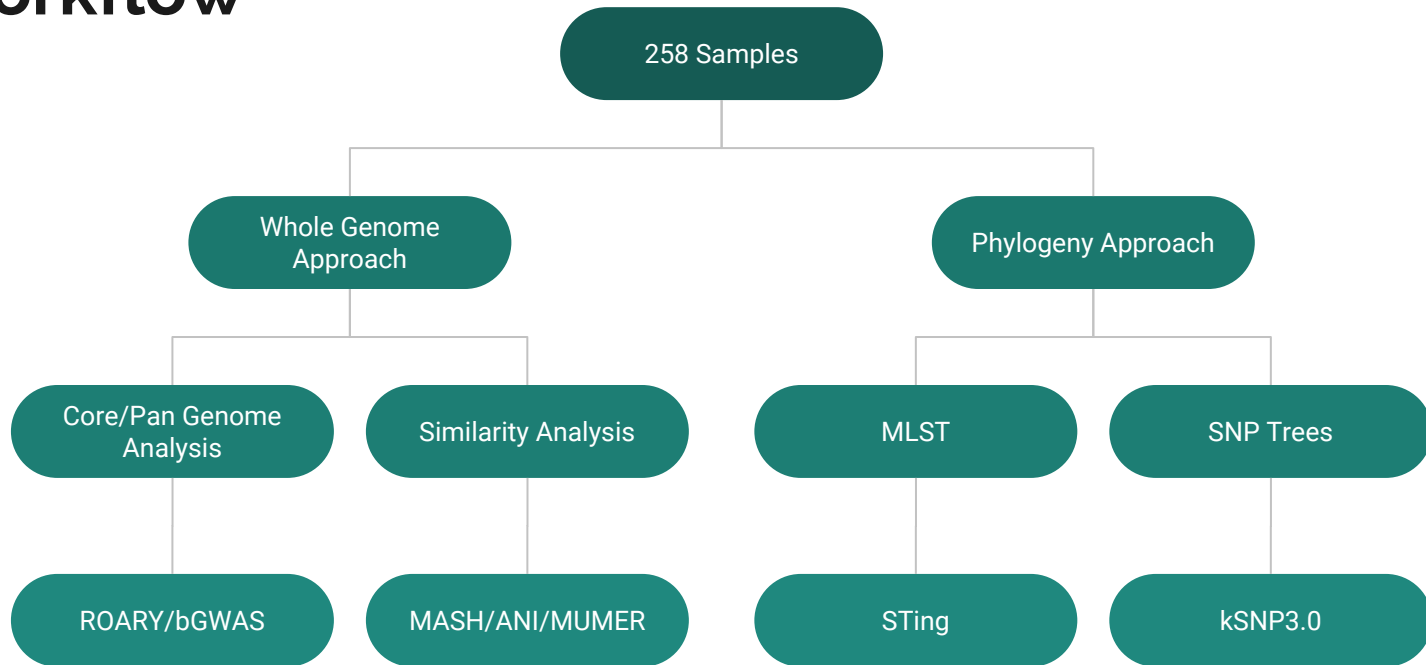
Comparative Genomics

Final Results

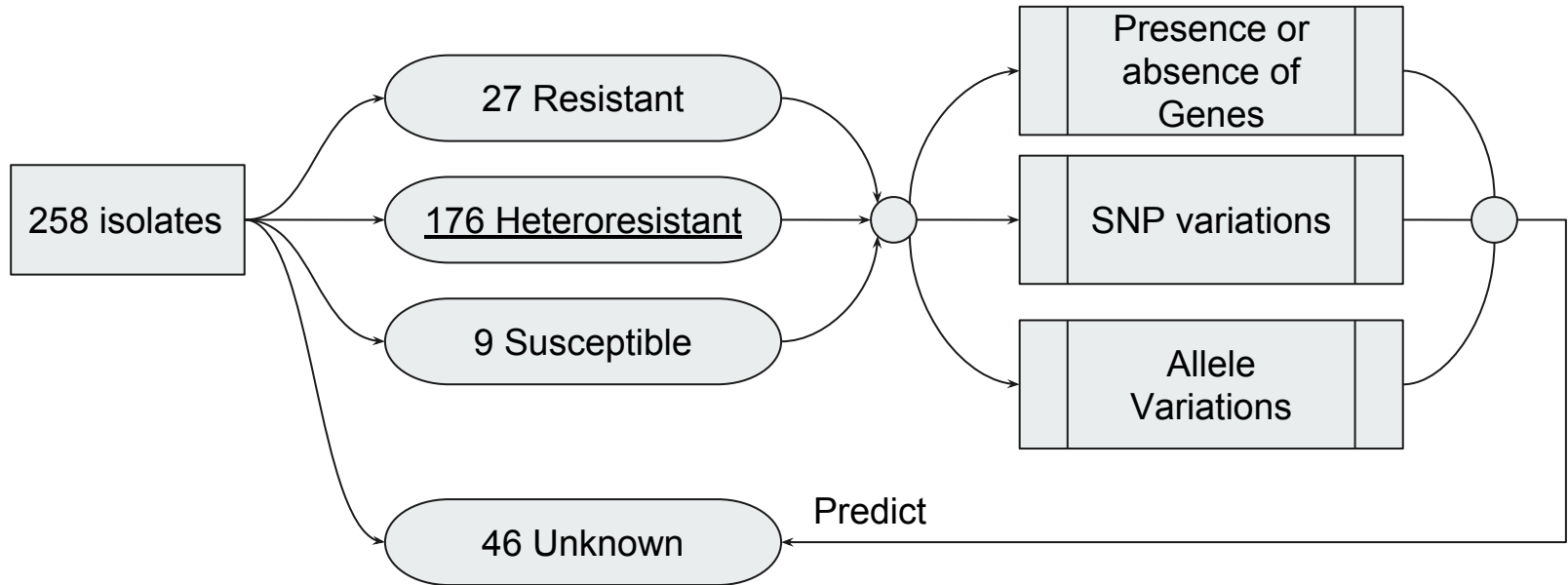
Team II: Fosfomycin Heteroresistance

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Sini Nagpal, Eunbi Park, Prachiti P. Prabhu, Vishnu Raghuram, Qi Zhang

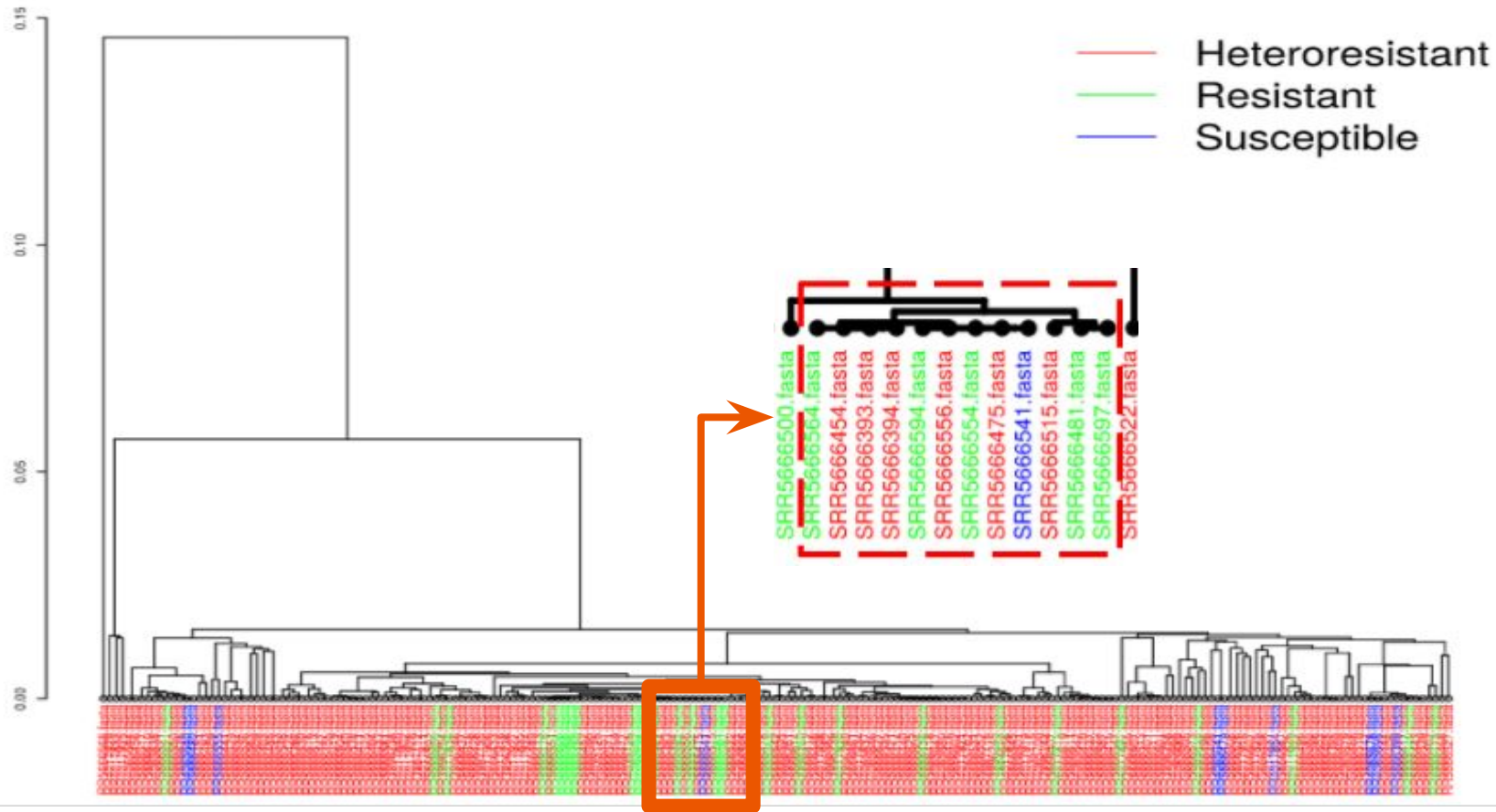
Workflow



Workflow



High level view



Presence or absence of genes

GWAS: Genome wide association study, aims to identify the genetic basis of phenotypic traits using the variation that exists within natural populations.

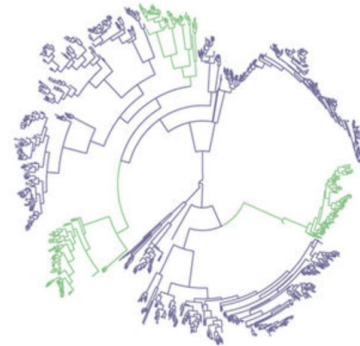
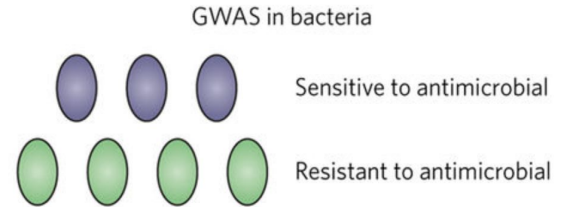
Attempts to correlate **phenotypic differences** to **genotypic differences**.

Control and case groups need to be well defined and represented in the population for reliable results.

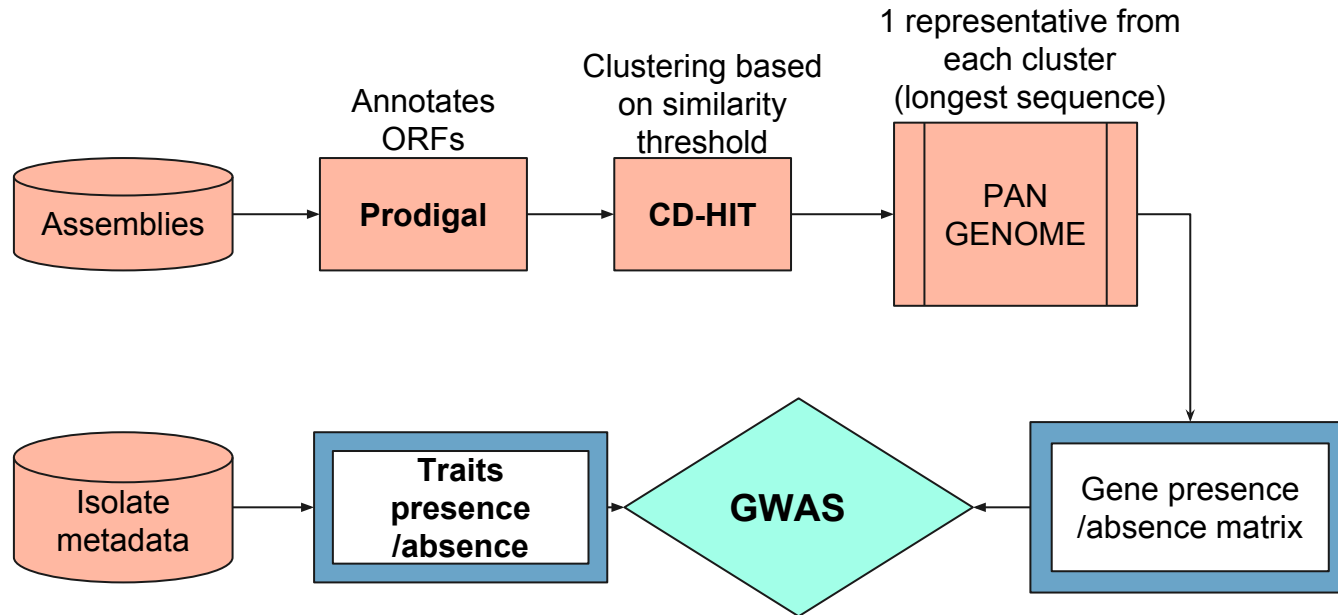
In our case:

Control: Non-HR samples (36) → **not well represented**

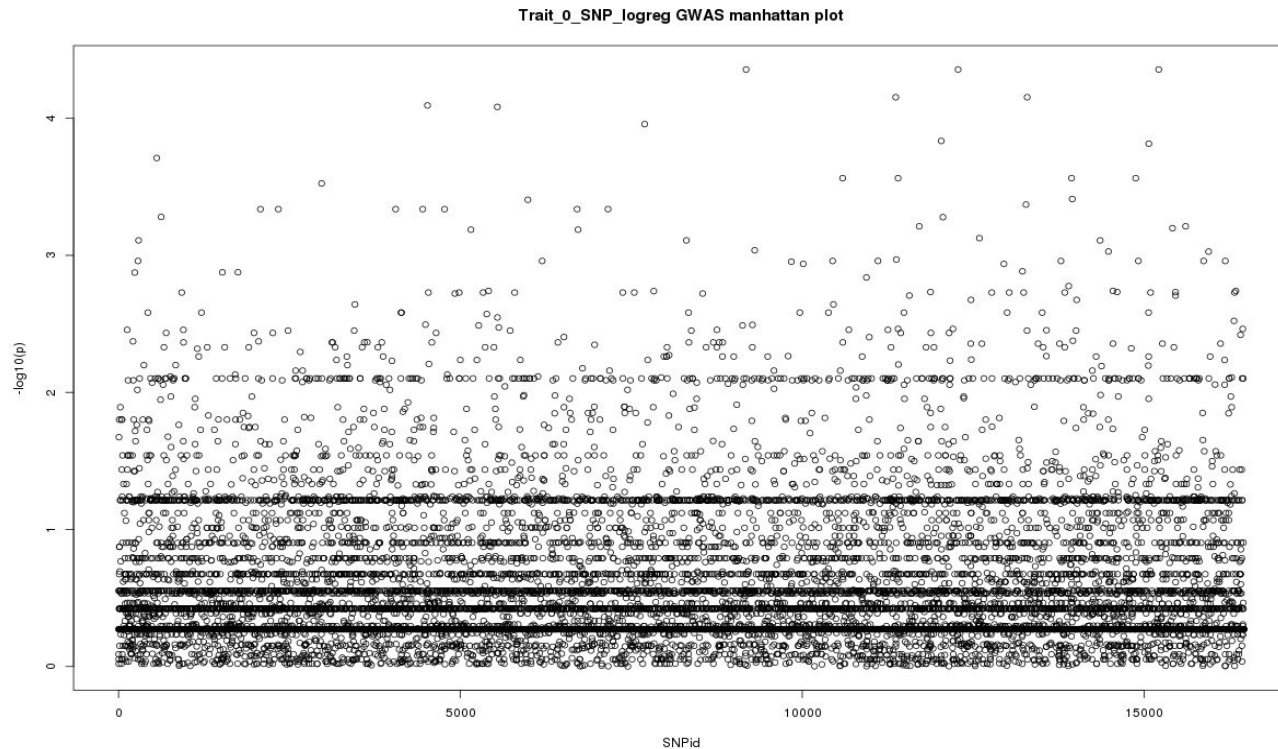
Case: Heteroresistant samples (176)



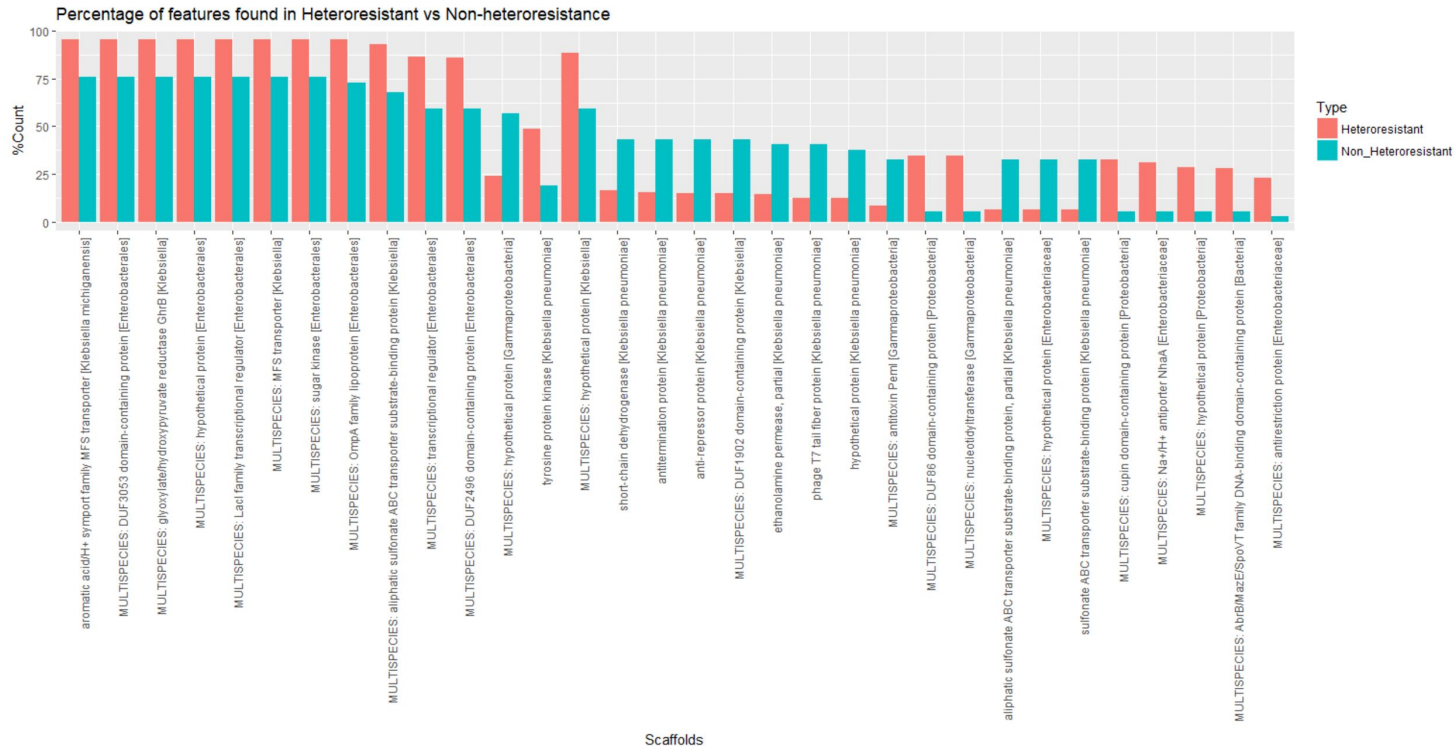
Tool: Bacterial GWAS



HR vs NonHR - Manhattan Plot



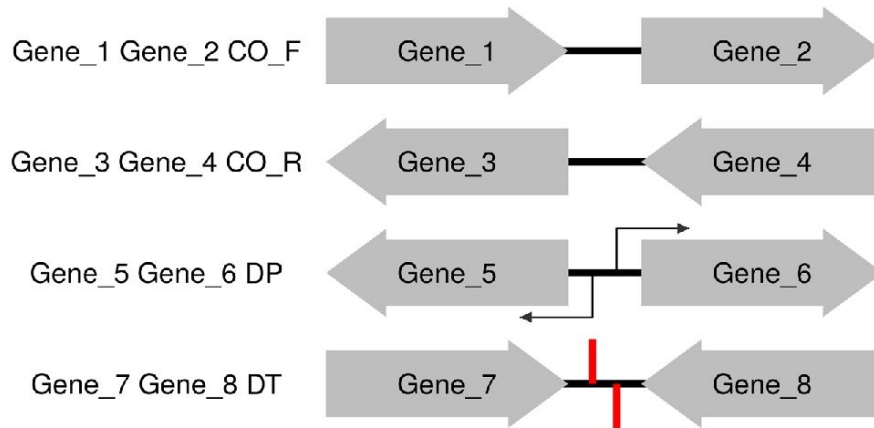
HR vs NonHR - %Feature found





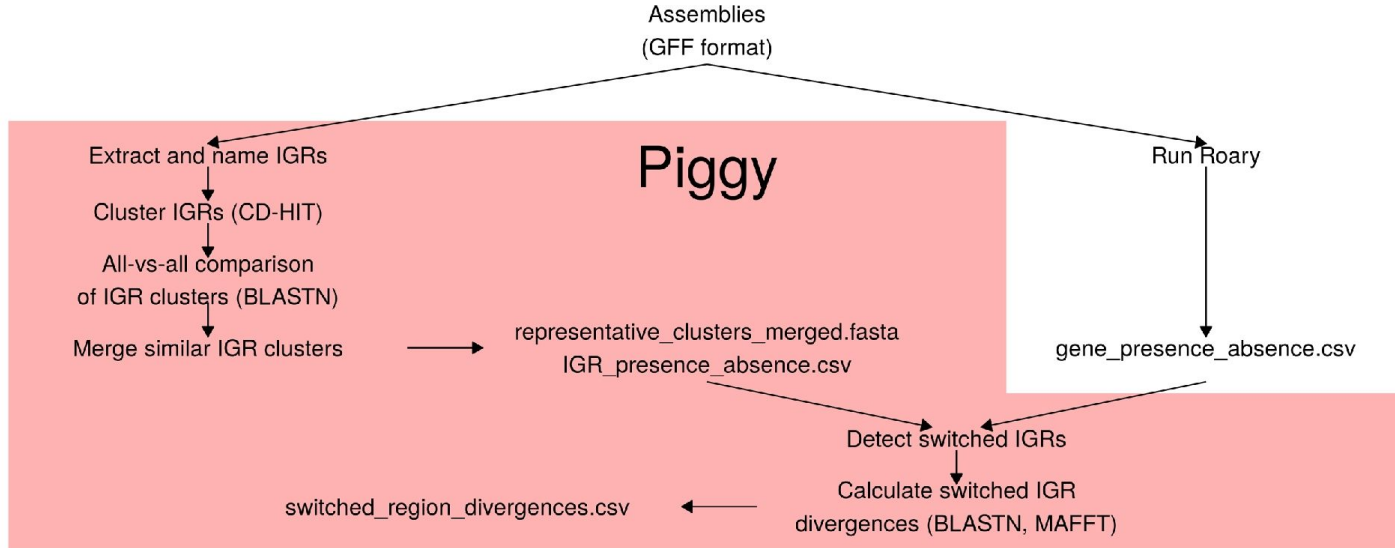
Piggy

A rapid, large-scale pan-genome analysis tool for intergenic regions in bacteria



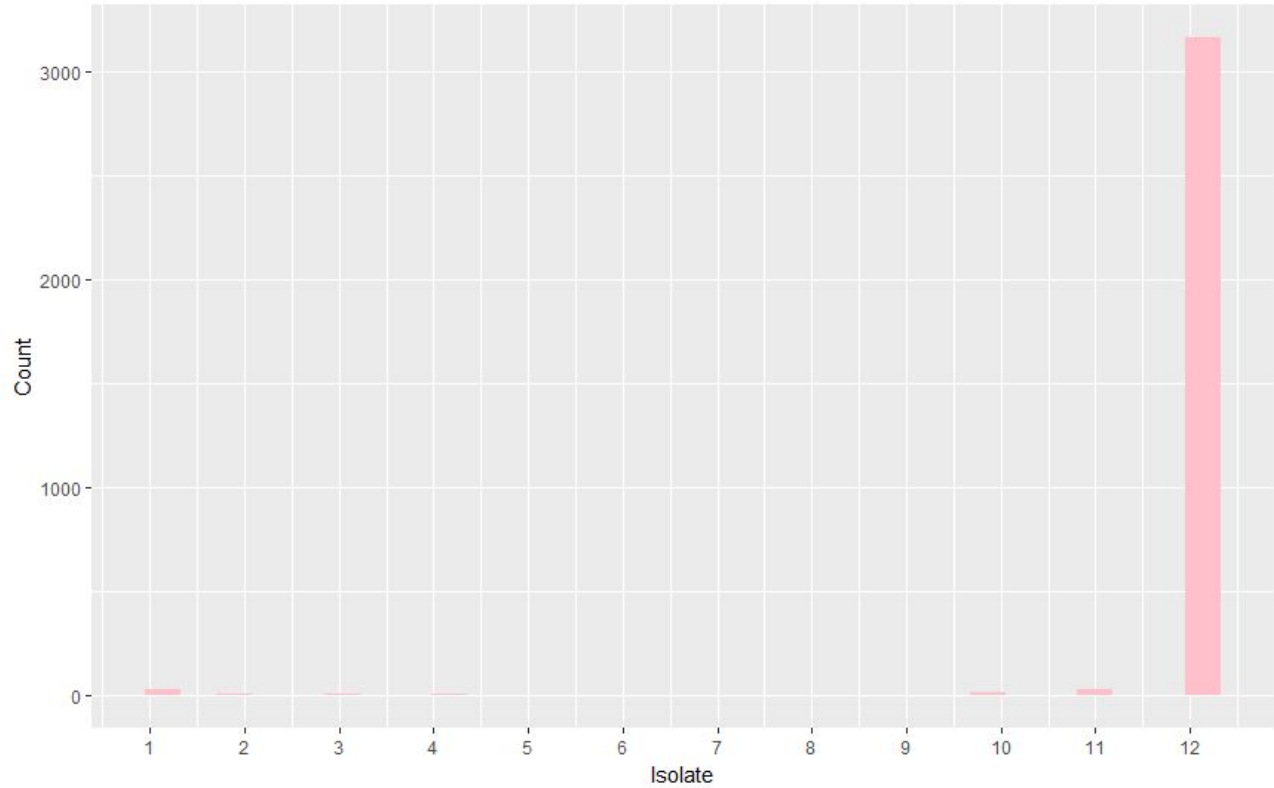


Piggy



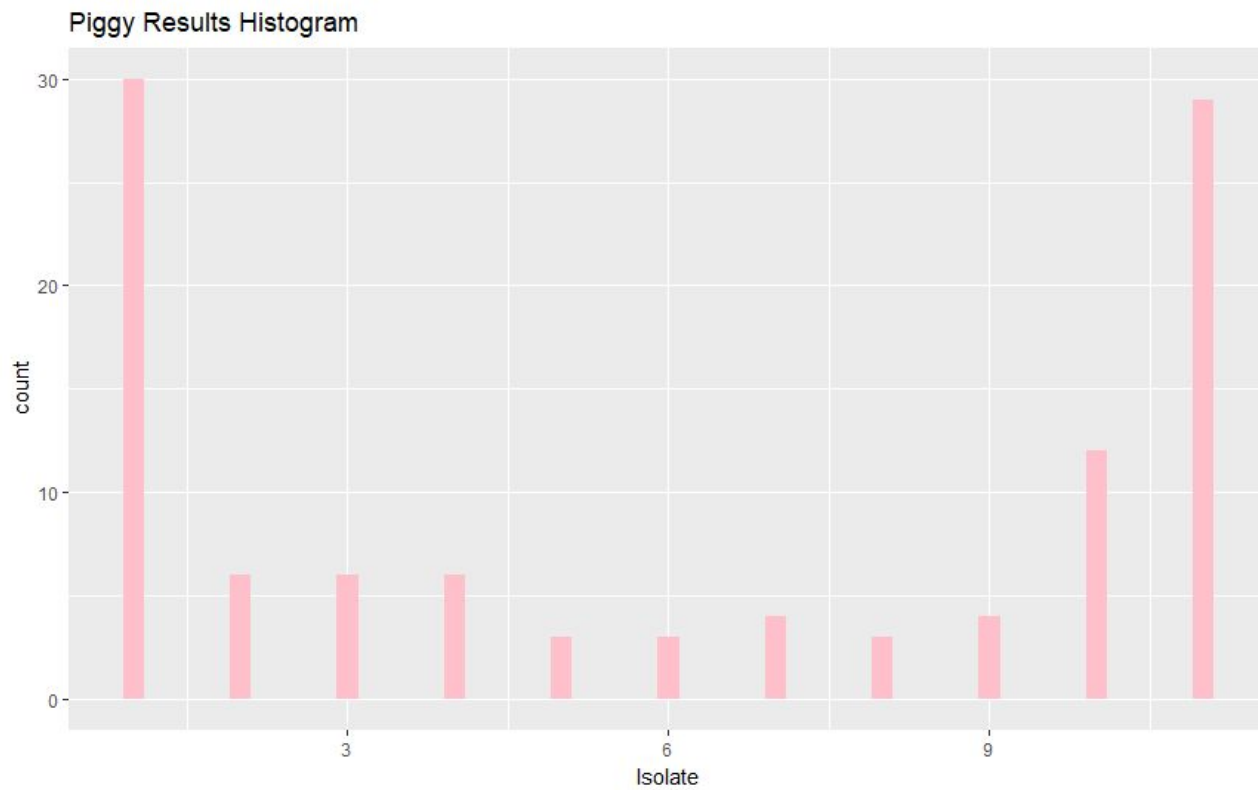


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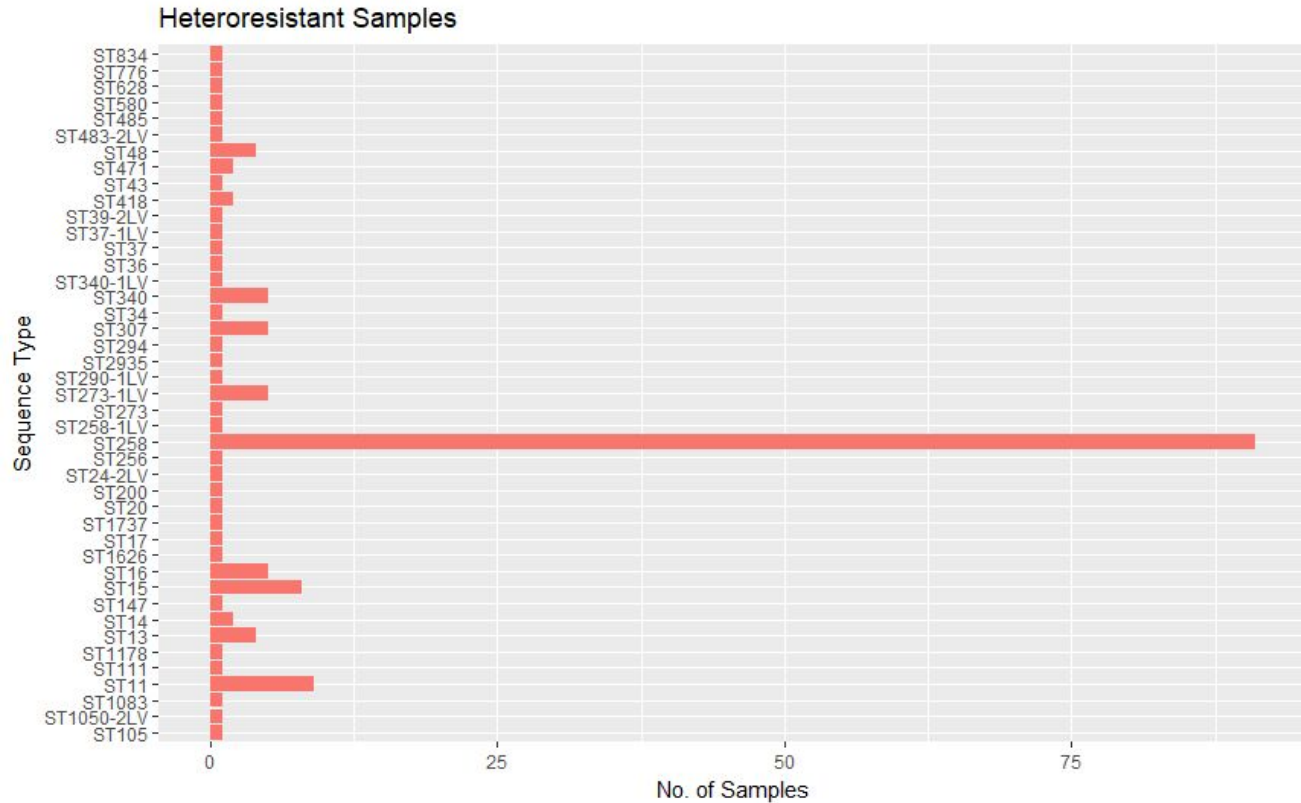




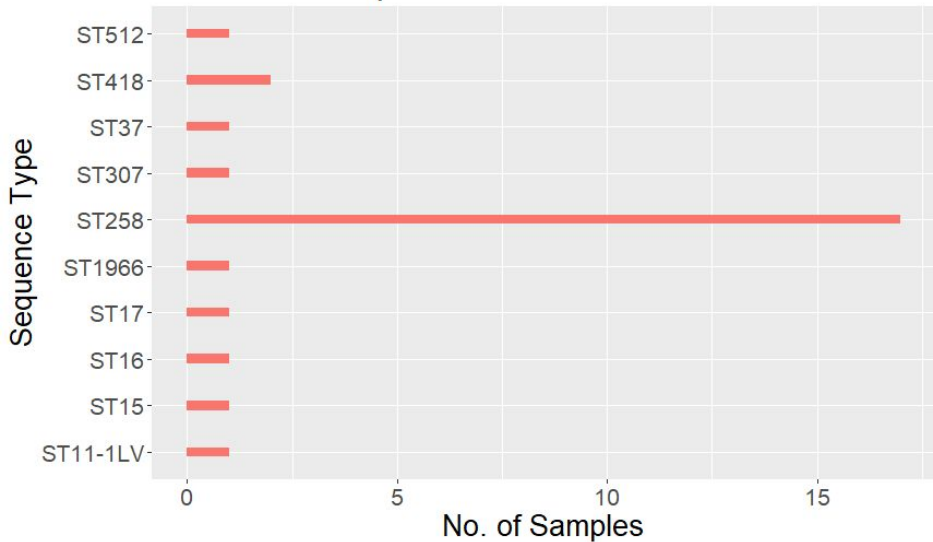
Piggy



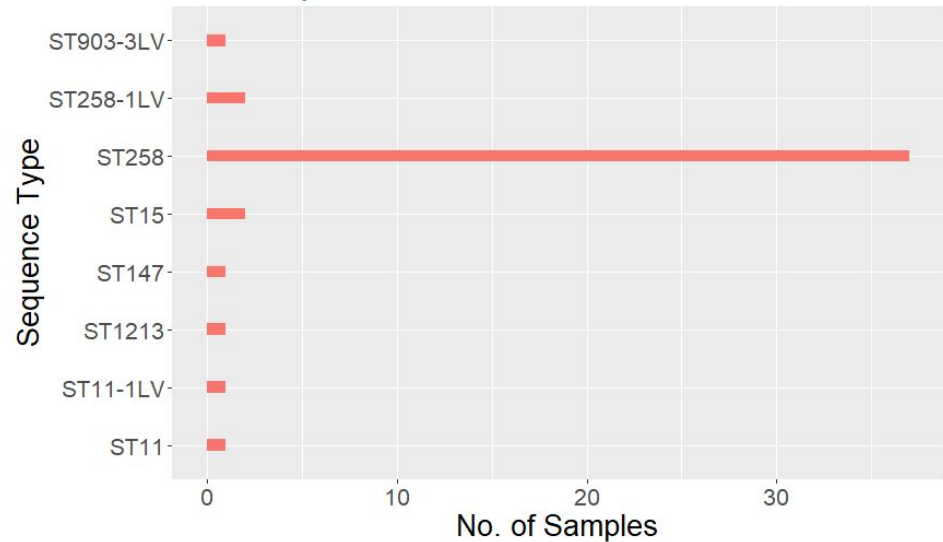
Phylogeny: MLST Results



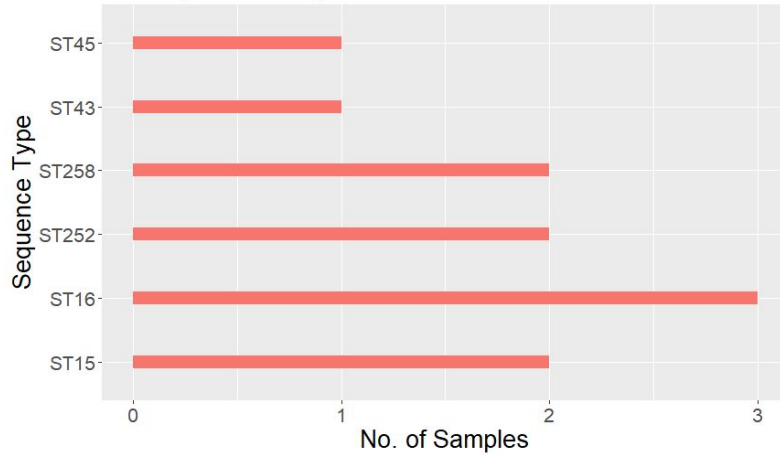
Resistant Samples



NA Samples

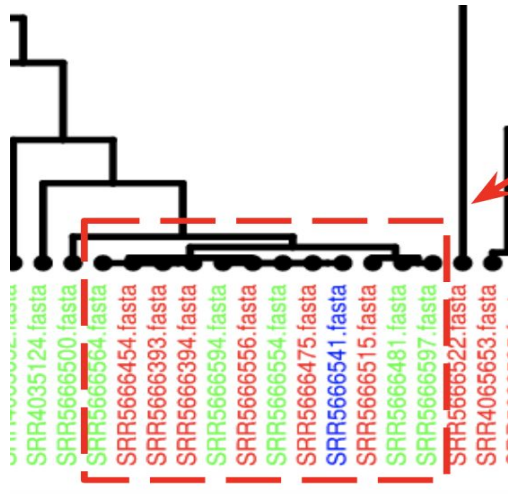


Susceptible Samples



Phylogeny: MLST Results

Cluster of Interest

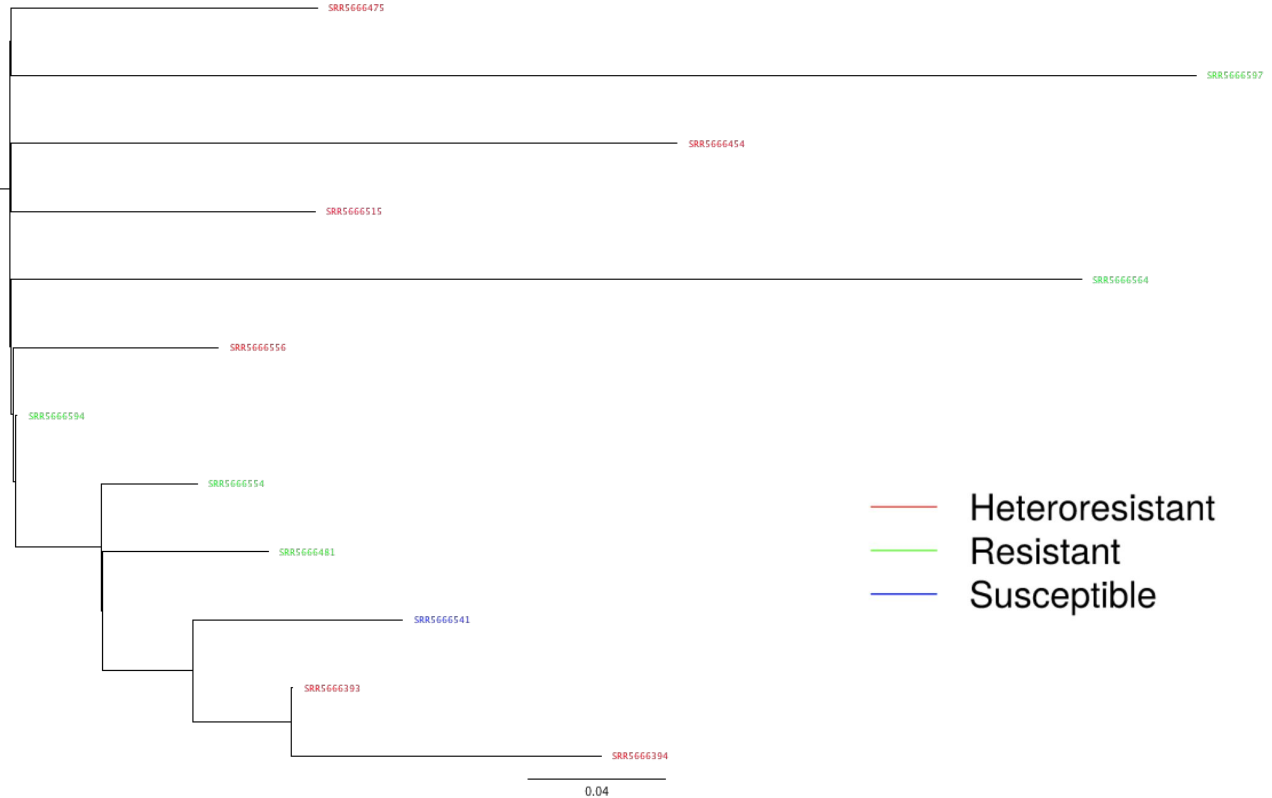
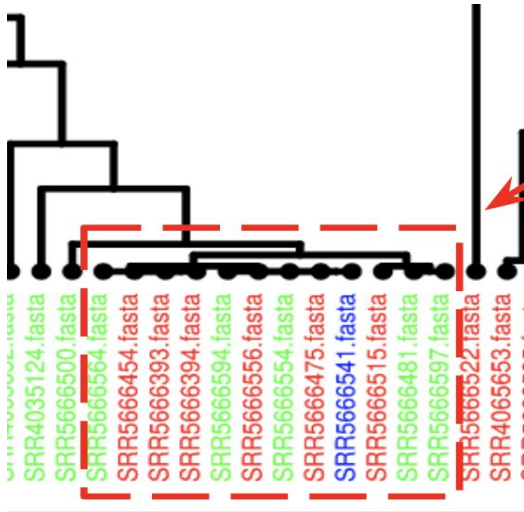


Sample Name	Phenotype	ST #
SRR5666393	Hetero	ST258
SRR5666394	Hetero	ST258
SRR5666454	Hetero	ST258
SRR5666475	Hetero	ST258
SRR5666515	Hetero	ST258
SRR5666556	Hetero	ST258
SRR5666481	Resist	ST258
SRR5666554	Resist	ST258
SRR5666594	Resist	ST258
SRR5666597	Resist	ST258
SRR5666564	Resist	ST258
SRR5666541	Suscept	ST258

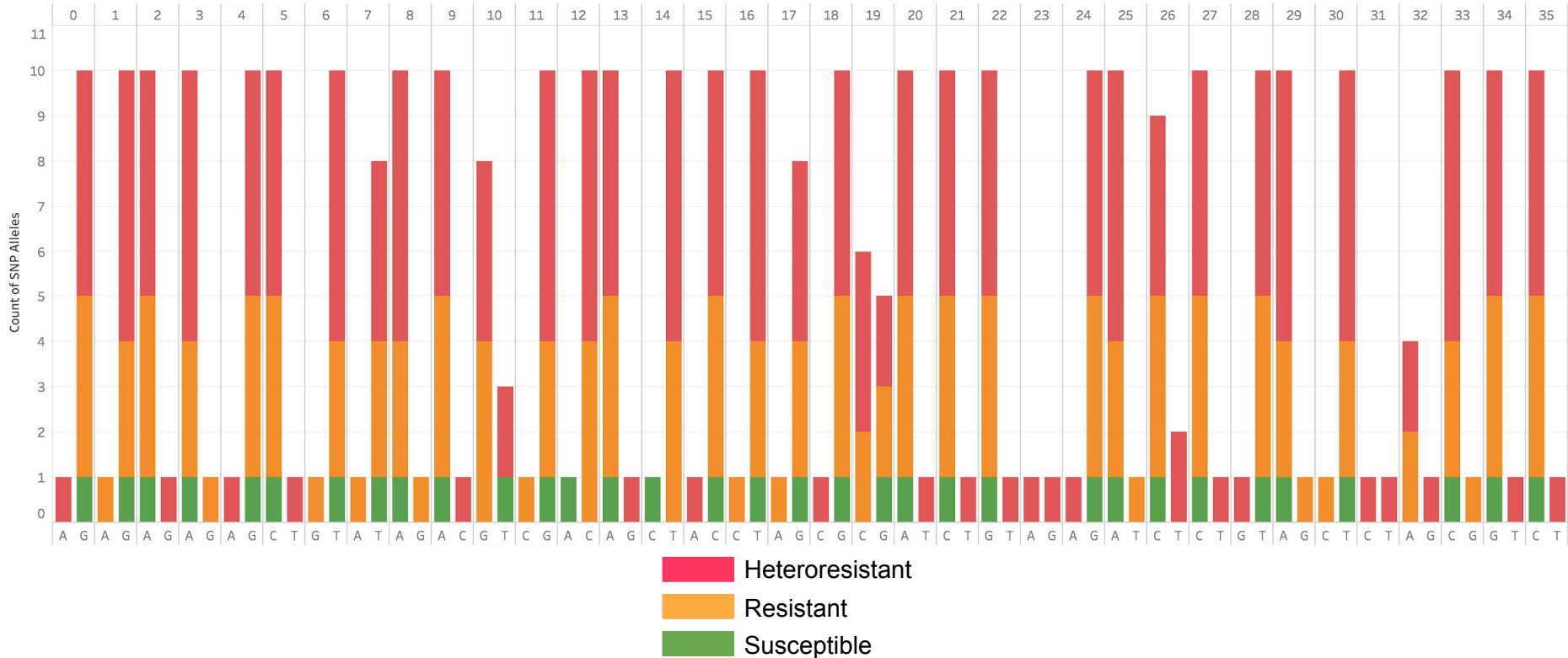
Phylogeny: kSNP Results



Phylogeny: kSNP Results



Phylogeny: kSNP Results





Conclusions:

1. Phylogenetic approaches were inconclusive.
2. Whole genome approaches were only useful in determining the relativity of our strains.
3. GWAS did not give significant results.



References

1. Castañeda-García, Alfredo, Jesús Blázquez, and Alexandro Rodríguez-Rojas. "Molecular mechanisms and clinical impact of acquired and intrinsic fosfomycin resistance." *Antibiotics* 2.2 (2013): 217-236.
2. Nikolaidis I, Favini-Stabile S, Dessen A. 2014. Resistance to antibiotics targeted to the bacterial cell wall. *Protein Sci* 23: 243–259.
3. Kidd, Timothy J et al. "A *Klebsiella Pneumoniae* Antibiotic Resistance Mechanism That Subdues Host Defences and Promotes Virulence." *EMBO Molecular Medicine* 9.4 (2017): 430–447.
4. Guo, Qinglan et al. "Glutathione-S-Transferase FosA6 of *Klebsiella Pneumoniae* Origin Conferring Fosfomycin Resistance in ESBL-Producing *Escherichia Coli*." *Journal of Antimicrobial Chemotherapy* 71.9 (2016): 2460–2465.
5. Gardner, Shea N., Tom Slezak, and Barry G. Hall. "kSNP3. 0: SNP detection and phylogenetic analysis of genomes without genome alignment or reference genome." *Bioinformatics* 31.17 (2015): 2877-2878.
6. Shea N Gardner, Tom Slezak, Barry G. Hall; kSNP3.0: SNP detection and phylogenetic analysis of genomes without genome alignment or reference genome, *Bioinformatics*, Volume 31, Issue 17, 1 September 2015, Pages 2877–2878.
7. Kim, Mincheol, et al. "Towards a taxonomic coherence between average nucleotide identity and 16S rRNA gene sequence similarity for species demarcation of prokaryotes." *International journal of systematic and evolutionary microbiology* 64.2 (2014): 346-351.