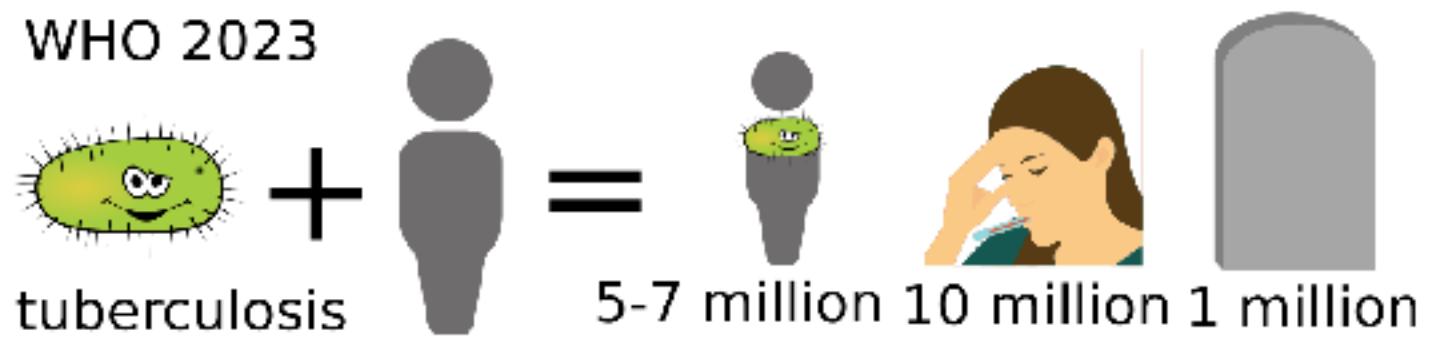
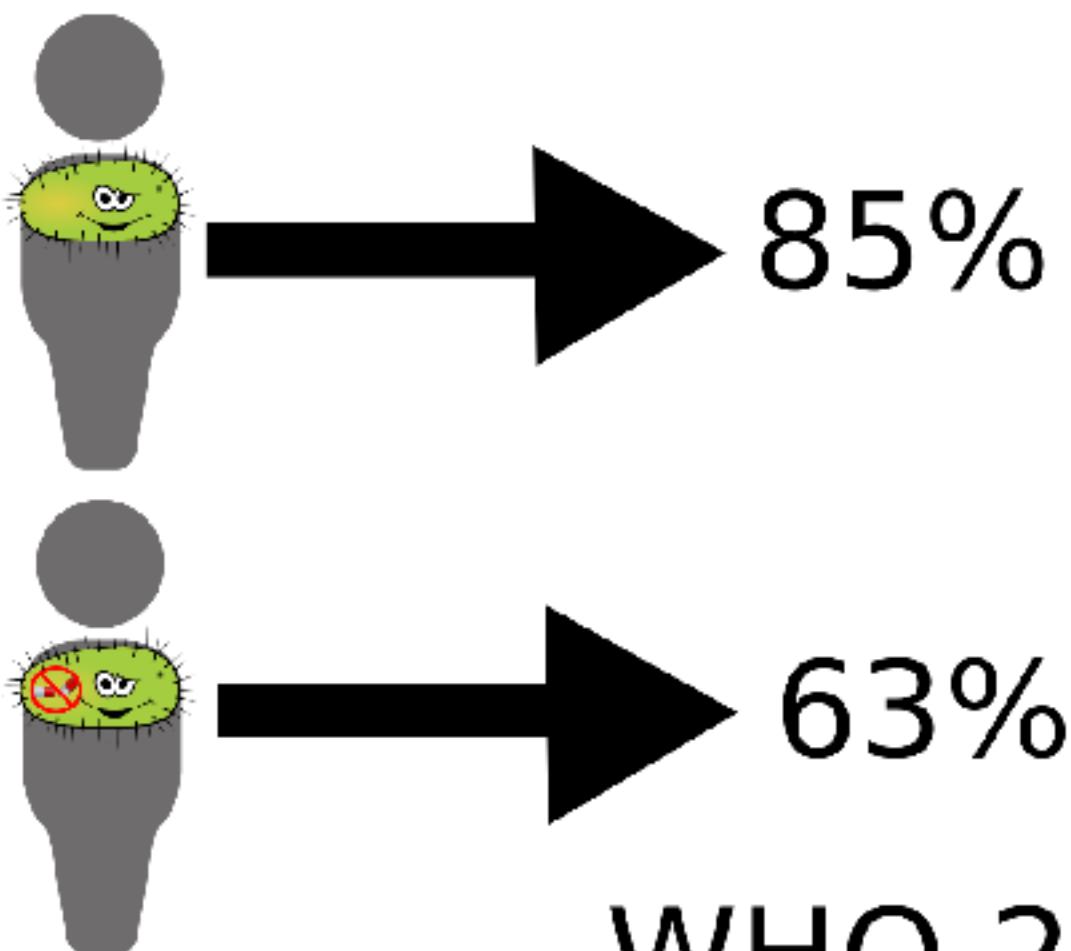


`freezeTb`; detecting anti-microbial resistance in TB

WHO 2023



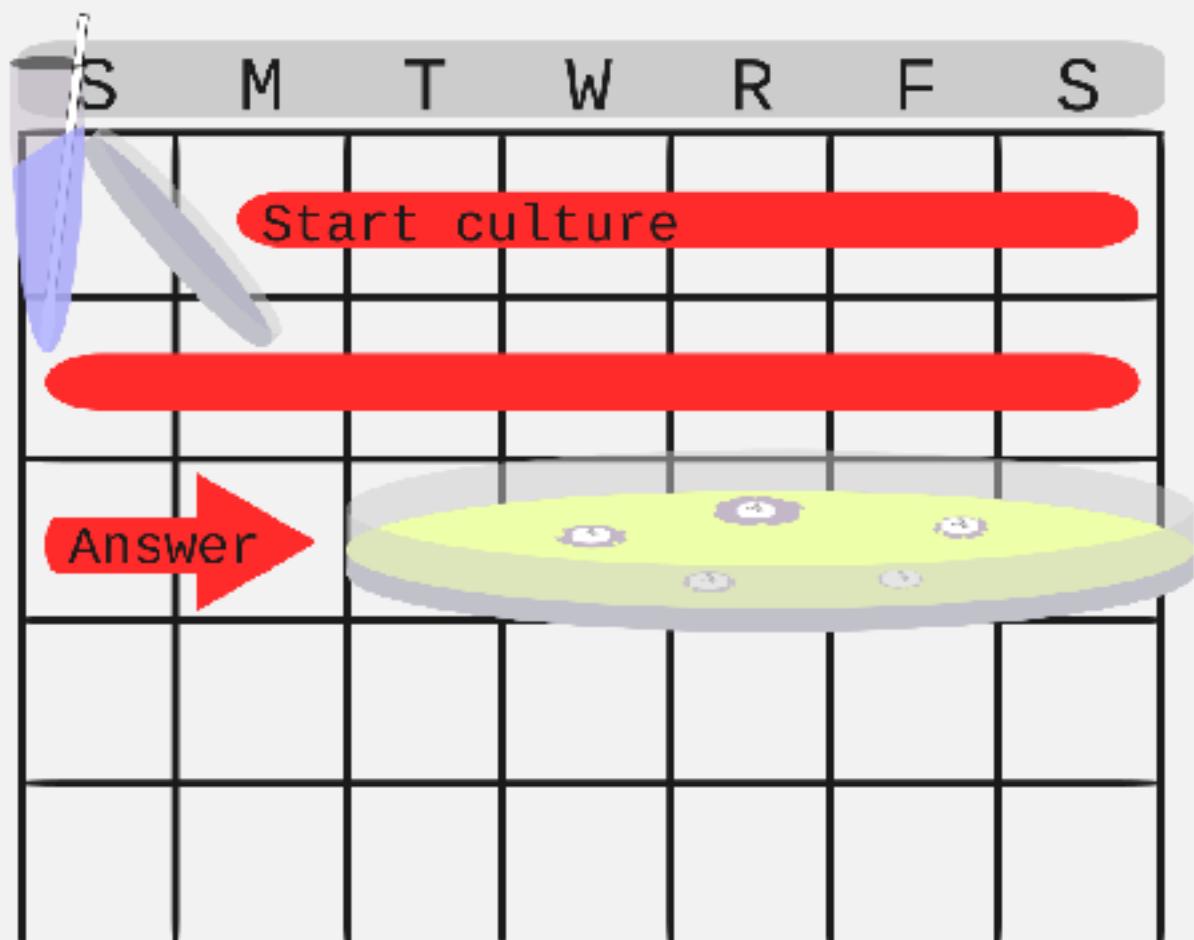
Treatment success



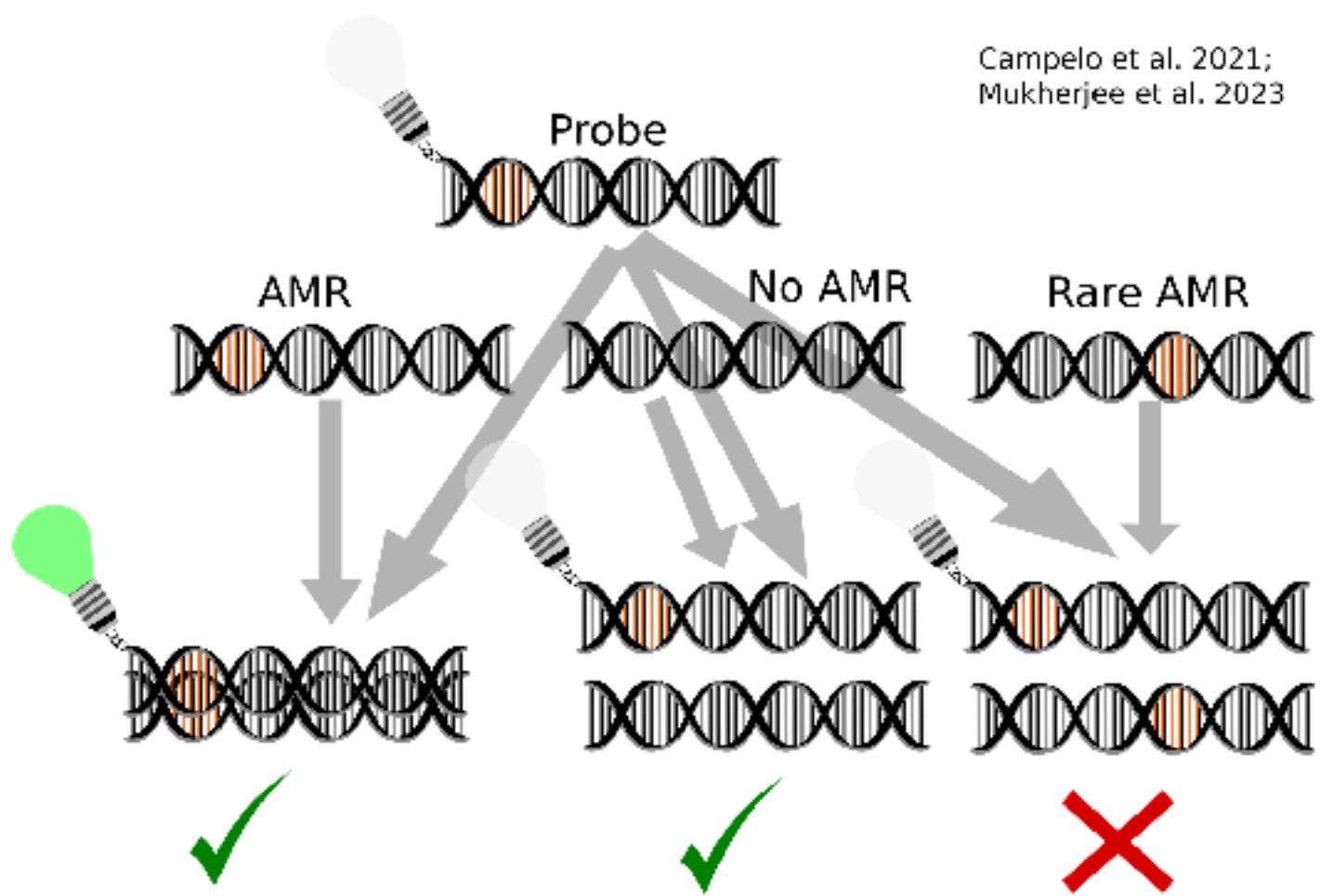
WHO 2023

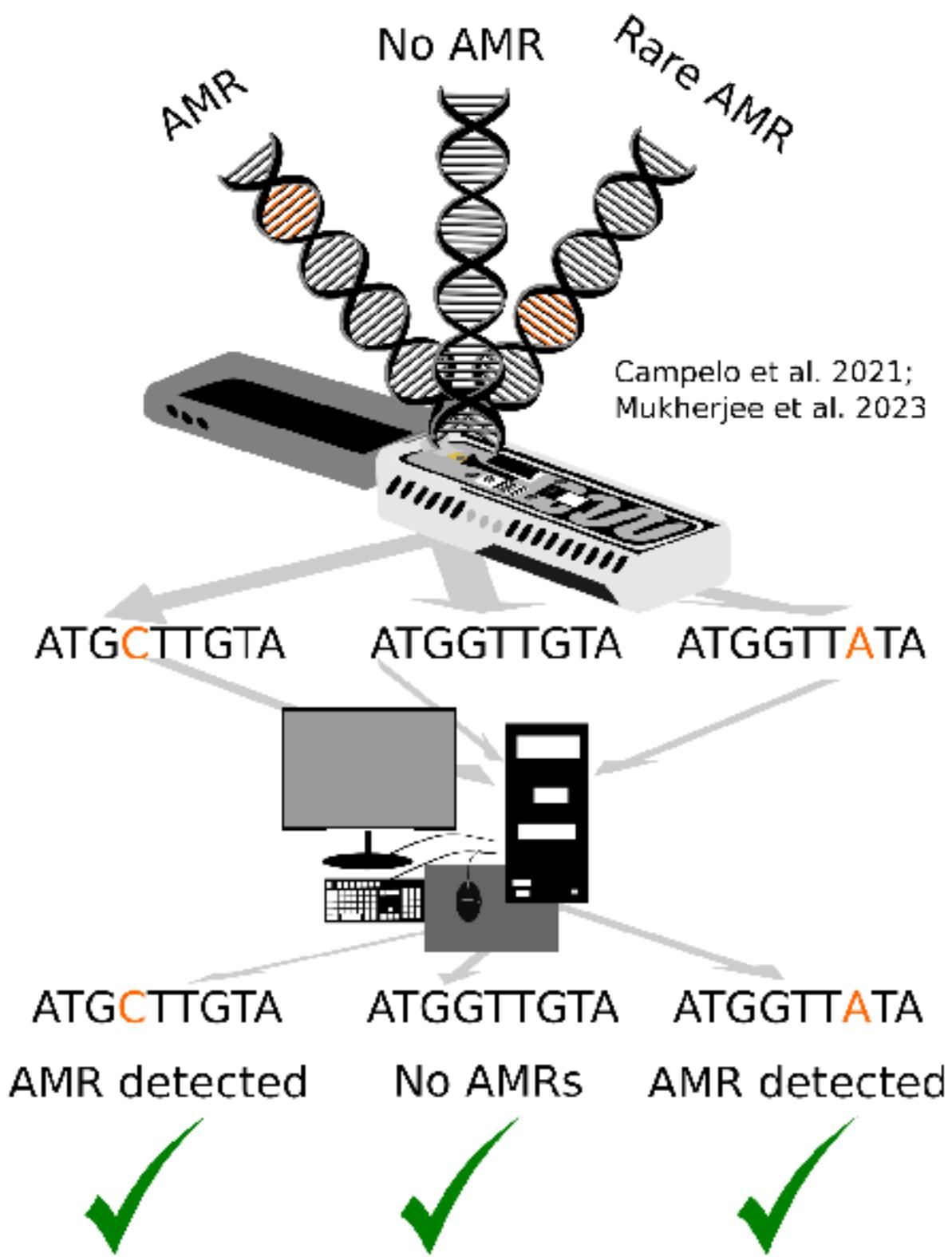
Drug resistant detection

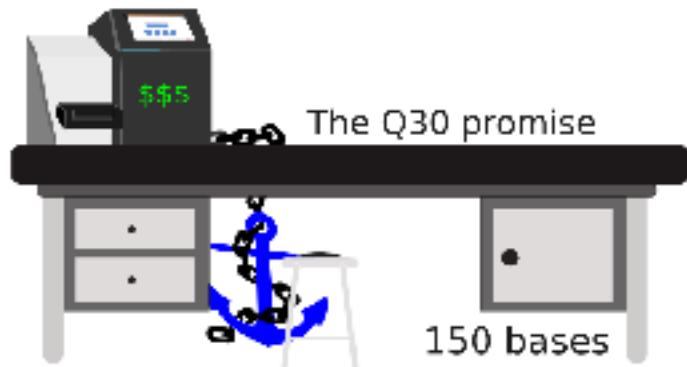
Month



Campelo et al. 2021;
Mukherjee et al. 2023



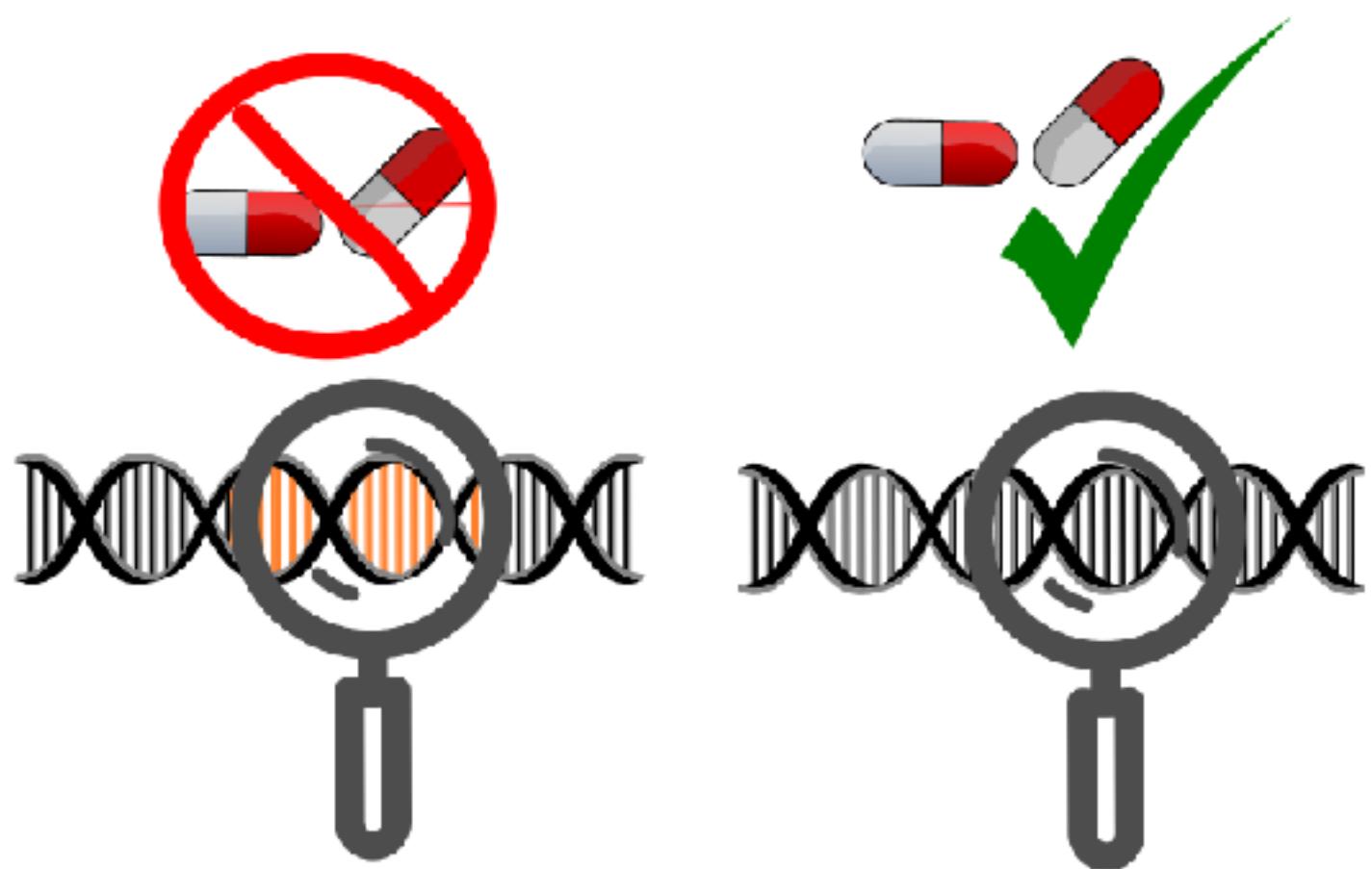




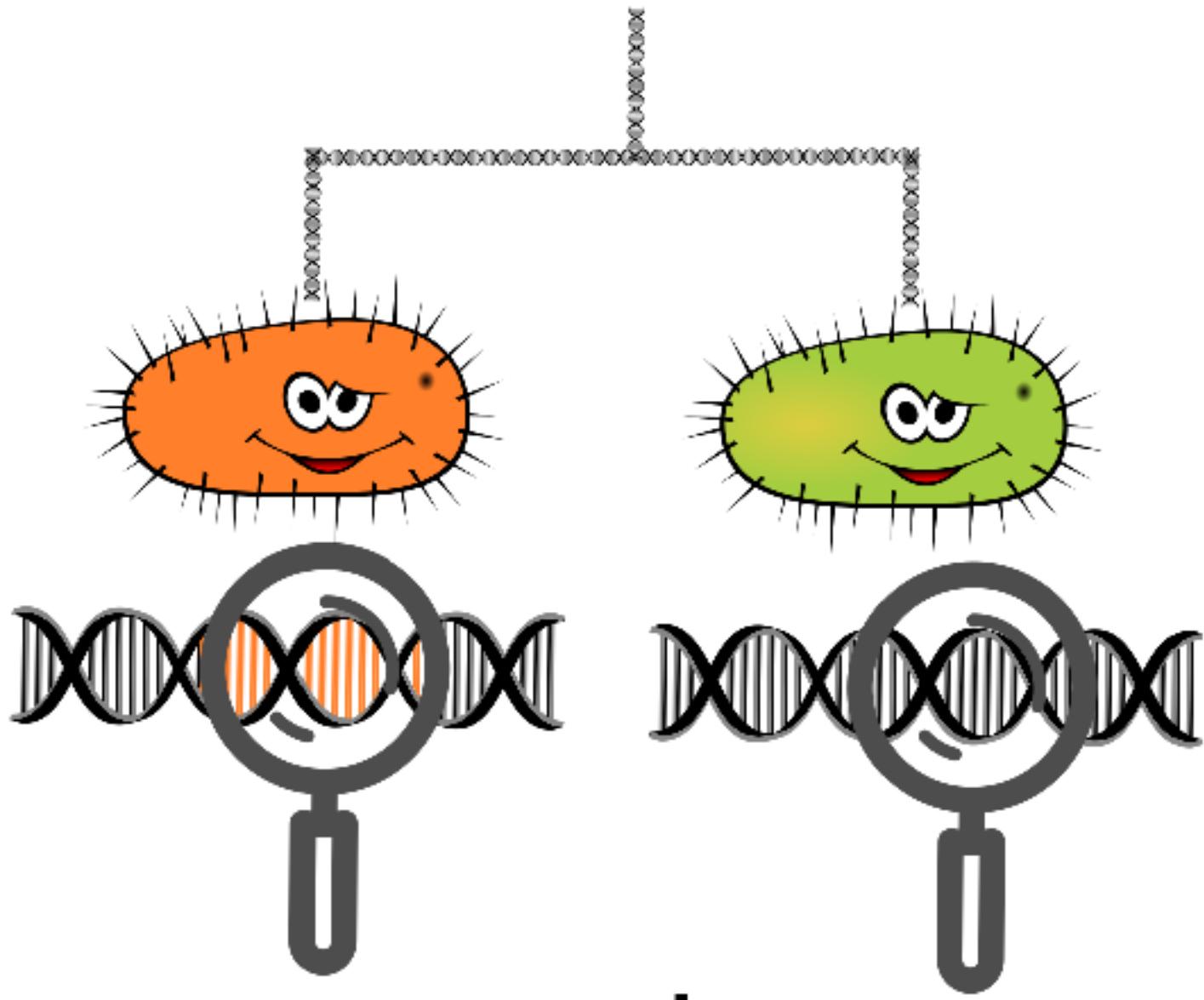
Xia et al. 2023

freezeTB; the software side

Expected output



Check for AMRs



Detect Lineages

2. a. MIRU-VNTR

- Amplifies 24 repeat regions across genome
- Lineage found by amplicon length
- Current gold standard

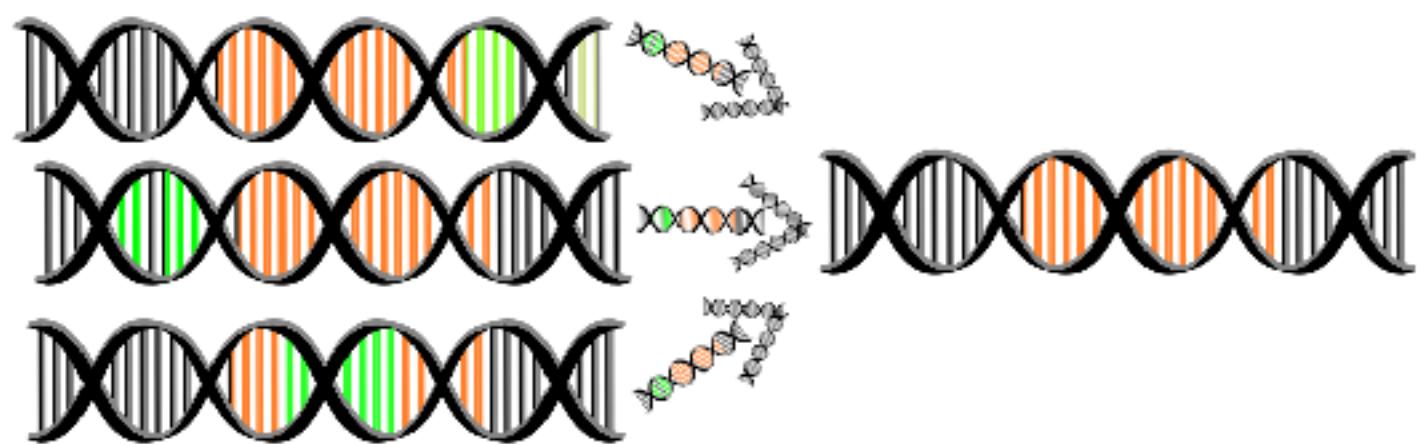
Direct repeat



101
+



Spoligotype
= Lineage



Build consensus

TBProfiler; the current resource

TBProfiler; pros

- AMR detection with WHO 2023 catalog
- Detects spoligotypes
- Outputs an vcf files

TBProfiler; cons

- > 5 dependencies or conda

Other solutions:

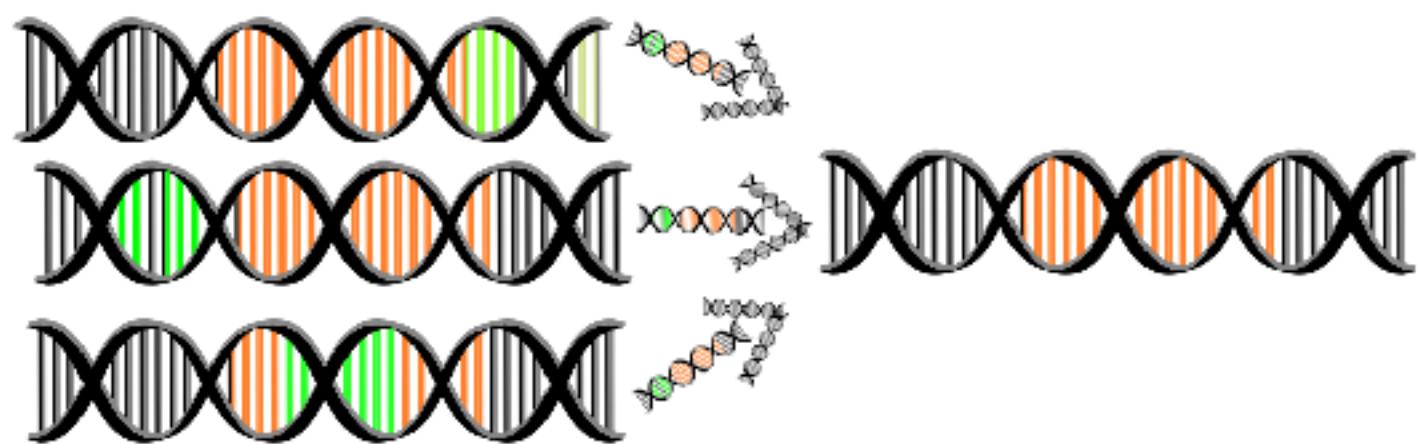
- Propitiatory (ONT)
- ??

freezeTB; the software side

- CLI: sam file
- GUI (R): fastq file + minimap2

Primer Masking [Optional]





Build consensus

Removes bases with Q-scores under 7

Break up consensuses

- Fragments with read depth > 19x
- Remove fragments under 200 bases

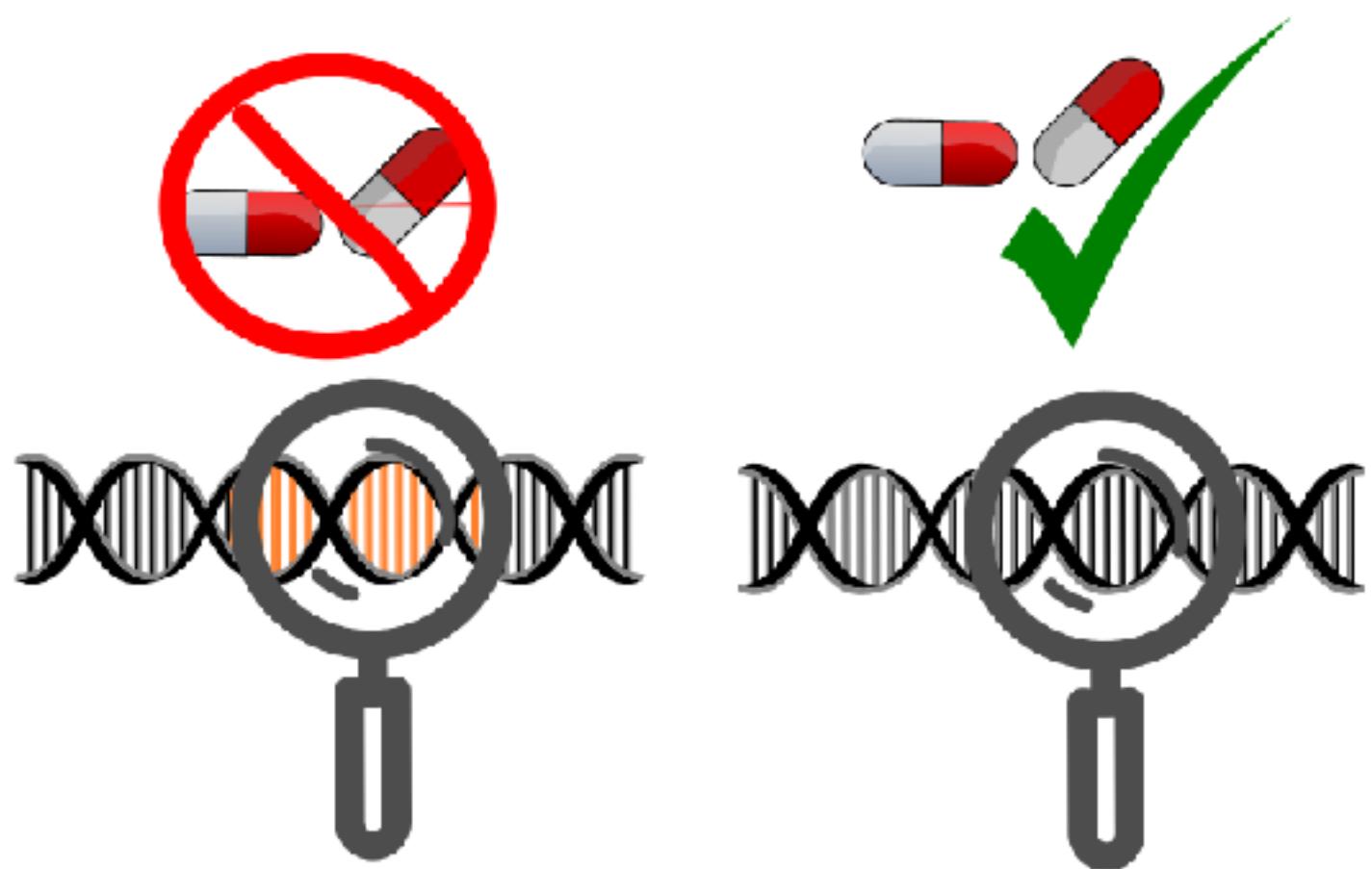
Masking:

- Find mapped reads (A + T + G + C + dels)
- Select base with most support
- Find base support (base / mapped)
- Mask bases under < 50% support

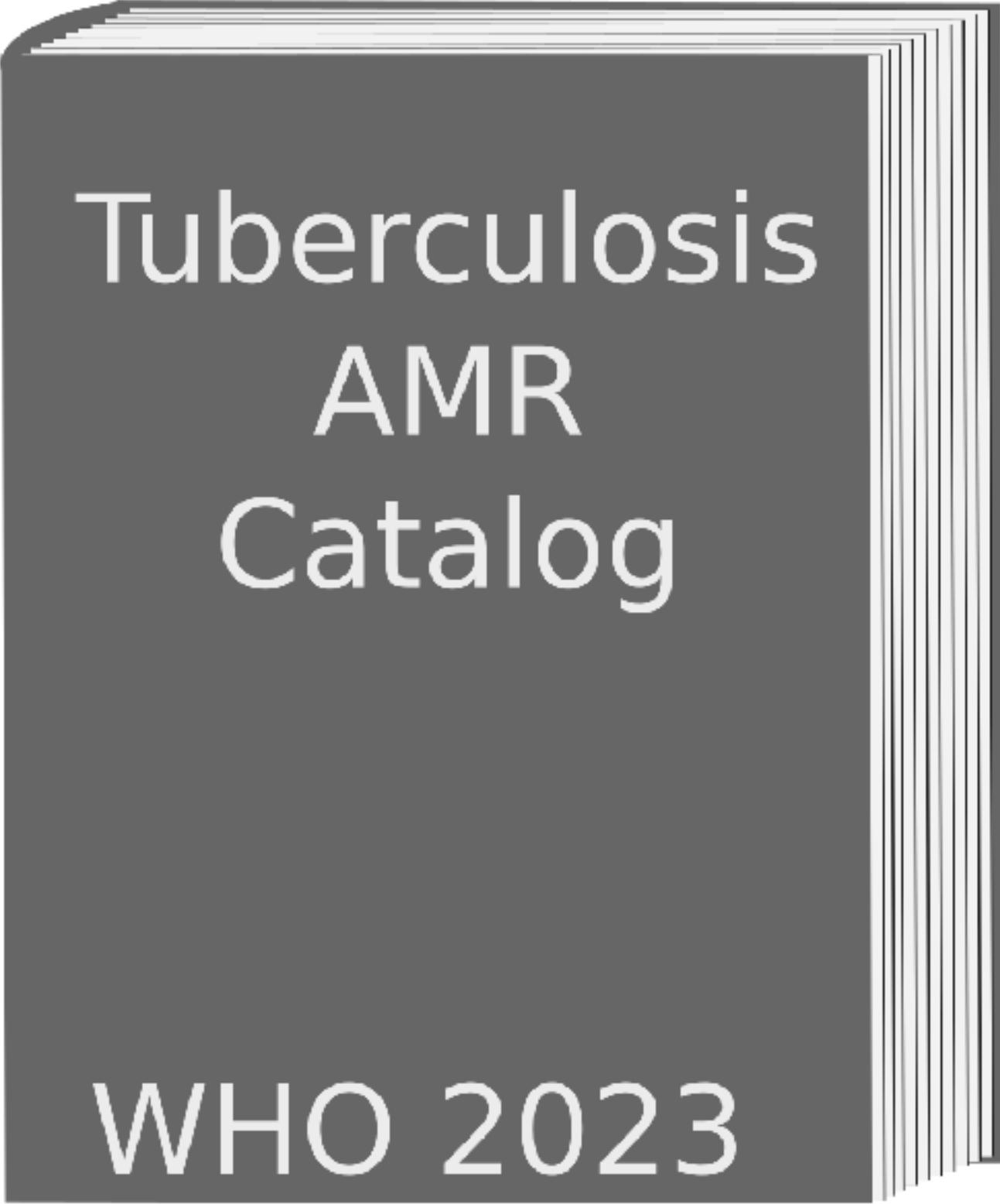
Indel removal:

- Find mapped reads (A + T + G + C + dels + N)
- Find indel support (indel / mapped)
- Remove indels under 70% support

Output fragments in sam file



Check for AMRs



Tuberculosis AMR Catalog

WHO 2023

Ignore gene deletions

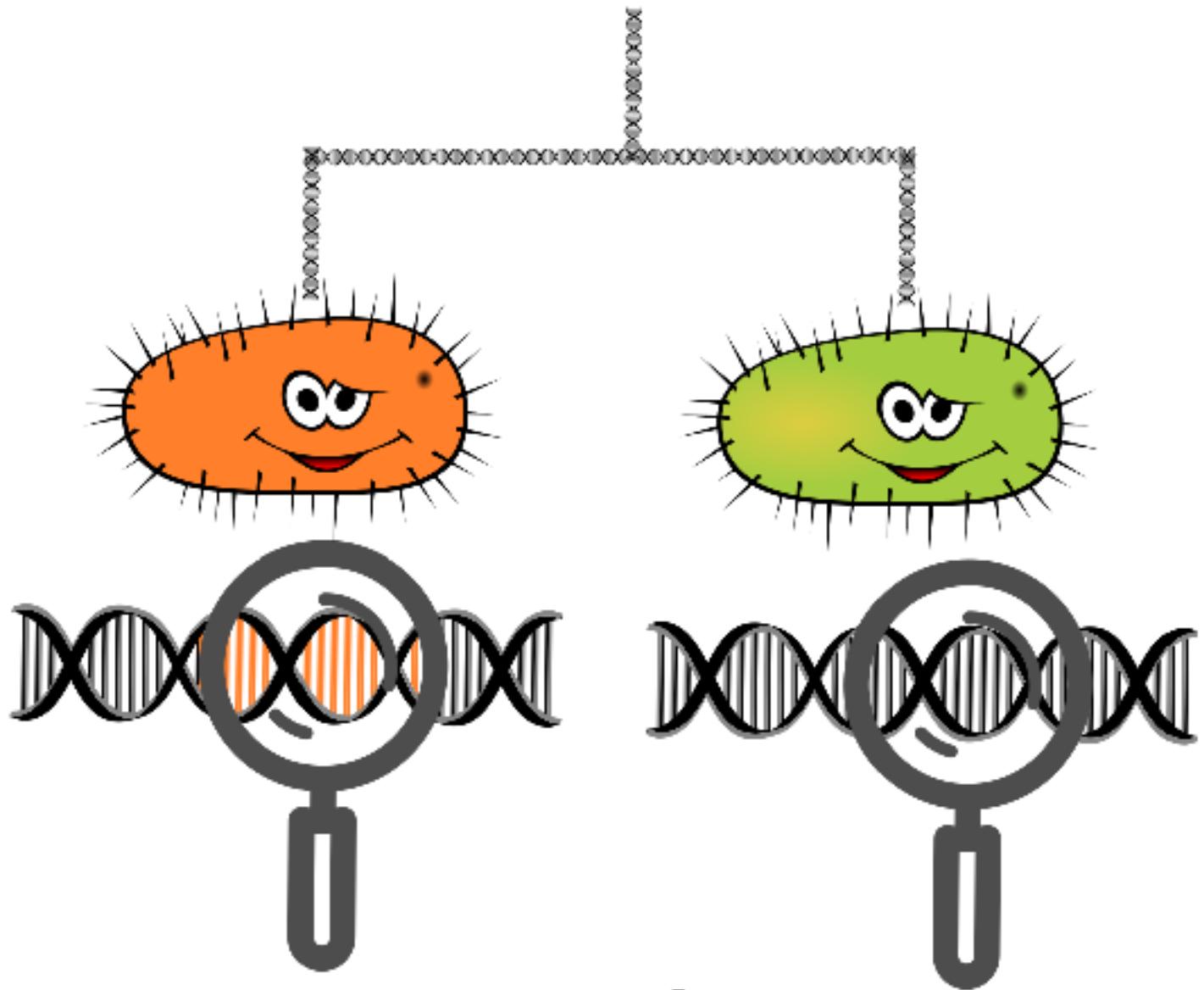
Frames shift and LoF:

- Only match patterns
- Less false positives from indel errors

Amino acid catalog AMRs
- Translate sequence AMR region

AMR called if:

- Sequences match
- Sequence AMR region length = AMR length



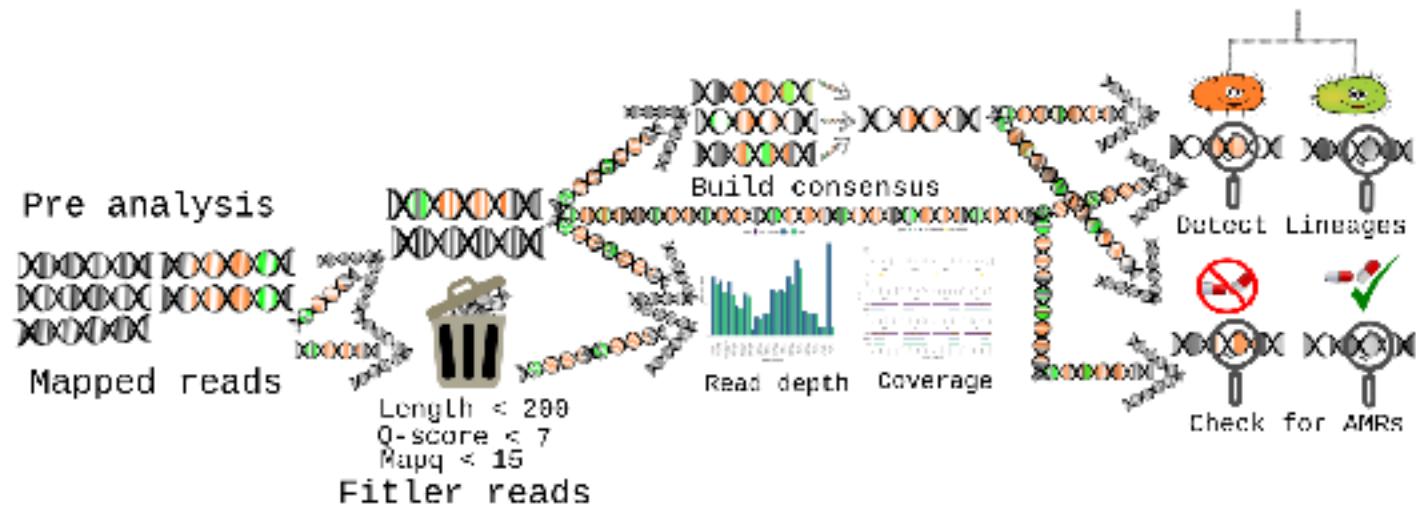
Detect Lineages

MIRU-VNTR lineages:

- See if sequence has repeat
- Check sequence repeat length
- Call lineage

Spoligotyping:

- Get direct repeat (DR) region
- Map spacers to DR with Waterman
- Find lineage



`freezeTB` is modular:

- Steps are separate programs
- All programs use sam files

FreezeTB; works, but not an replacement

?