AMR Prediction tools and databases: an overview

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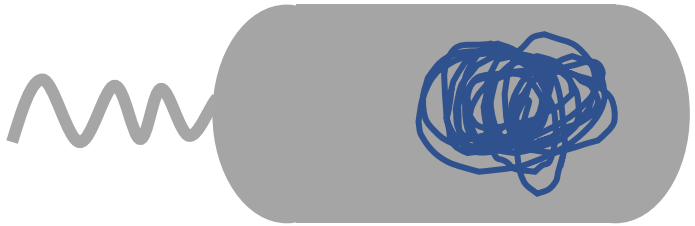
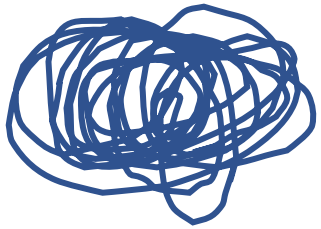
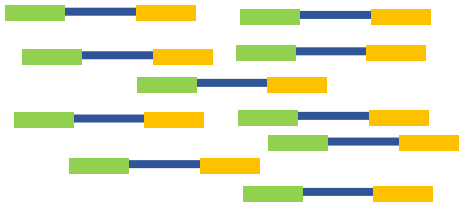
Whole genome sequencing



Bacteria



Genomic DNA isolation



Library Preparation

Reads

Read 1 Read 2

Illumina Sequencer

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Applications

Whole Genome Sequencing

1. Pathogen diversity and surveillance
2. Transmission tracking
3. Outbreak investigation
4. AMR prediction and surveillance

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Predicting antimicrobial resistance

1. **Information on resistance mechanisms**
   - Acquired - Example: *mecA*
   - Chromosomal mutations - Example: *gyrA* mutations
   - Resistance databases: **CARD, ResFinder and AMRFinder**
2. **Whole Genome Sequence**
3. **Analysis and interpretation tools**

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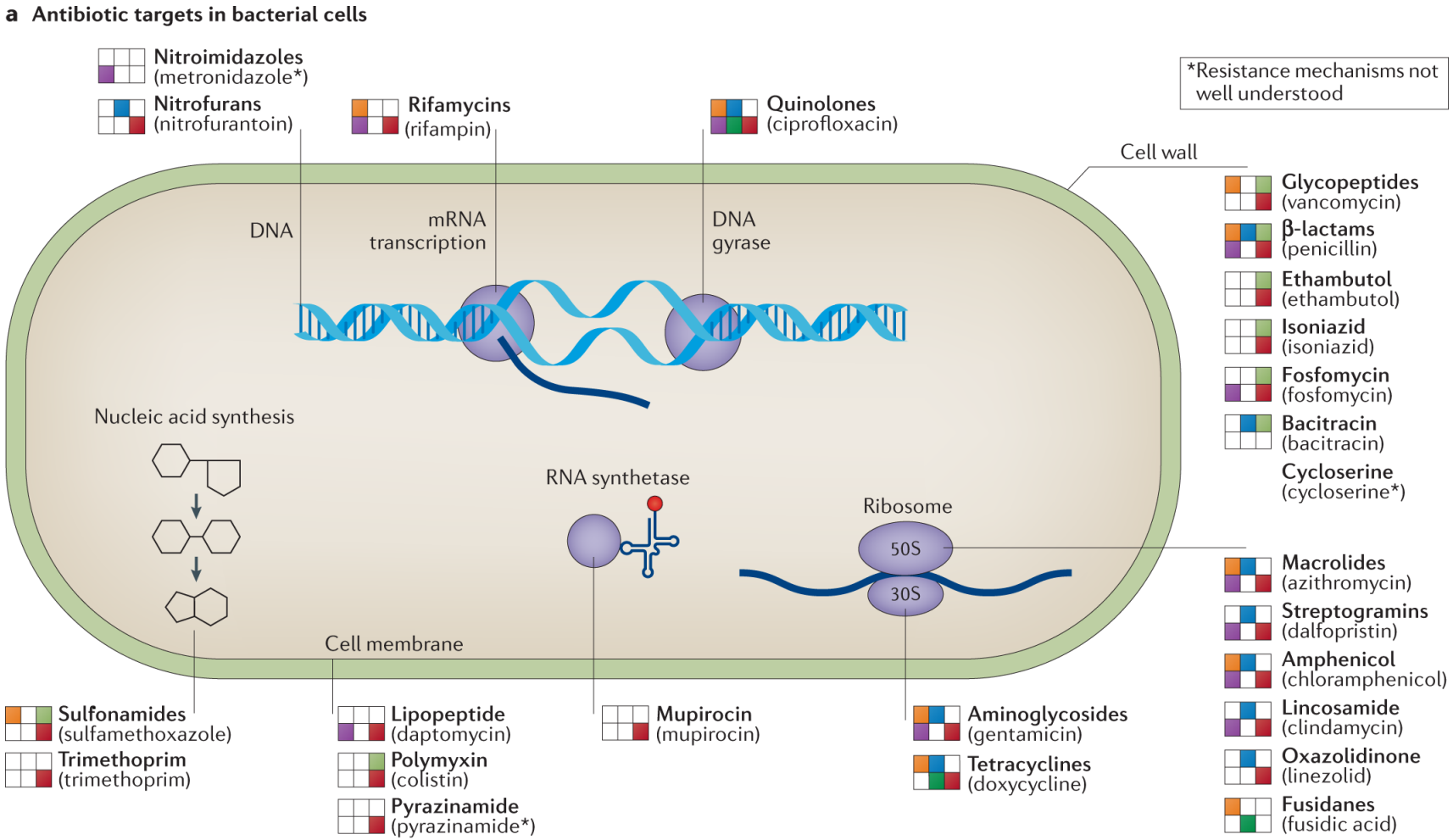
Antibiotics



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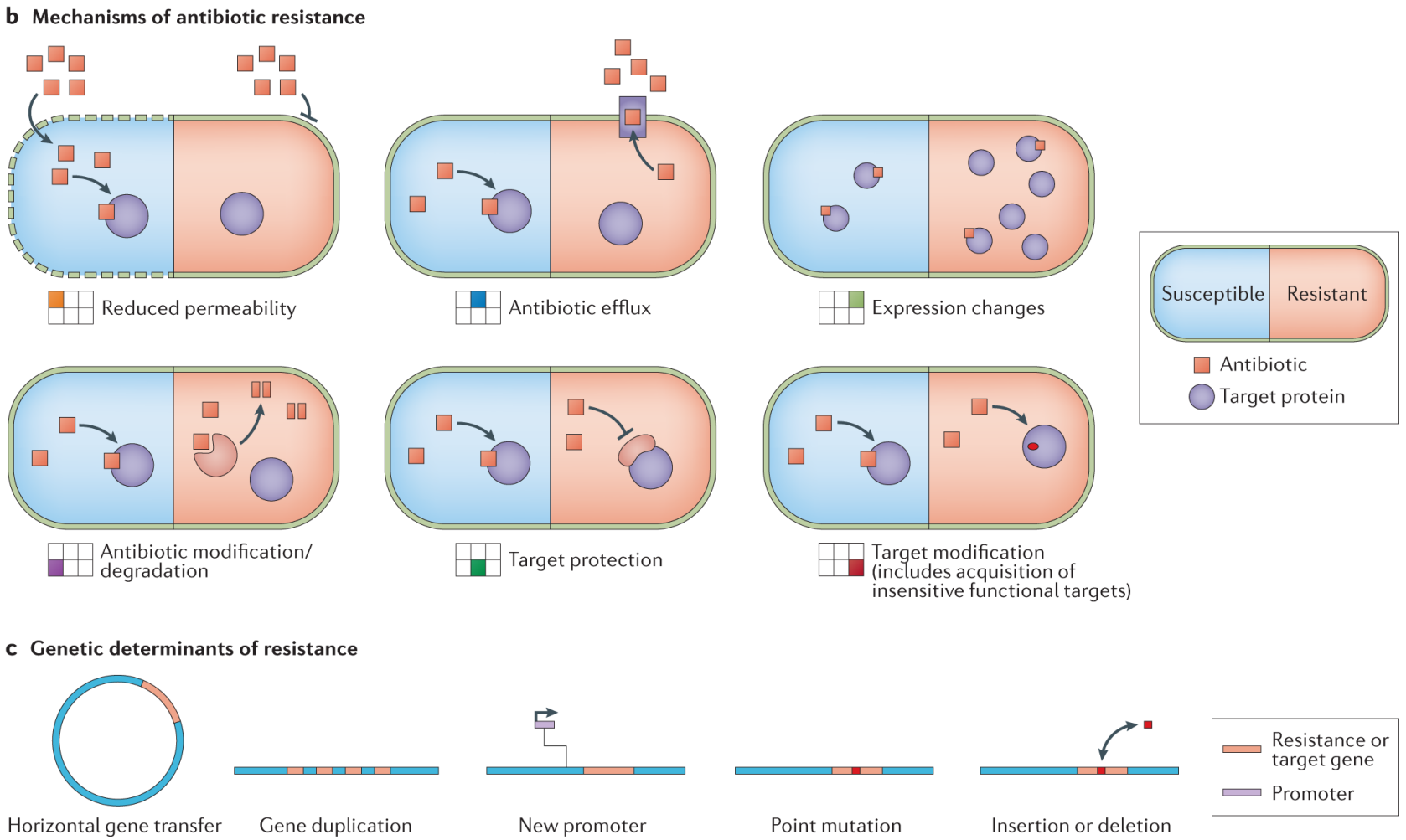
Nature, 2019, doi: 10.1038/s41576-019-0108-4

Resistance mechanisms



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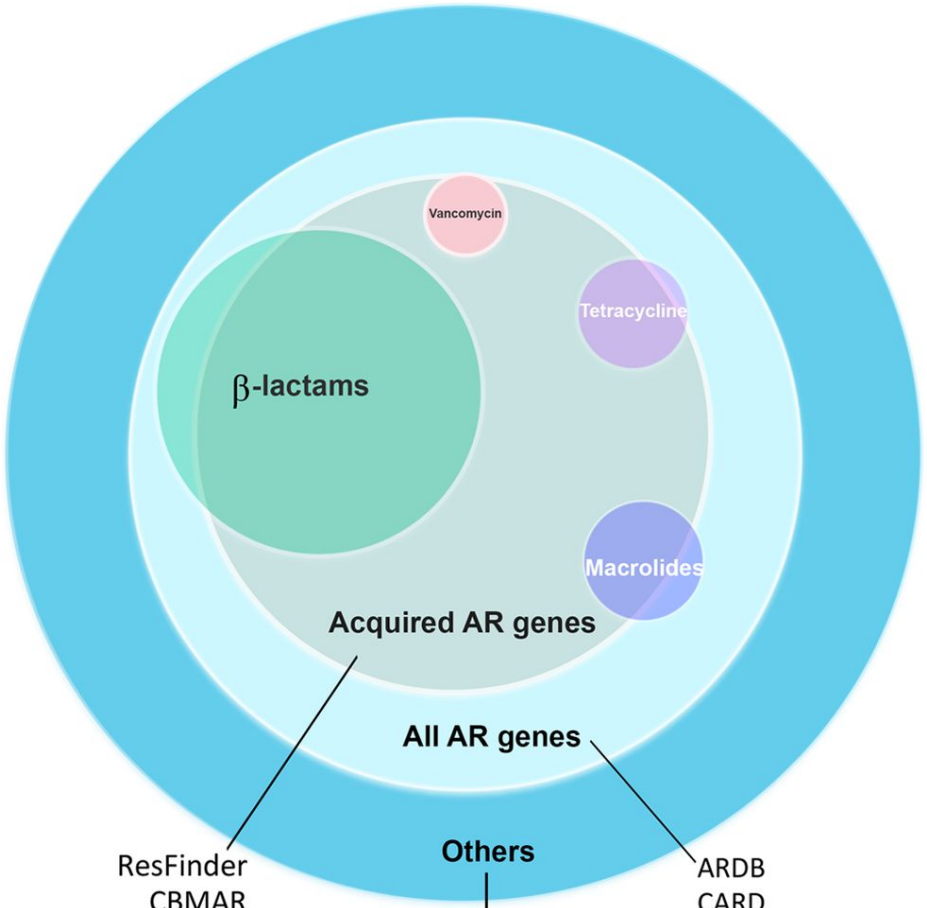
Antimicrobial resistance databases



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Xavier et al. 2016, JCM

Predicting phenotypic resistance

AMRFinder (*Feldgarden M et al. 2019*):

Validated on 6,242 isolates across 3 different species

concordance >98%

Mycobacterium tuberculosis (*Hunt et al. 2019*):

validated against 10207 isolates

concordance 94%

Staphylococcus aureus (*Kumar N et al. 2020*):

validated against 778 isolates

concordance 99%

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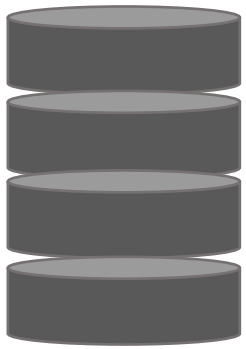
CARD



- Determinants from 263 pathogens (N > 100,000) genes, SNPs and plasmids
- Gene ontology structure (6453 GO Terms) for characterization
- Uses both BLAST, homology and SNP models
- latest versions with Kmer based algorithms
- Integrated within easy-to-use webtool

Usage considerations:

- Results need to be filtered based on the cutoffs used (manual curation)
- Species nonspecific predcitions
- Prediction limited to class of drugs in certain instances
- Limited upload size not suitable for large scale usage
- Accepts only assembled sequences

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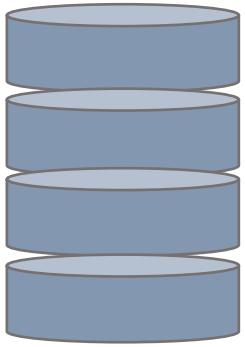
ResFinder



- Reference database contains 2919 genes, 266 SNPs and >57 antimicrobials
- Regularly curated and updated
- Uses Kmer based algorithms
- Integrated within easy-to-use webtool and command line version also available

Usage considerations:

- Species specific predictions
- Minimal curation of the results needed
- Prediction limited to class of drugs in certain instances
- Can accept multiple sequences at a time
- Accepts both assembled sequences and reads

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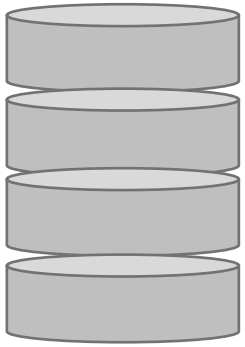
AMRFinder



- Reference database contains 4579 proteins, 560 HMM
- Regularly curated and updated maintained by NCBI
- Allows identification of potentially novel mechanisms

Usage considerations:

- Command line only tool
- Results include drug class
- Can accept multiple sequences at a time
- Accepts assembled sequences

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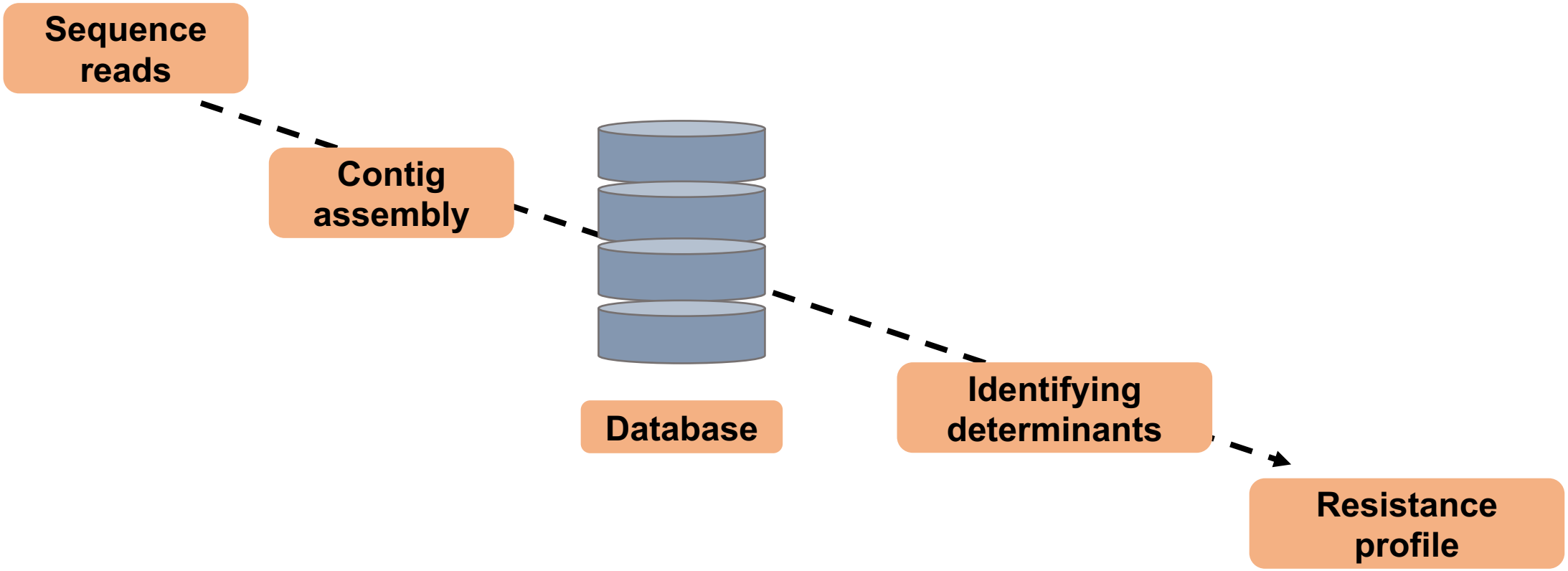
Detecting resistance



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Prediction tools

Prediction tools	Databases used
Web tools	
Pathogenwatch	own
ResFinder	own
CARD-RGI	own
Command line tools	
NCBI AMRFinder	own
ResFinder	own
SRST2	Derived from ARG-ANNOT
ABRICATE	ResFinder, CARD, AMRFinder, PlasmidFinder, VFDB

Considerations

- Input files reads/assemblies
- Comprehensiveness
- Curation
- Regularly updated
- Easy to access
- Comparability
- Discrepancies between phenotype and genotype

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Acknowledgement

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Prof. Stephen Bentley

SAGESA network

Thank you

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