





- First-year MSc student
 - Undergrad: Biotechnology (B. Tech at Mac)
 - Mandatory programming courses (C++, Java, Python)
- Dabbled in both academia and industry
 - Academic experience was largely wet lab (Biohybrids Lab, Chem Eng. & fourth-year capstone)
 - Industry experience at two Coca-Cola production facilities
 - First introduction to real "ontologies"



ANTIBIOTIC
RESISTANCE
ONTOLOGY
KNOWLEDGE SPACE

Antibiotic molecule

Resistance-modifying agents

Mechanism of antibiotic resistance

Determinant of antibiotic resistance

Antibiotic target

Antibiotic biosynthesis

Component of AMR phenotype terminology

MODEL ONTOLOGY ALGORITHM SPACE

Protein homolog model

Protein variant model

Protein overexpression model

rRNA gene variant model

Toxin system meta model

Protein knockout model

Nonfunctional insertion model

Efflux pump system meta-model

Protein domain meta-model

CARD CURATED MODEL TYPES AND DETECTION PARAMETERS

efflux pump system meta-model 33 efflux pump components 33 gene cluster meta-model 12 gene order 12 protein domain meta-model 1 domain order 1 protein homolog model 4577 BLASTP bit-score 4577 protein knockout model 111 BLASTP bit-score 11 protein knockout model 32 single resistance variant 13 BLASTP bit-score 13 multiple resistance variants 1 deletion mutation from peptide sequence 1 nonsense mutation 1 deletion mutation from nucleotide sequence 1 insertion mutation from nucleotide sequence 1 frameshif mutation 1 protein variant model 462 BLASTP bit-score 163 single resistance variant 163 no association with resistance TB 17 multiple resistance variants 163 deletion mutation from nucleotide sequence 17 <tr< th=""><th>lodel Type / Model Parameter</th><th>Sum of Model Parameter Count</th></tr<>	lodel Type / Model Parameter	Sum of Model Parameter Count
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Supported by RGI

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A diverse intrinsic antibiotic resistome from a cave bacterium

Andrew C. Pawlowski¹, Wenliang Wang¹, Kalinka Koteva¹, Hazel A. Barton², Andrew G. McArthur¹ & Gerard D. Wright¹



Matches reference sequence



KNOWN UNKNOWNS
Similarity within model



LOOSE/DISCOVERY

UNKNOWN UNKNOWNS
Similarity outside of model



Measures sequence similarity independent of database size





Fine-tune bitscore cut-offs to reduce false positive and false negative hits

PROJECT TL;DR

2

Implement additional statistics to further reduce false positive hits

3

Develop additional code to address current gaps in RGI resistome prediction



(691 sequenced MDR genomes)



86.48%

- Presence/absence of homologous proteins
- 2) Similarity to CARD curated reference sequences based on **BLAST bitscore cut-offs**

NDM-1 (metallo-beta-lactamase)

PROTEIN VARIANT 7.33%

- Presence/absence of homologous proteins
- Secondary search for curated antibiotic resistance-conferring mutations

SNP in *Staphylococcus aureus* gyrB (confers resistance to aminocoumarin antibiotics)

PROTEIN OVEREXPRESSION

6.19%

| |-| |

Detects overexpression based on the presence or absence of mutations

Mutations in MexR (repressor of multi-drug efflux operon) of *Pseudomonas aeruginosa*

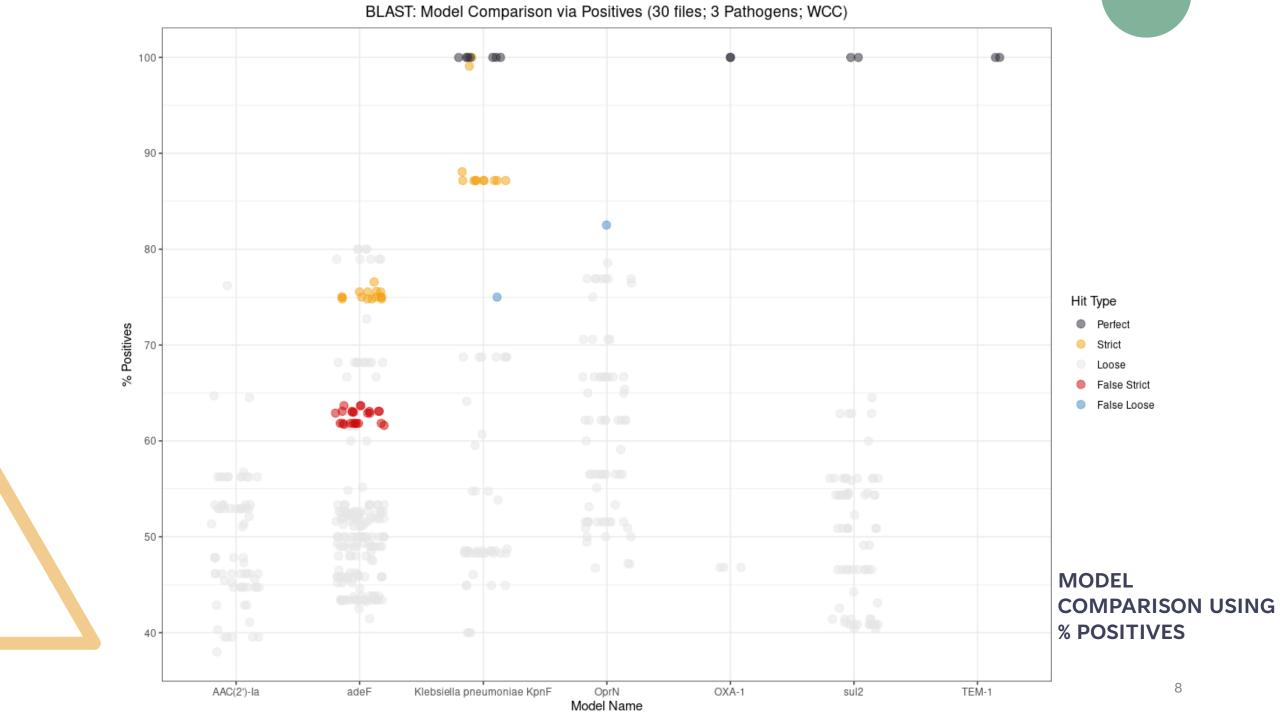
rrna gene variant

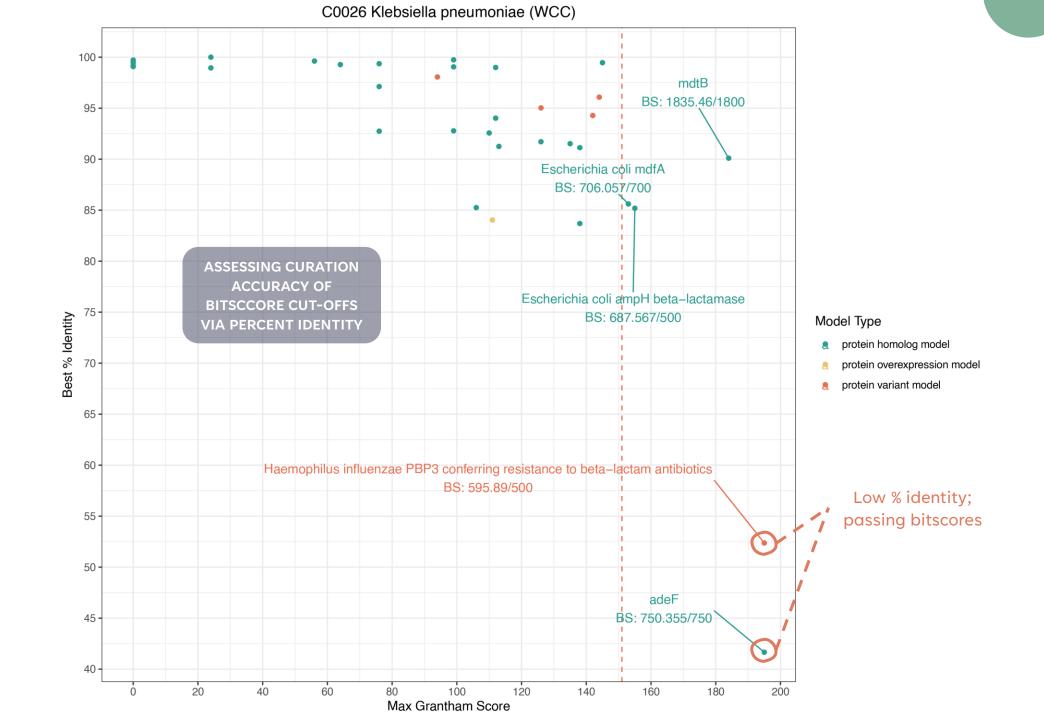
0%

Detects rRNA genes containing AMR mutations, differentiating them from their wild type

counterparts

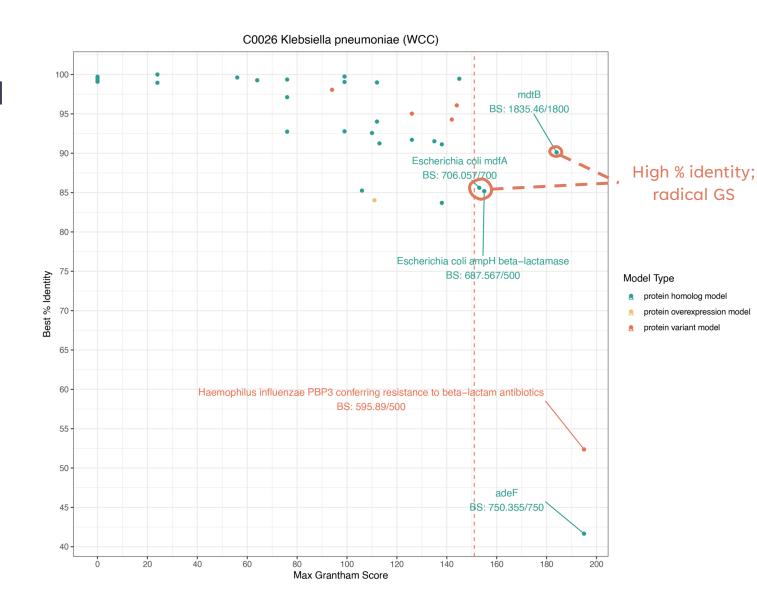
Point mutation in 16S rRNA of *Mycobacteroides* abscessus that confers aminoglycoside resistance





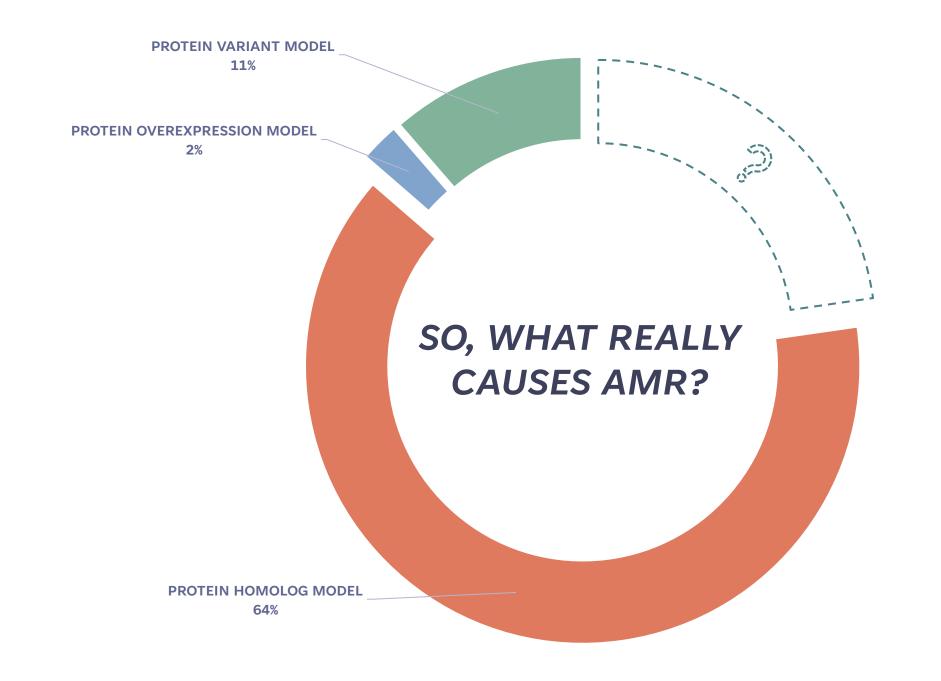
ADDITION OF GRANTHAM SCORES (GS) FOR RGI RESULT VALIDATION

- Categorizes amino acid substitutions and their level of dissimilarity
- Effect of substitutions is further categorized into four classes:
 - Conservative (0-50)
 - Moderately conservative (51-100)
 - Moderately radical (101-150)
 - Radical (≥151)



WHAT ABOUT THE CODE?







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