Outbreaks, typing and AMR/Day 7

Antimicrobial resistance genes and point mutations detection in *Salmonella*

Section of Foodborne infections, Dep. of bacteria, parasites and fungi, Statens Serum Institute

March 2024

Specific objectives of the AMR session

Lecture:

1. Explain what is AMR, how it develops and how it spreads
2. Explain the difference between antimicrobial resistance phenotype and genotype

Practical exercise:

1. Utilise command-line tools to identify AMR genes and point mutations (PMs).
2. Explain why different bioinformatic tools may give different results.
3. Discuss the difference between a tool, a database, and a method.
4. Explain the difference between genotype and phenotype.

Outline

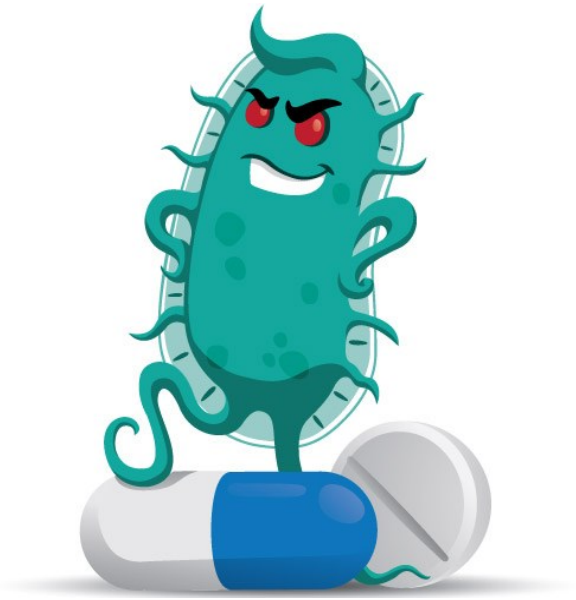
This session consists of the following elements:

14.30-14.50	**Introduction to AMR**
14.50-15.50	**Practical exercise**
15.50-16.00	**Discussion**

Introduction to AMR

What is AMR

Antimicrobial resistance (AMR) is the ability of microorganisms to **persist or grow in the presence of drugs** designed to inhibit or kill them



ID 160274360
© Luciano Cosmo Barbosa Gomes | Dreamstime.com

How bacteria become resistant?

Acquired resistance

Microorganisms have a **natural ability to evolve genetically** to counter/resist the drugs

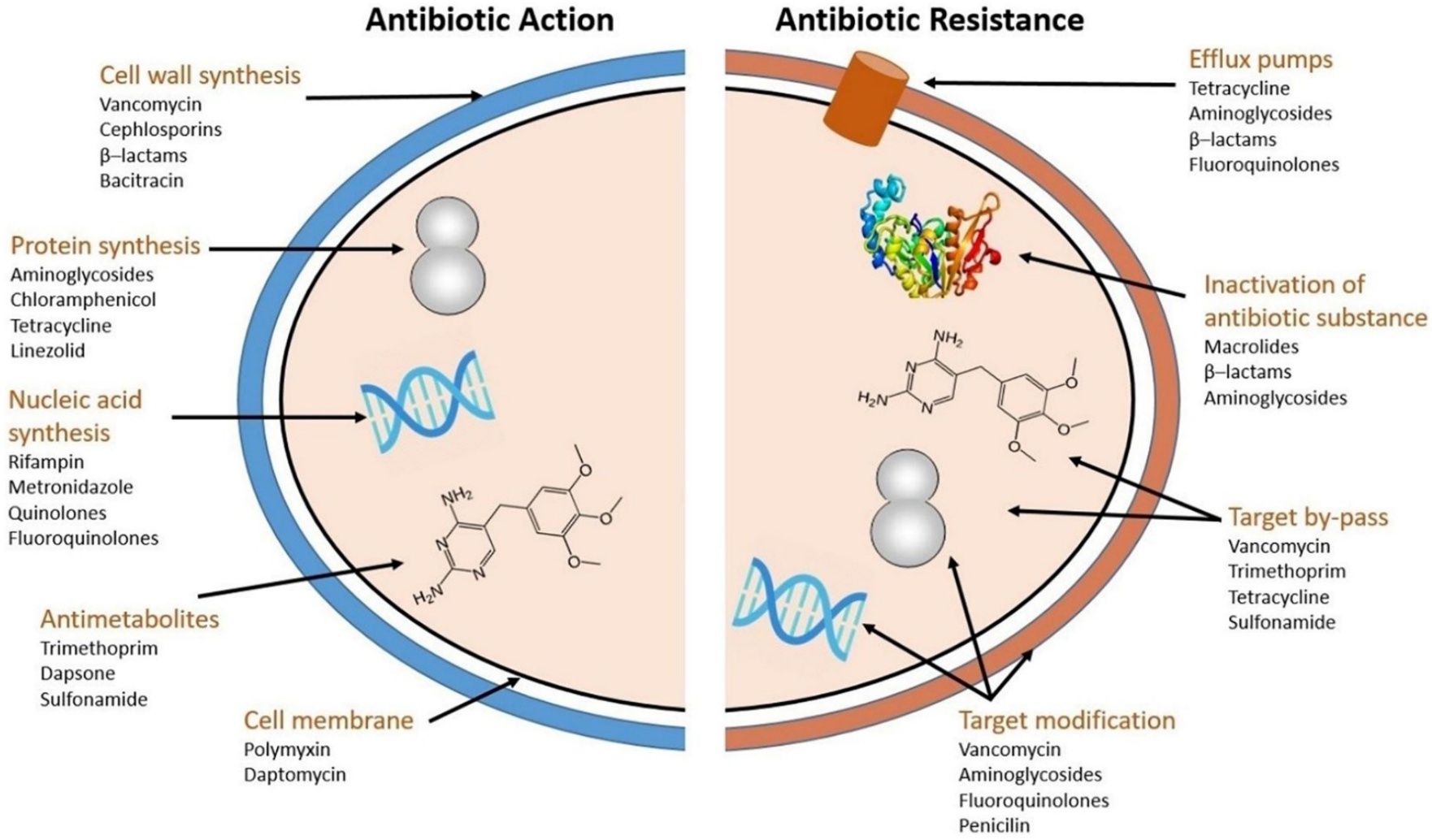
- The changes occur inside their genomes **when they are exposed to antimicrobial** drugs

Intrinsic resistance
Some bacteria have an innate ability to resist antibiotics without being exposed to a drug

Antimicrobial action and resistance mechanisms

Genetic resistance determinants:

- Genes
- Chromosomal point mutations



Antibiotic action and resistance mechanisms by Uluseker et al. (2021) CC BY 4.0 DEED

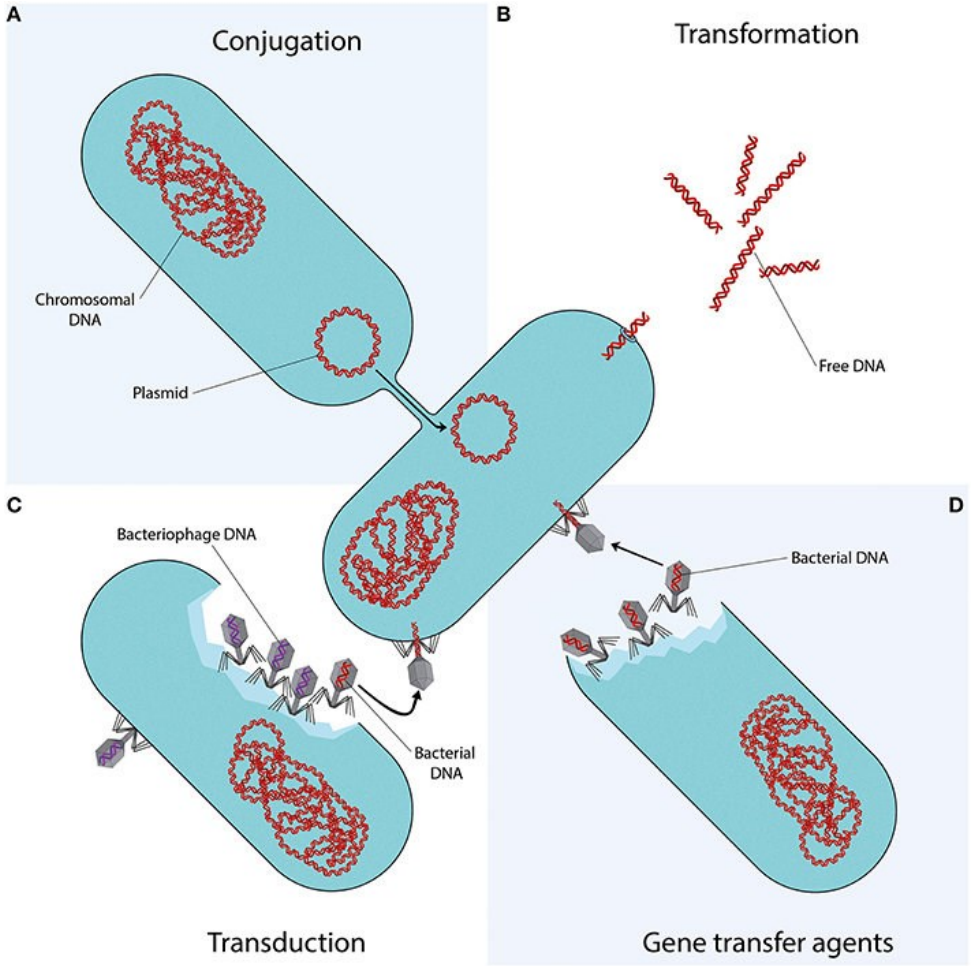
How resistance spread between the bacteria

Vertical transmission:

- genes and point mutations
- reproductive

Horizontal transmission:

- genes
- non-reproductive
- intra- and inter- species spread
- most concerning



Mechanisms of horizontal gene transfer by Wintersdorff et al. (2016) CC BY 4.0 DEED

Question

How do we detect resistance to antimicrobials?

How do we detect AMR?

Phenotypic antimicrobial susceptibility testing:

- Bacteria growth at higher antibiotic concentrations compare to the wild type (non-resistant) populations

Genotypic detection of AMR:

- Presence of genes/chromosomal mutations mediating AMR

Phenotypic vs. Genotypic resistance

Discordance between the results:

- Phenotypic +/genotypic -
- Phenotypic -/genotypic +

What are the possible causes of discordance?

Phenotypic vs. Genotypic resistance

Possible causes of discordance:

- Errors in the phenotypic/genotypic testing (skills, options, reporting, different strains, etc.)
- Loss of plasmid during cultivation/DNA extraction
- Phenotypic resistance is not expressed or is close to the breakpoint (weakly expressed)
- Gene/point mutation is absent from the sequence (poor quality, assembly issues, etc.)
- Gene/point mutation absent from the database(s) in use

Recommended article: Yee et al. 2021

Why we look at AMR?

To inform PH actions:

- National level surveillance (DanMap)

- EU level surveillance (ECDC)

- Global surveillance (GLASS)

Benchmarking of bioinformatic tools for AMR

No standard approach of testing and reporting genetic resistance

- Ring-Trial (FWD AMR-refLabCap)
  - various combinations tools, databases, thresholds reporting strategies are in use: difficult to compare the results

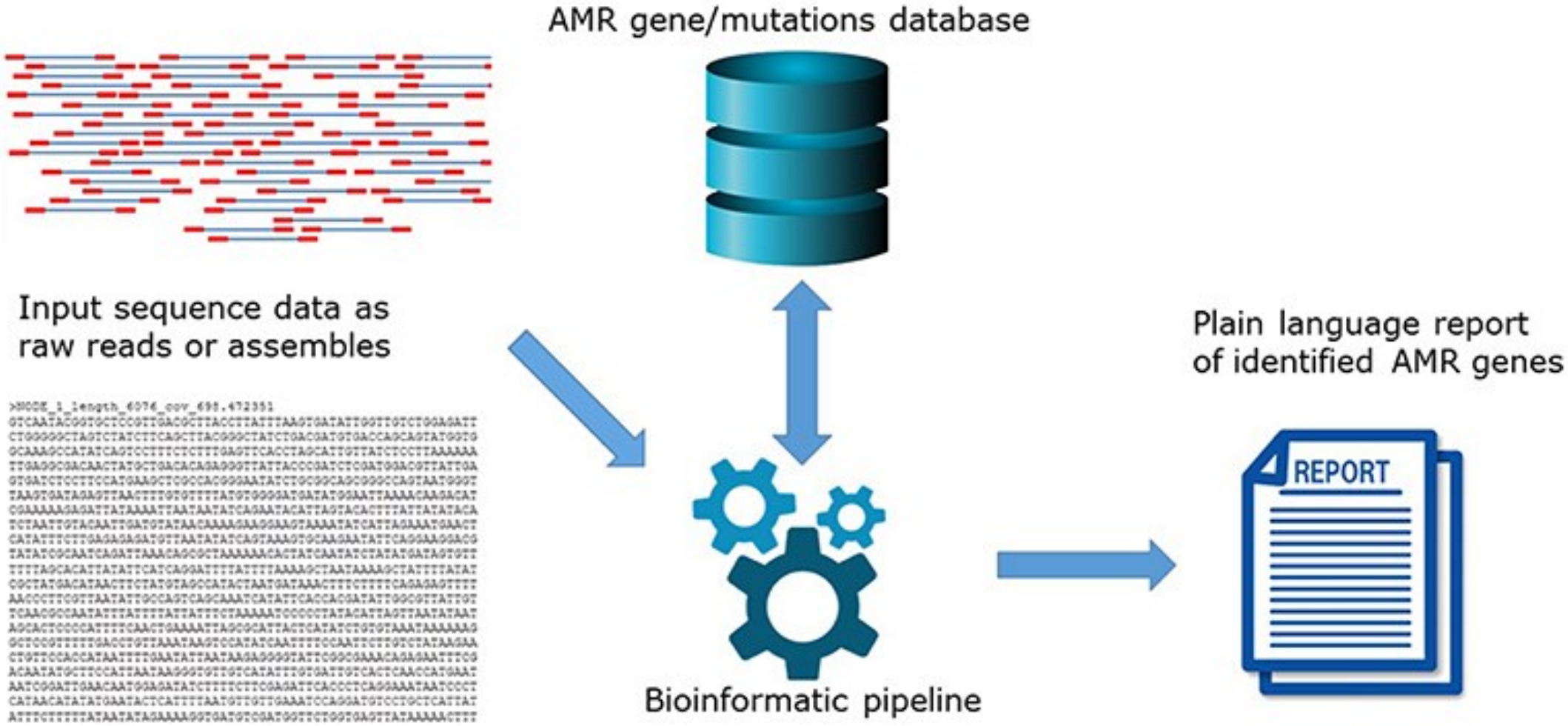
In general good agreement in the results, except for some specific AMR determinants

Take home

- Bacteria evolve to survive antibiotics
- Resistance can be acquired or intrinsic
- Resistance is determined by genes and point mutations found in bacterial genomes:
  - account for certain resistance mechanisms to various types of antimicrobials
  - can be transmitted between bacteria either vertically or horizontally
- Resistance can be detected with phenotypic and genotypic methods
  - discordance between the results is possible and often can be explained
- Standartised testing and reporting of AMR is necessary to follow the trends and to inform PH actions for it’s reduction

Interactive lecture #1: ResFinder + PointFinder

AMR detection *in silico*



The principle of in silico AMR determinant detection using a search algorithm to query input DNA by Hendriksen et al. (2019) CC BY 4.0 DEED

ResFinder

Databases

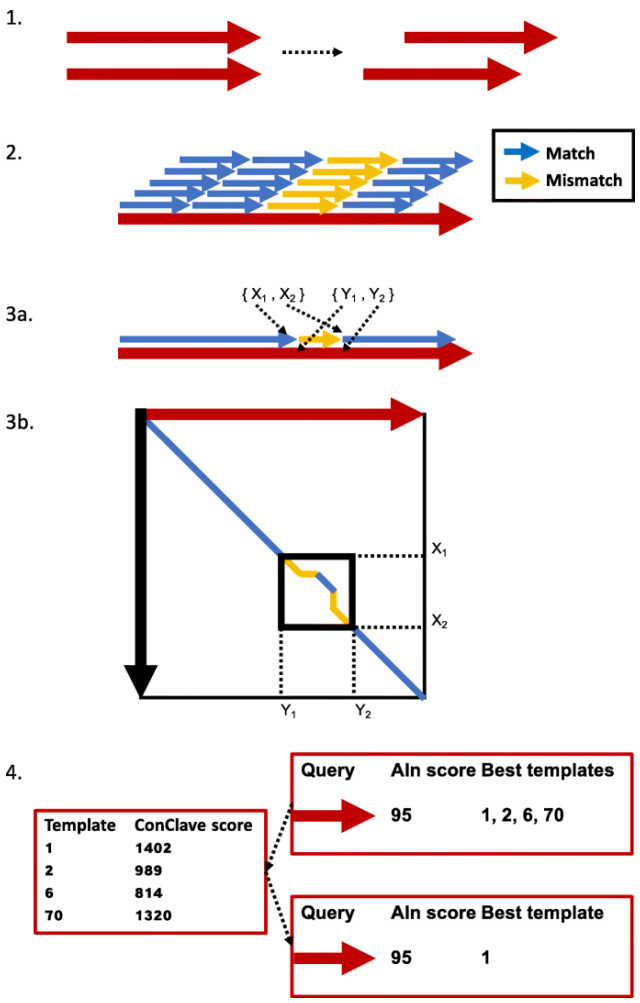
- ResFinderdb
  - Nucleotide
  - AMR ECOFF (epidemiological cut-off) predictions
- PointFinderdb

Softwares

- ResFinder
- PointFinder

ResFinder					
genes			point mutations		
input	**method**	**db**	**input**	**method**	**db**
DNA fastq	KMA	nucleotide	DNA fastq	KMA	nucleotide
DNA fasta	BLASTN		DNA fasta	BLASTN	
Protein fasta	-	-	Protein fasta	-	-

Method: KMA



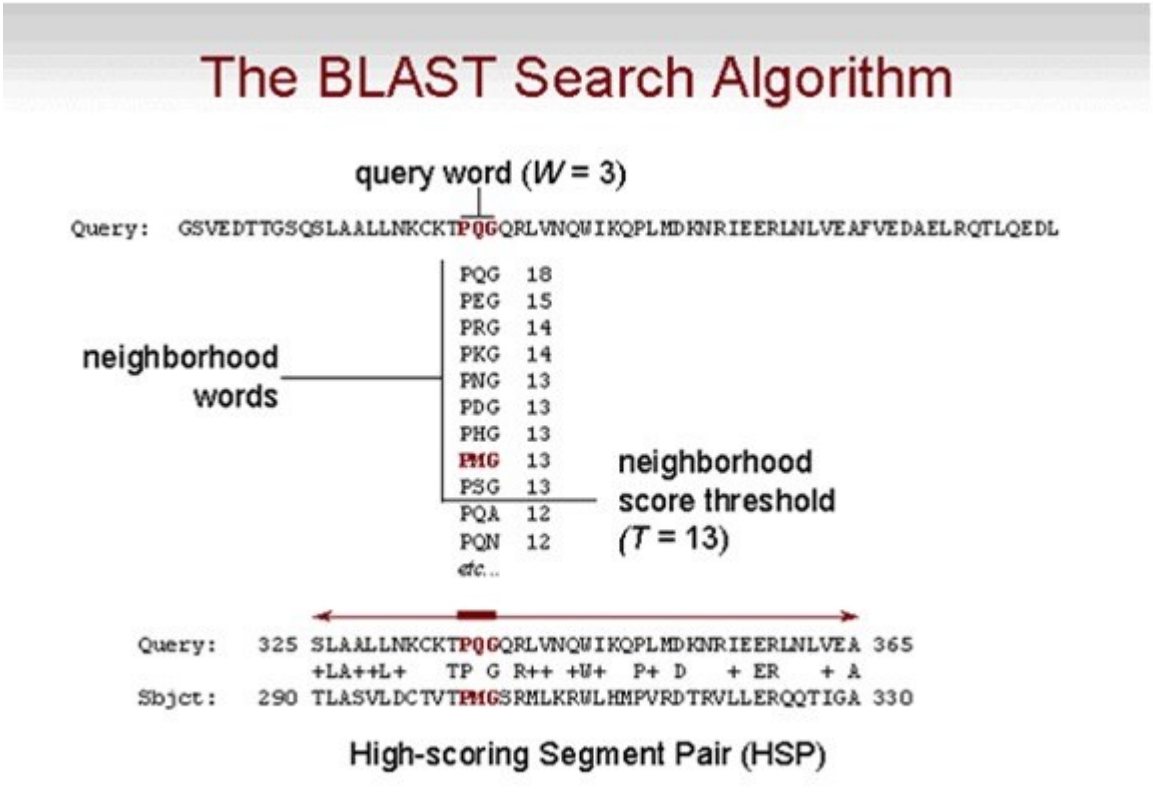
KMA (k-mer alignment) is able to map raw reads directly against redundant databases, it also scales well for large redundant databases.

KMA uses k-mer seeding to speed up mapping and the Needleman-Wunsch algorithm to accurately align extensions from k-mer seeds.

Multi-mapping reads are resolved using a novel sorting scheme (ConClave scheme), ensuring an accurate selection of templates.

Overview of step 1–4 of the KMA algorithm by Clausen et al. (2018) CC BY 4.0 DEED

Method: BLAST



https://www.ncbi.nlm.nih.gov/books/NBK62051/

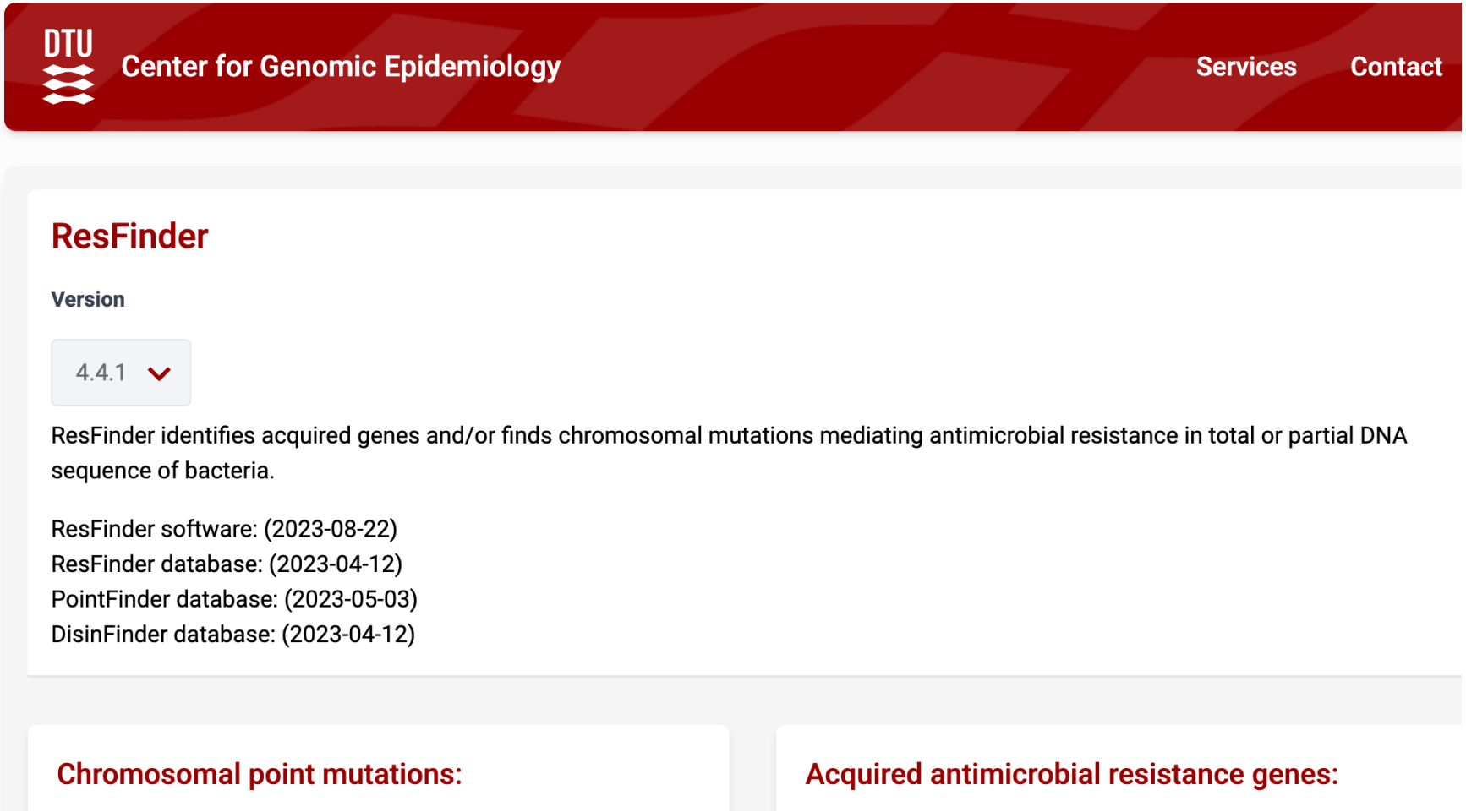
Basic Local Alignment Search Tool (BLAST) is a sequence comparison algorithm optimized for speed used to search sequence databases for optimal local alignments to a query.

The initial search is done for a word of length "W" that scores at least "T" when compared to the query using a substitution matrix.

Word hits are then extended in either direction in an attempt to generate an alignment with a score exceeding the threshold of "S".

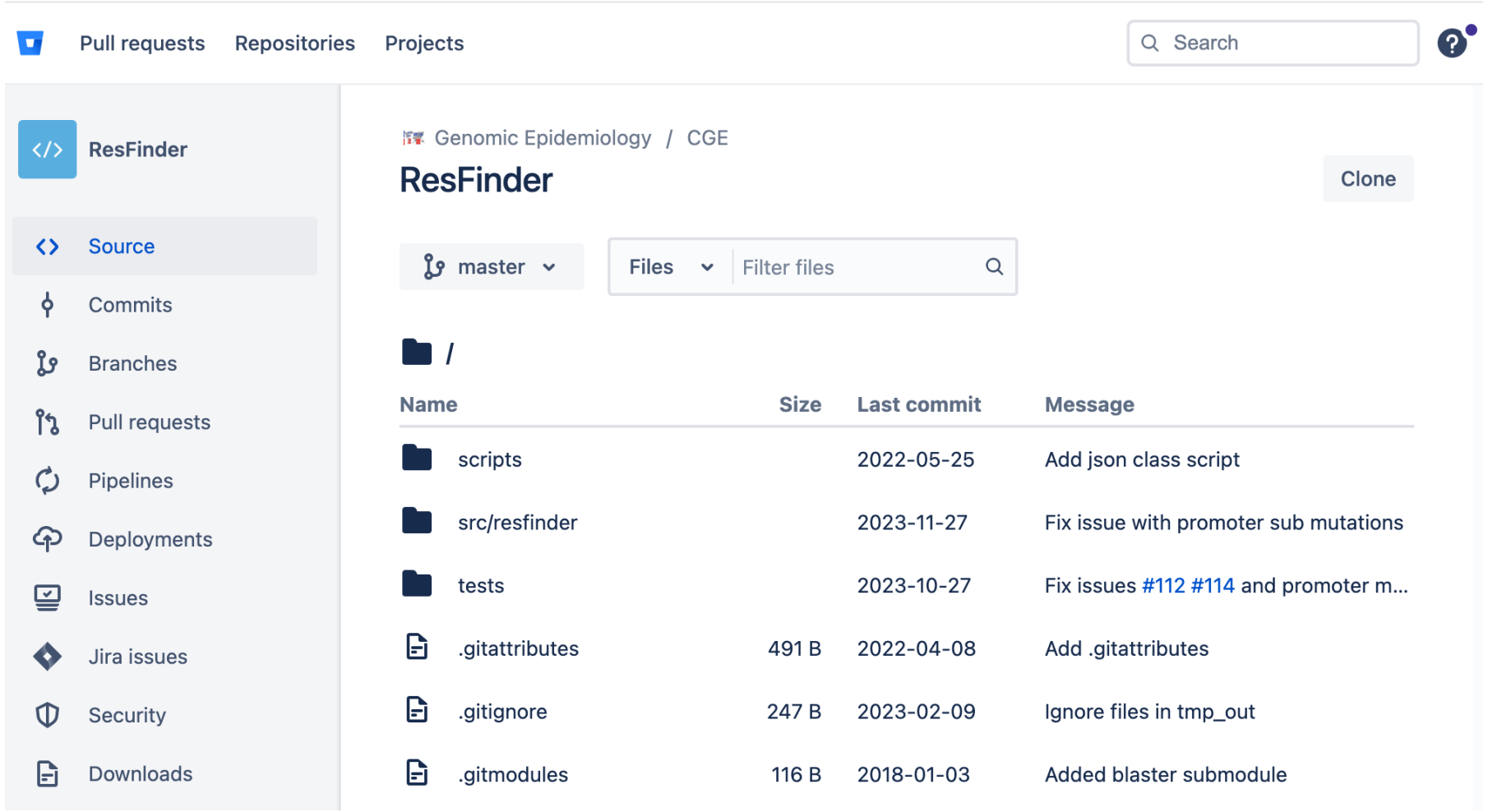
The "T" parameter dictates the speed and sensitivity of the search.

Web tool



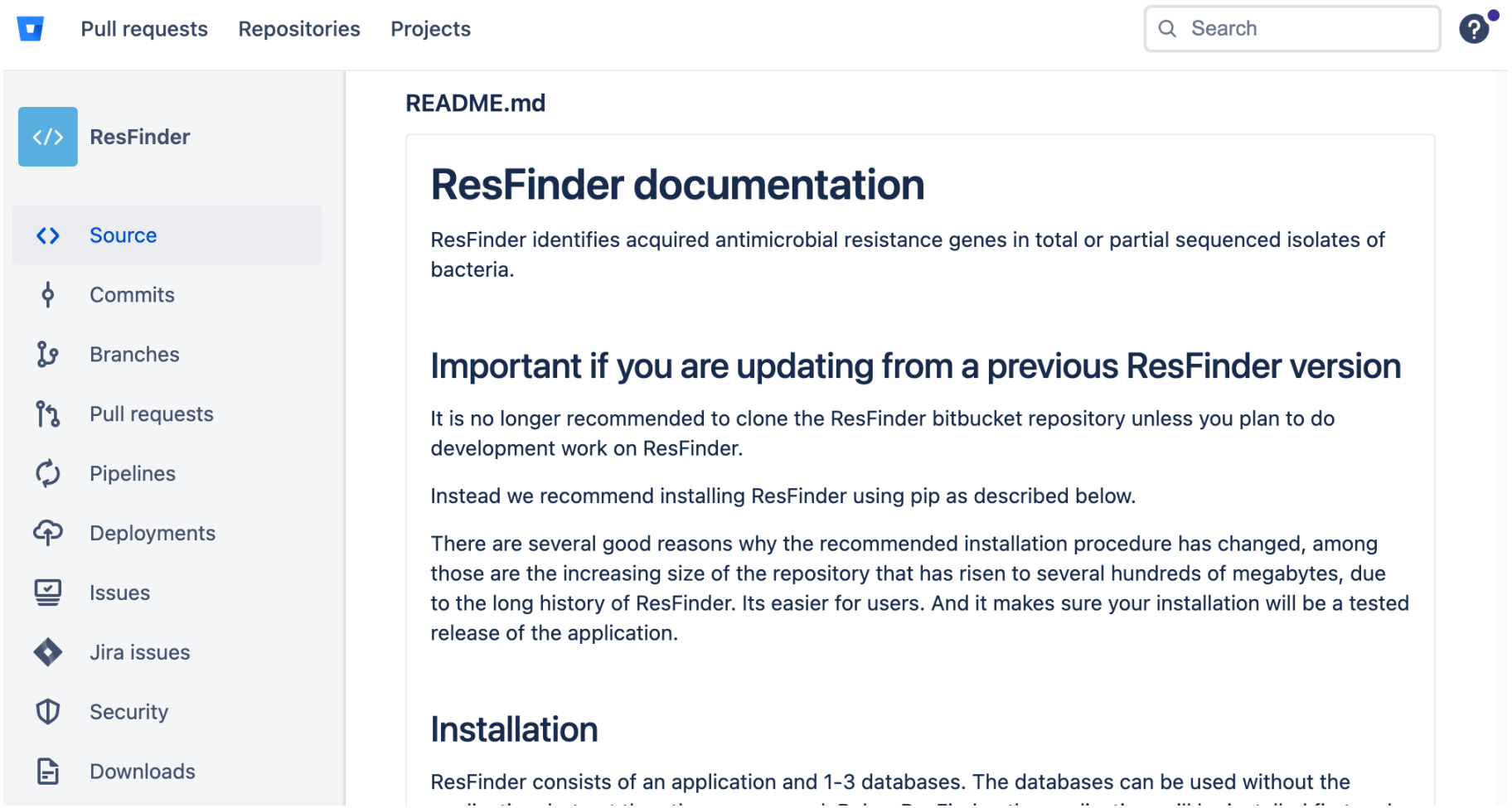
http://genepi.food.dtu.dk/resfinder

Command line tool



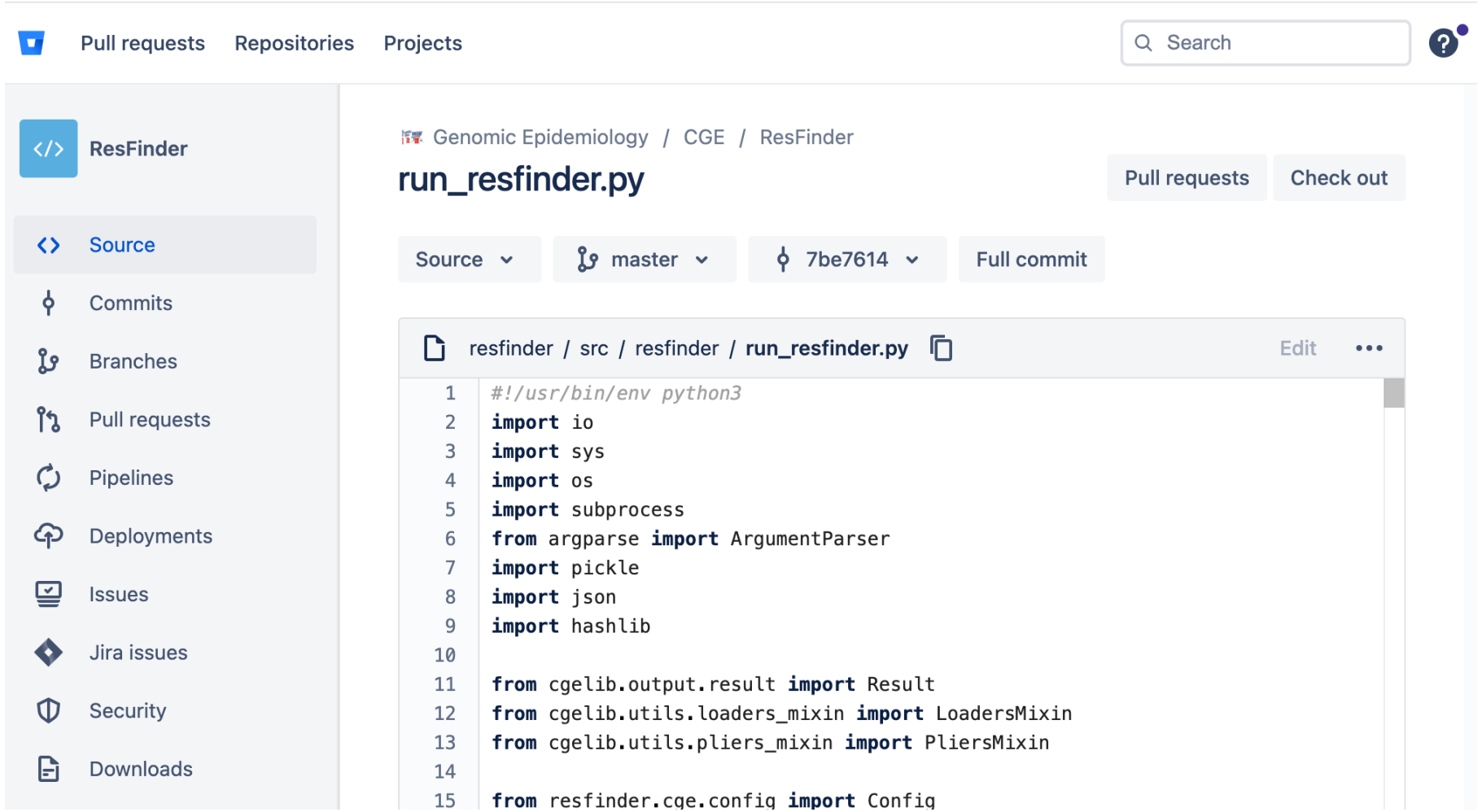
https://bitbucket.org/genomicepidemiology/resfinder/src/master/

Documentation



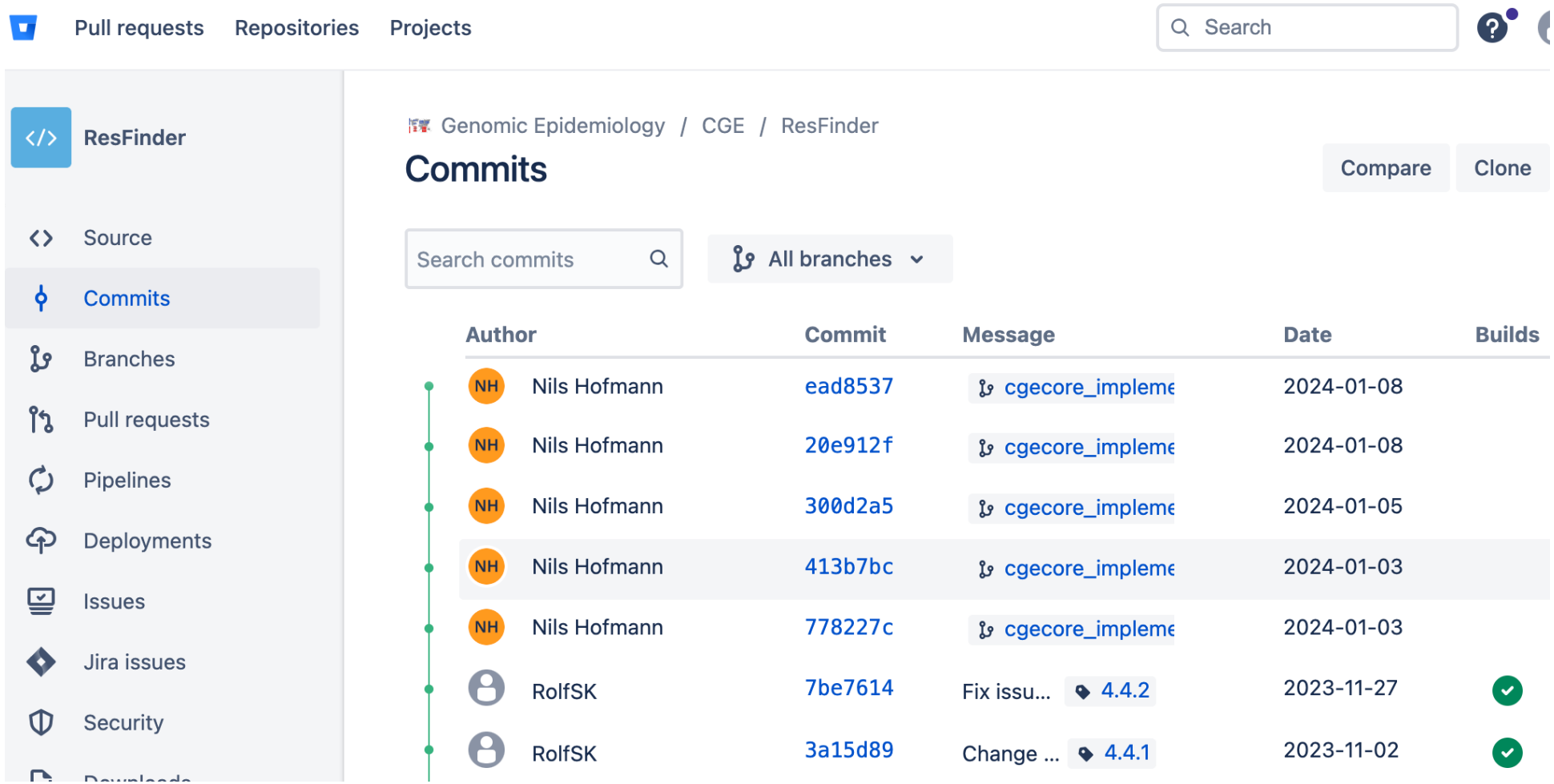
https://bitbucket.org/genomicepidemiology/resfinder/src/master/

Main script



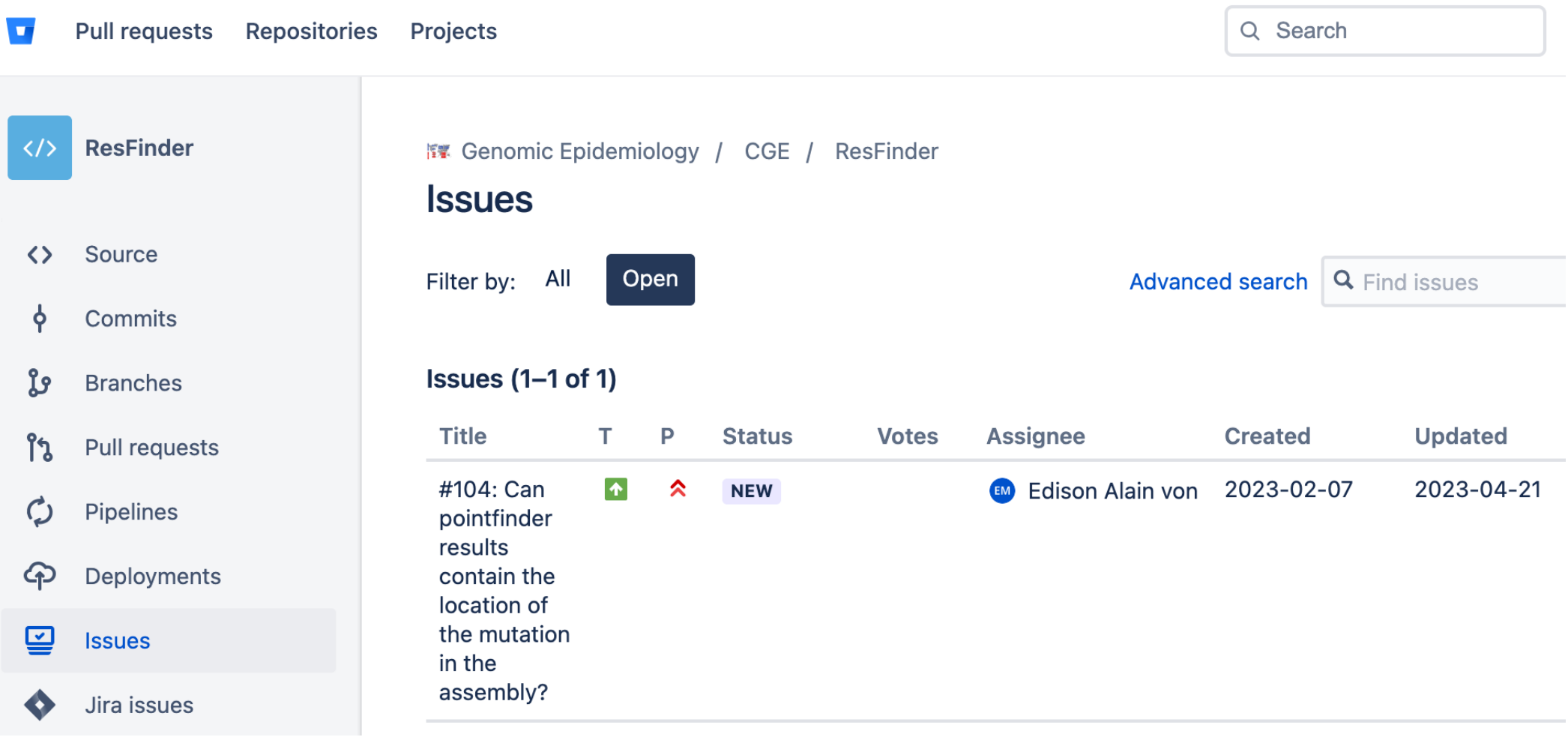
https://bitbucket.org/genomicepidemiology/resfinder/src/master/src/resfinder/run_resfinder.py

History



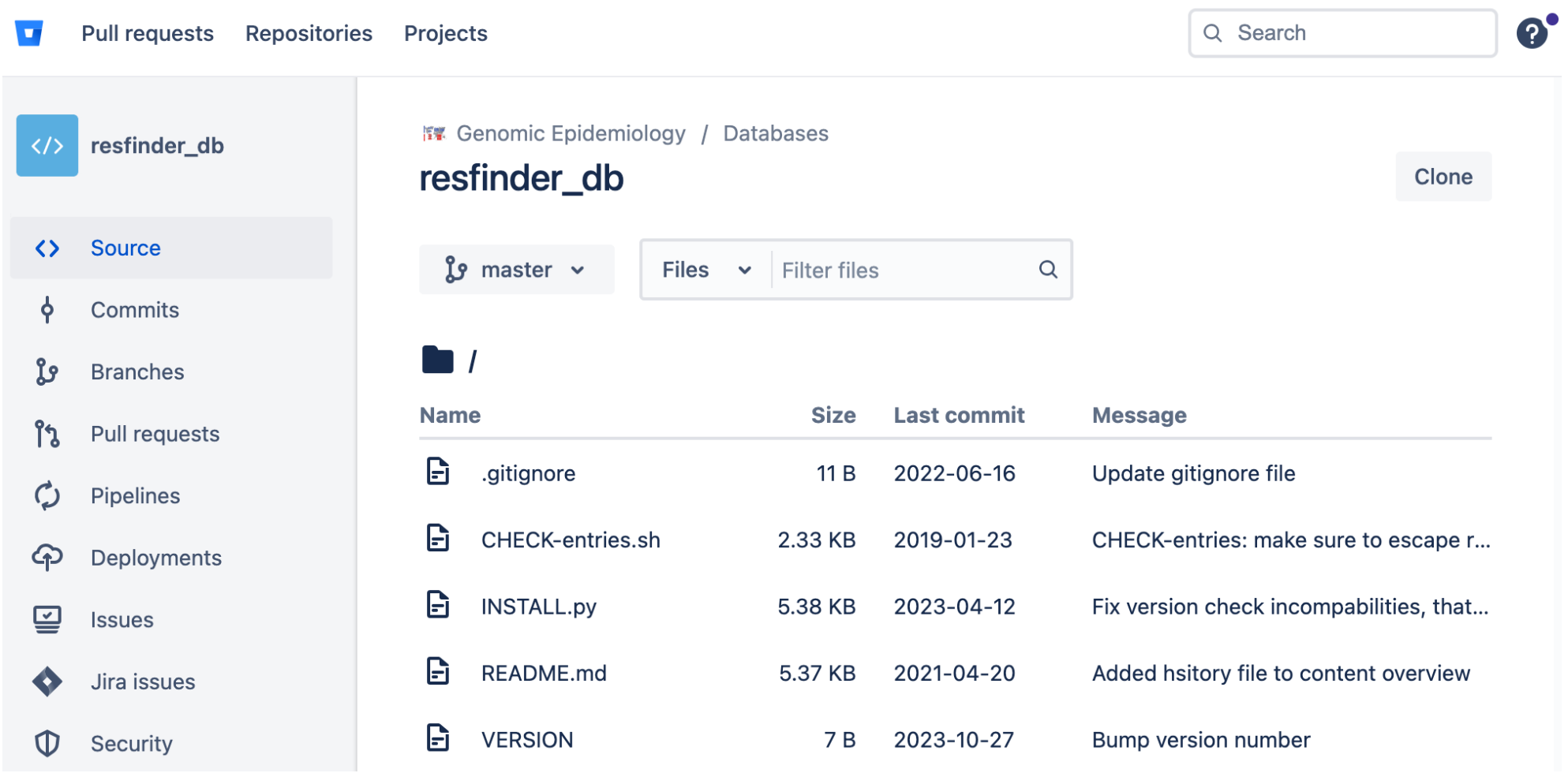
https://bitbucket.org/genomicepidemiology/resfinder/commits/

Issues/Questions



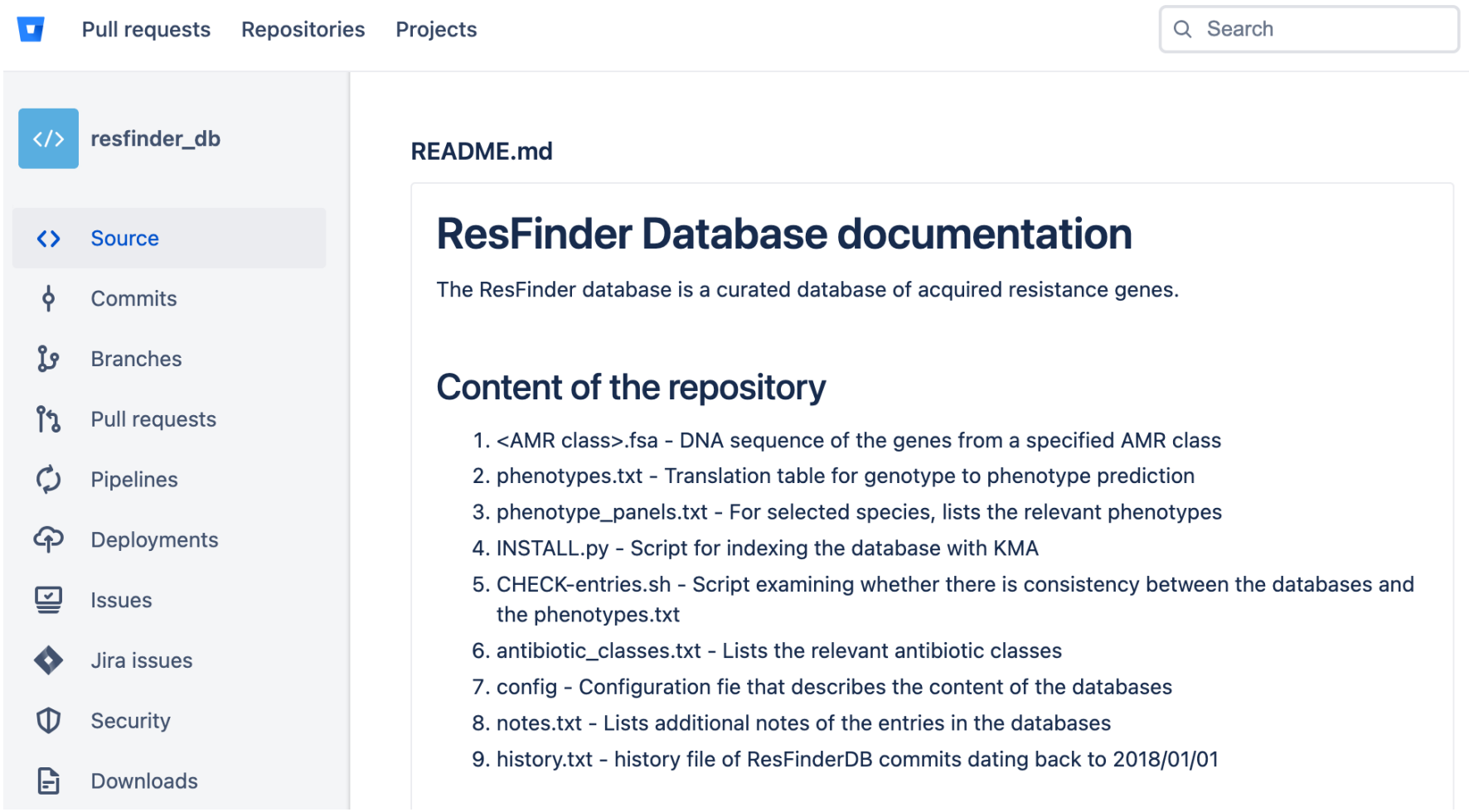
https://bitbucket.org/genomicepidemiology/resfinder/issues?status=new&status=open

Database



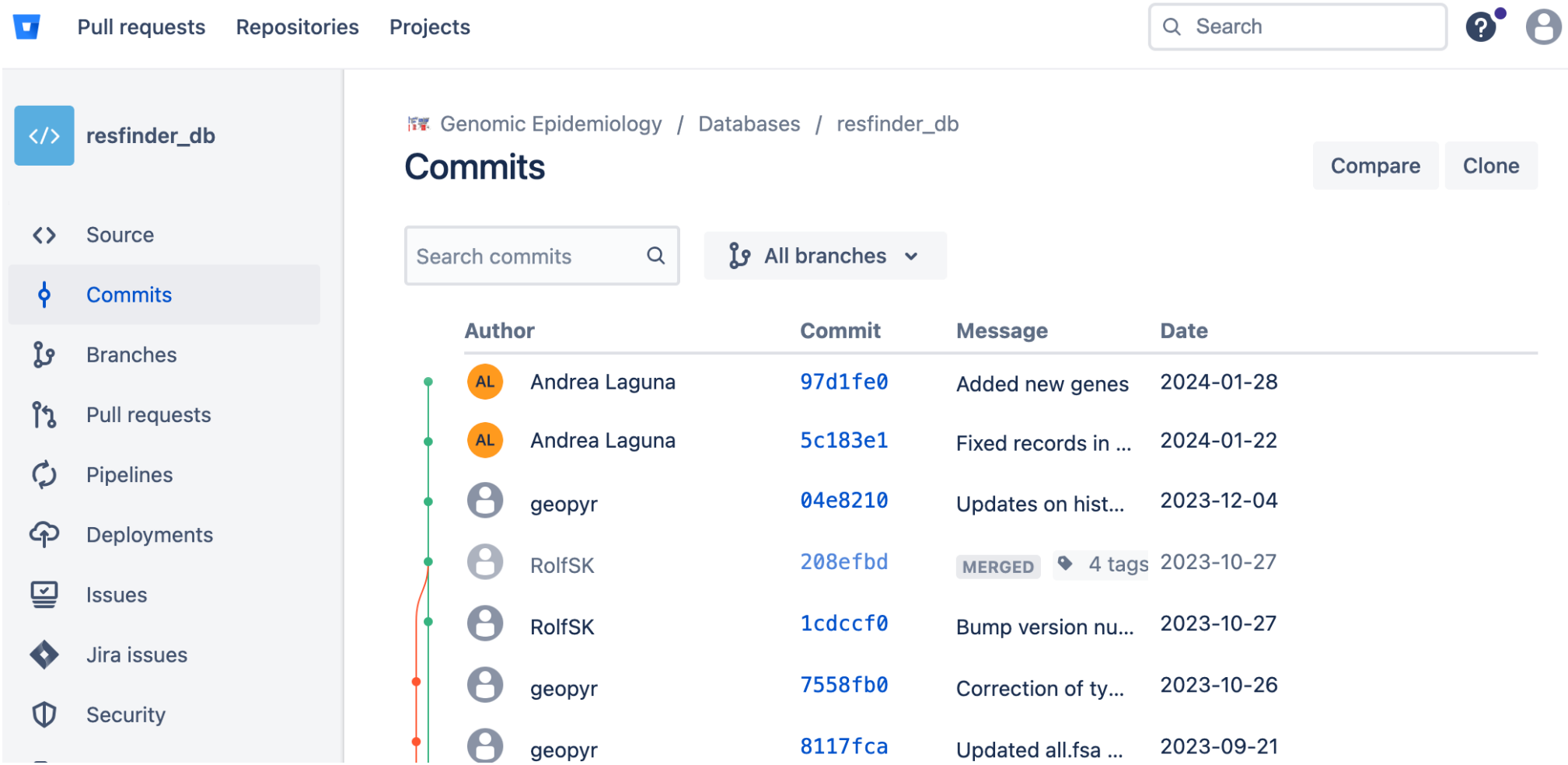
https://bitbucket.org/genomicepidemiology/resfinder_db/src/master/

Database documentation



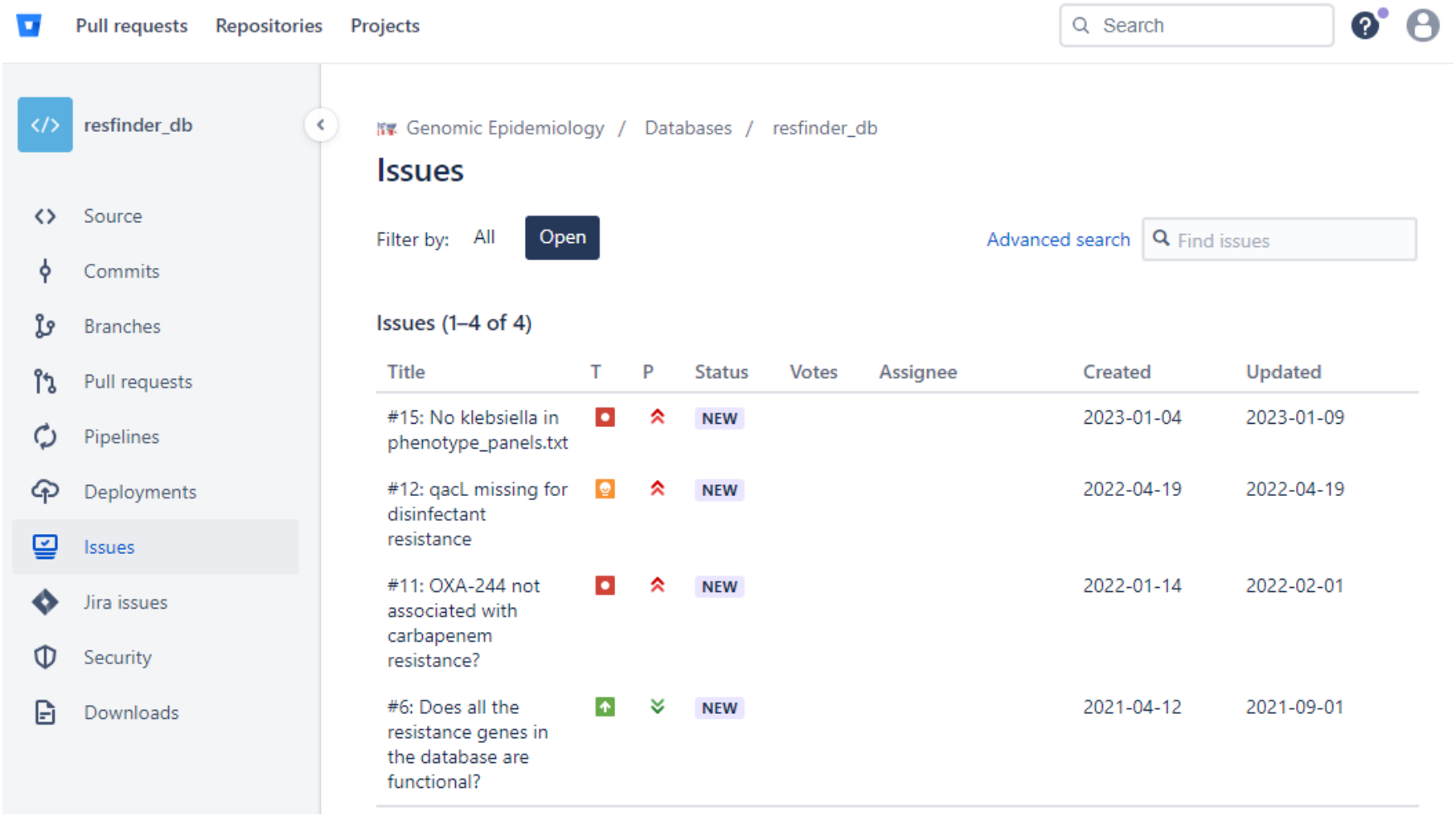
https://bitbucket.org/genomicepidemiology/resfinder_db/src/master/

Database history



https://bitbucket.org/genomicepidemiology/resfinder_db/commits/

Database issues/questions



https://bitbucket.org/genomicepidemiology/resfinder_db/issues?status=new&status=open

Practice #1: ResFinder + PointFinder

Introduction to the exercise

practicals/manuals: AMR_practicals.docx

See: How to use this document

Conda environment with required software: CGEfinders and NCBItypers

Path to working folder: ~/BTG_2024

Path to assemblies: ~/BTG_2024/precomputed_data/day7/amr

Path to databases: ~/BTG_2024/data/databases

Path to output: ~/BTG_2024/amr/output

Path to precomputed output: ~/BTG_2024/precomputed_data/day7/amr

Introduction to the exercise (example)

Conda environment with required software: CGEfinders

Path to working folder: ~/BTG_2024/amr

Path to assemblies: ~/BTG_2024/precomputed_data/day7/amr/SRR27241771/SRR27241771.fasta

Path to databases:

~/BTG_2024/data/databases/resfinder_db

~/BTG_2024/data/databases/pointfinder_db

Path to output:

~/BTG_2024/amr/output/SRR27241771/ResFinder_results_tab.txt

~/BTG_2024/amr/output/SRR27241771/ PointFinder_results.txt

Path to precomputed output:

~/BTG_2024/precomputed_data/day7/amr/SRR27241771/resfinder/ResFinder_results_tab.txt

~/BTG_2024/precomputed_data/day7/amr/SRR27241771/resfinder/PointFinder_esults.txt

Recap #1

SRR27241771 (Genes)

Resistance gene	Identity	Alignment Length/Gene Length	Coverage	Position in reference	Contig	Position in contig	Phenotype	Accession no.
aac(6')-Iaa	99.54	438/438	100	1..438	SRR27241771_12/1	52440..52877	Amikacin, Tobramycin	NC_003197
aadA16	99.65	846/846	100	1..846	SRR27241771_27/1	78..923	Spectinomycin, Streptomycin	EU675686
blaTEM-1B	100	861/861	100	1..861	SRR27241771_37/1	534..1394	Amoxicillin, Ampicillin, Cephalothin, Piperacillin, Ticarcillin	AY458016
mph(A)	100	906/906	100	1..906	SRR27241771_47/1	4965..5870	Erythromycin, Azithromycin, Spiramycin, Telithromycin	D16251
floR	98.19	1214/1215	99.9177	1..1214	SRR27241771_105/1	3191..4404	Chloramphenicol, Florfenicol	AF118107
qnrB6	100	645/645	100	1..645	SRR27241771_117/1	192..836	Ciprofloxacin	EF523819
ARR-3	100	453/453	100	1..453	SRR27241771_27/1	3636..4088	Rifampicin	JF806499
sul1	100	840/840	100	1..840	SRR27241771_53/1	4..843	Sulfamethoxazole	U12338
tet(B)	100	1206/1206	100	1..1206	SRR27241771_72/1	1421..2626	Doxycycline, Tetracycline, Minocycline	AP000342
dfrA27	100	474/474	100	1..474	SRR27241771_27/1	1104..1577	Trimethoprim	FJ459817

SRR27241771 (Point mutations)

Mutation	Nucleotide change	Amino acid change	Resistance	PMID

SRR27241772 (Genes)

Resistance gene	Identity	Alignment Length/Gene Length	Coverage	Position in reference	Contig	Position in contig	Phenotype	Accession no.
aph(6)-Id	99.88	837/837	100	1..837	SRR27241772_44/1	7618..8454	Streptomycin	M28829
aph(3'')-Ib	100	804/804	100	1..804	SRR27241772_44/1	8454..9257	Streptomycin	AF321551
aac(6')-Iaa	98.63	438/438	100	1..438	SRR27241772_51/1	48278..48715	Amikacin, Tobramycin	NC_003197
aph(3')-Ia	100	816/816	100	1..816	SRR27241772_68/1	115..930	Unknown Aminoglycoside, Kanamycin, Kanamycin, Neomycin, Neomycin, Kanamycin, Lividomycin, Paromomycin, Ribostamycin	V00359
aadA2	100	564/792	71.212121	229..792	SRR27241772_100/1	1..564	Spectinomycin, Streptomycin	JQ364967
aadA2	100	564/819	68.864469	256..819	SRR27241772_100/1	1..564	Spectinomycin, Streptomycin	NC_010870
aadA1	100	792/792	100	1..792	SRR27241772_113/1	1556..2347	Spectinomycin, Streptomycin	JQ414041
blaCTX-M-15	100	876/876	100	1..876	SRR27241772_63/1	254..1129	Amoxicillin, Ampicillin, Aztreonam, Cefepime, Cefotaxime, Ceftazidime, Ceftriaxone, Piperacillin, Ticarcillin	AY044436
mph(A)	99.5	604/921	65.472313	319..921	SRR27241772_100/1	7203..7806	Erythromycin, Azithromycin, Spiramycin, Telithromycin	U36578
floR	98.19	1214/1215	99.917695	1..1214	SRR27241772_44/1	3269..4482	Chloramphenicol, Florfenicol	AF118107
cmlA1	99.92	1260/1260	100	1..1260	SRR27241772_113/1	204..1463	Chloramphenicol	M64556
sul2	99.88	816/816	100	1..816	SRR27241772_44/1	9318..10133	Sulfamethoxazole	AY034138
sul1	100	840/840	100	1..840	SRR27241772_100/1	1069..1908	Sulfamethoxazole	U12338
sul3	100	792/792	100	1..792	SRR27241772_113/1	4029..4820	Sulfamethoxazole	AJ459418
tet(A)	99.92	1275/1275	100	1..1275	SRR27241772_44/1	5083..6357	Doxycycline, Tetracycline	AF534183
dfrA12	100	498/498	100	1..498	SRR27241772_7/1	614..1111	Trimethoprim	AM040708

SRR27241772 (Point mutations)

Mutation	Nucleotide change	Amino acid change	Resistance	PMID
gyrA p.S83F	TCC -> TTC	S -> F	Nalidixic Acid, Ciprofloxacin	10471553
gyrA p.D87G	GAC -> GGC	D -> G	Nalidixic Acid, Ciprofloxacin	11283069
parC p.T57S	ACC -> AGC	T -> S	Nalidixic Acid, Ciprofloxacin	15388468
parC p.S80I	AGC -> ATC	S -> I	Nalidixic Acid, Ciprofloxacin	15388468

Interactive lecture #2: AMRFinderPlus

AMRFinderPlus

Database

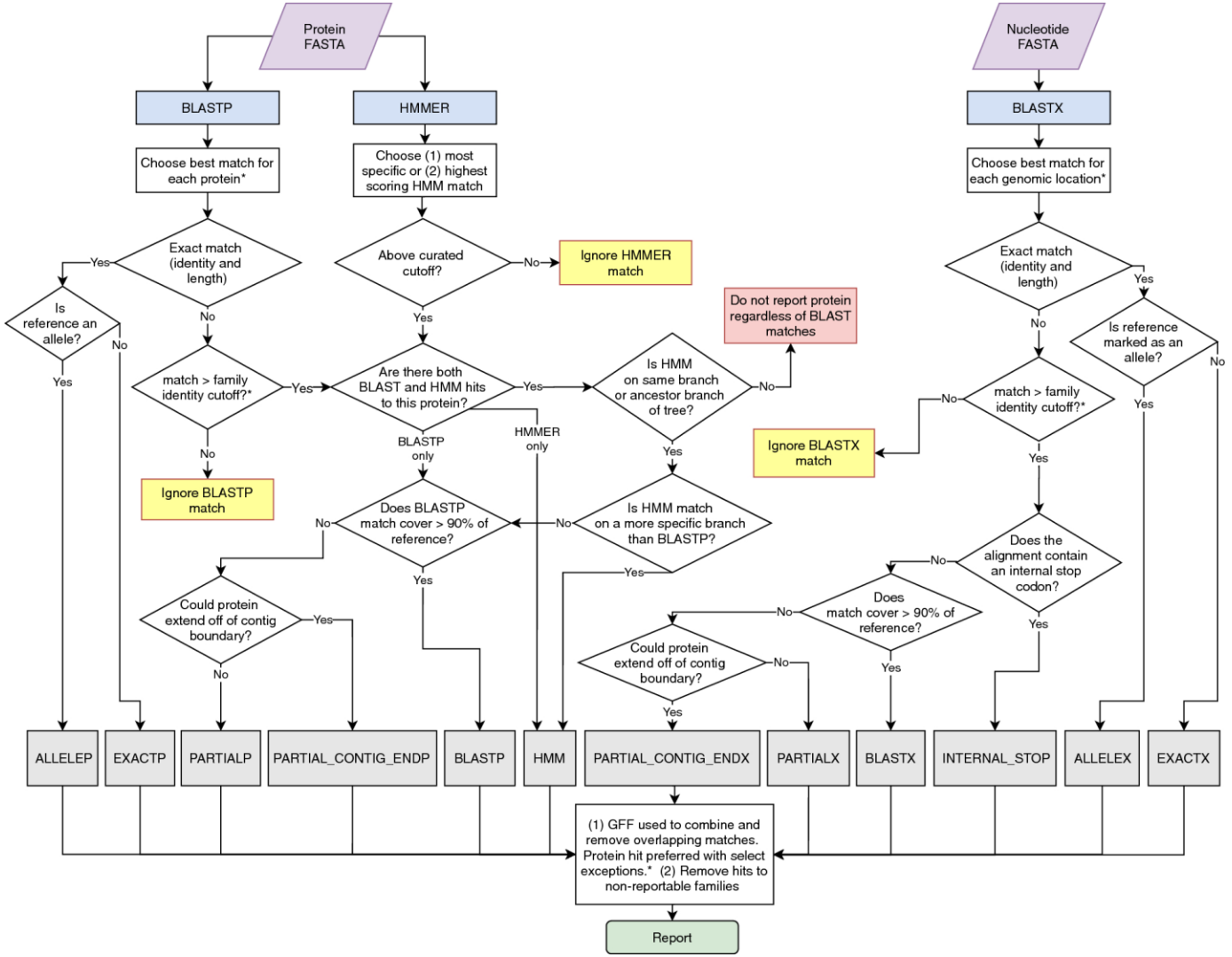
- Genes
  - Protein
  - Highly curated database
  - Hierarchical structure for AMR proteins
  - Manually curated cutoffs
  - Associated hierarchical names
- Point mutations
  - Literature, CARD and ResFinder.

Software

- BlastRules
- Protein fasta
  - BLASTP
  - HMMER
- Nucleotide fasta
  - BLASTX (translated nucleotide)

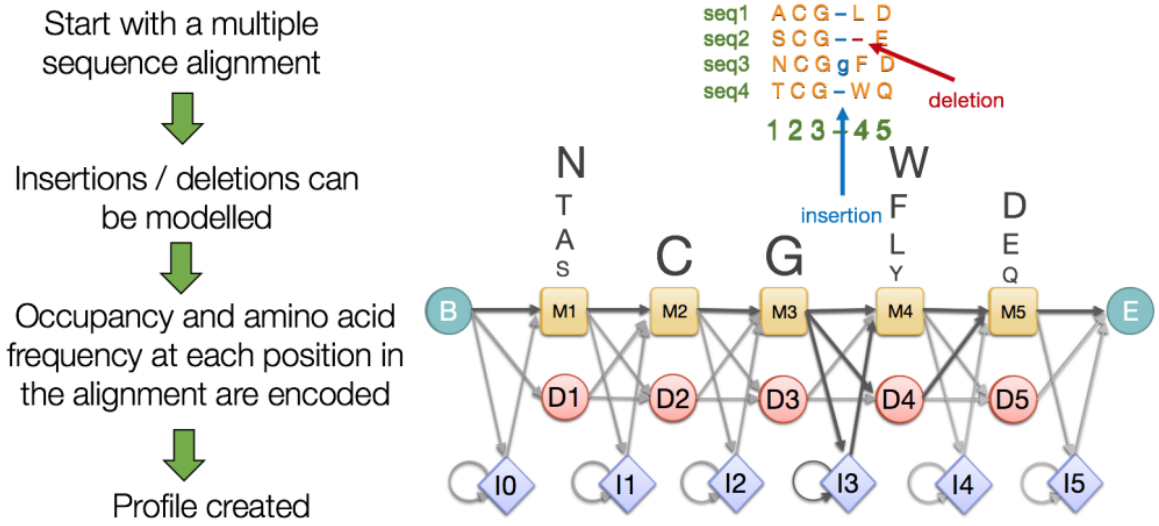
AMRFinderPlus					
genes			point mutations		
input	method	db	input	method	db
DNA fastq	-	-	DNA fastq		-
DNA fasta	BLASTX	protein	DNA fasta	BLASTN	nucleotide
Protein fasta	BLASTP		Protein fasta	-	-

AMRFinderPlus



Overview of AMRFinderPlus gene identification method using protein and nucleotide sequences by Feldgarden et al. (2021) CC BY 4.0 DEED

Method: HMMER



http://eddylab.org/software/hmmer/Userguide.pdf
Copyright (C) 2023 Howard Hughes Medical Institute. HMMER and its documentation are freely distributed under the 3-Clause BSD open source license

HMMER is used for searching sequence databases for sequence homologs, and for making sequence alignments. It implements methods using probabilistic models called profile hidden Markov models (profile HMMs).

Sensitive homology searches. You're working on a specific sequence family, and you've carefully constructed a representative multiple sequence alignment. The HMMER hmmbuild program lets you build a profile from your alignment, and the hmmsearch program lets you search your profile against a sequence database looking systematically for more homologs.

AMRFinderPlus database

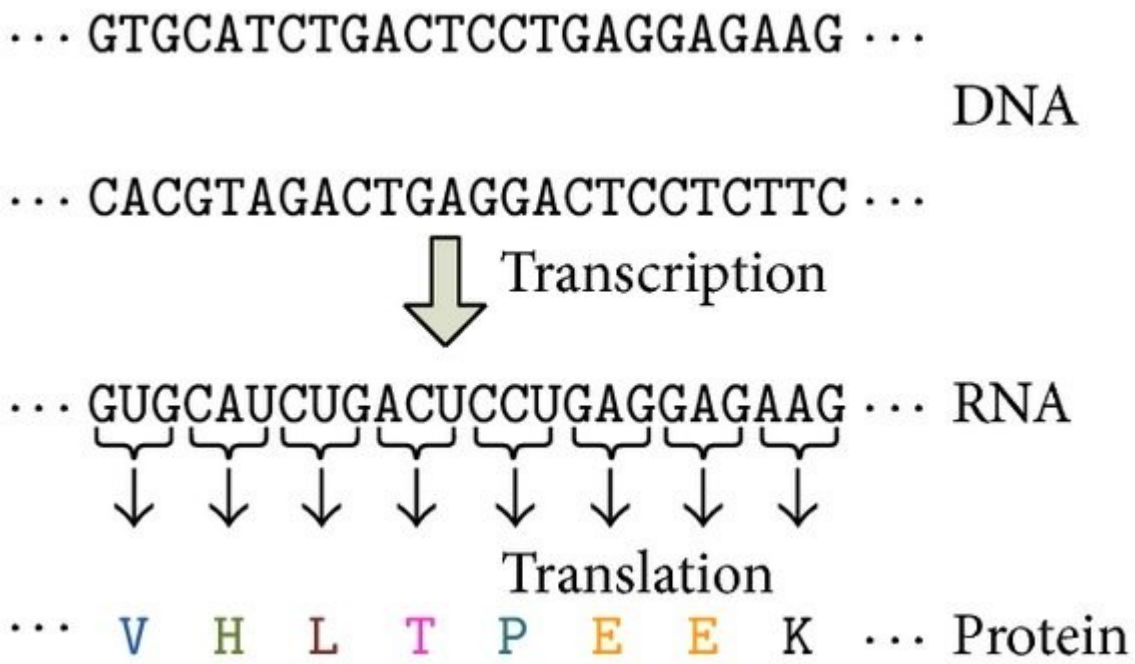
Core

- AMR elements (genes and proteins)
- Point mutations

Plus

- Stress and virulence
  - Biocide resistance
  - Heat resistance
  - Acid resistance
  - Metal resistance
- Other “AMR” genes

AMRFinderPlus

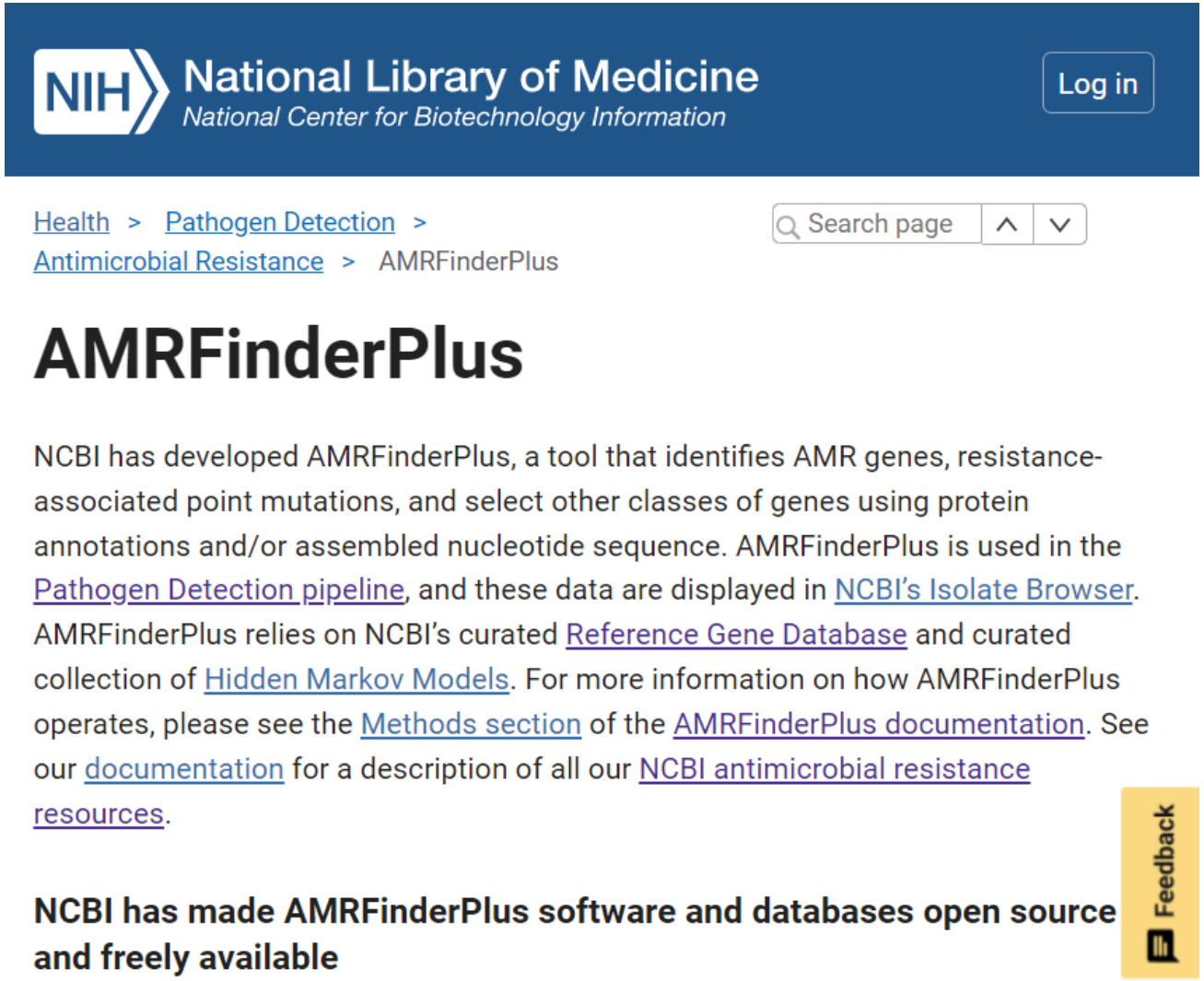


No web tool

AMR genes

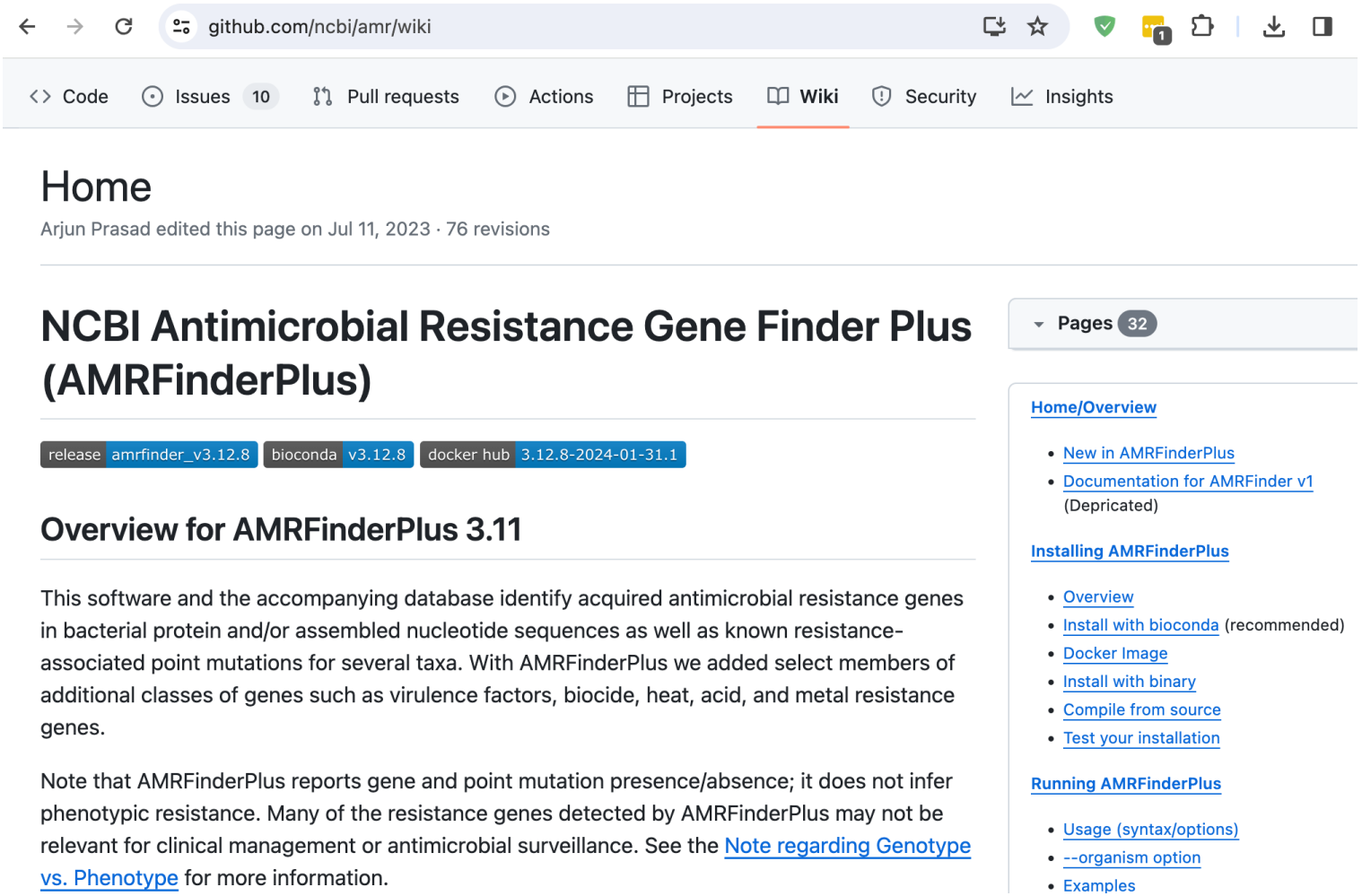
Resistance-associated point mutations

Other genes (stress, virulence)



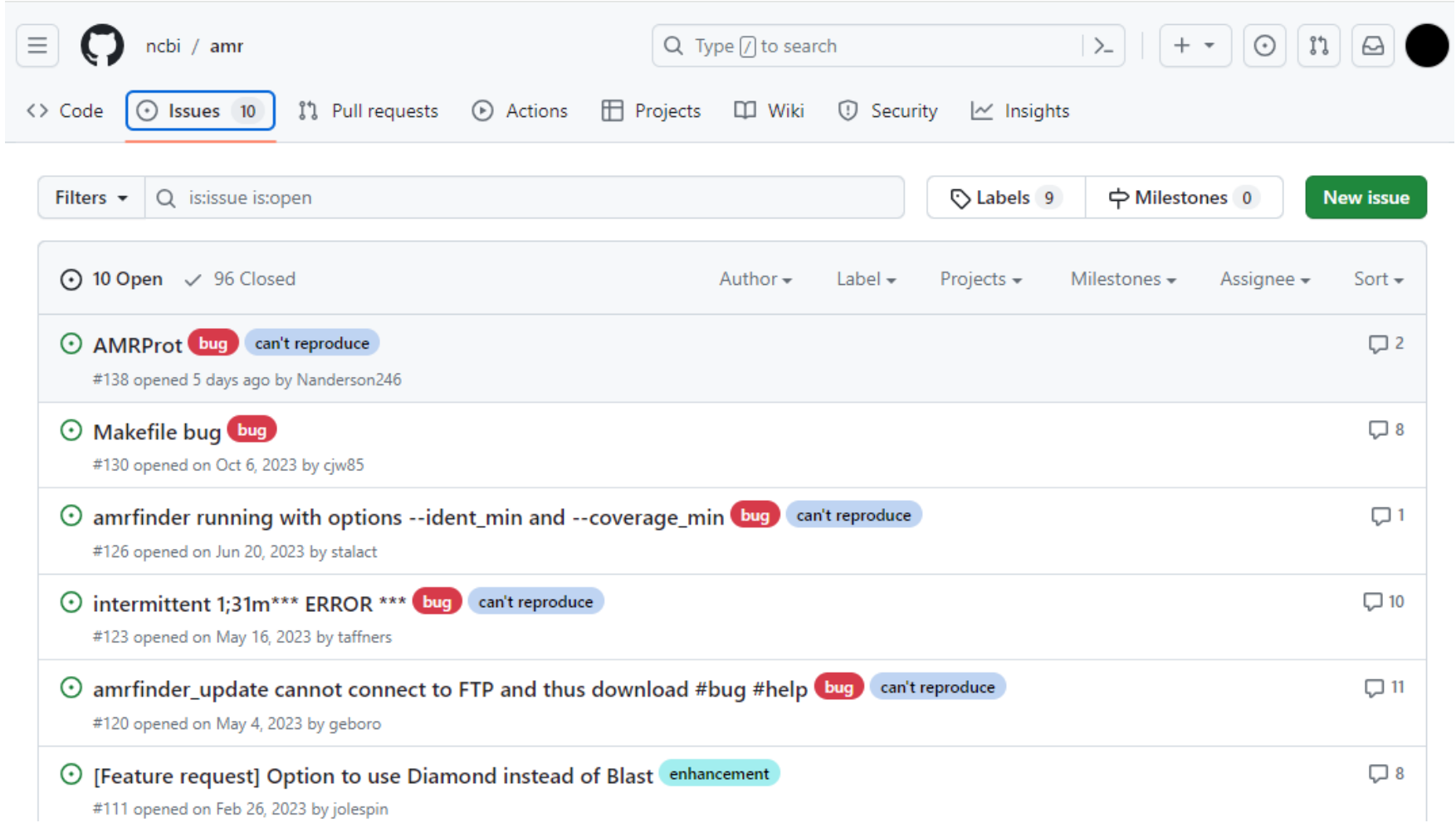
https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/AMRFinder/

Documentation



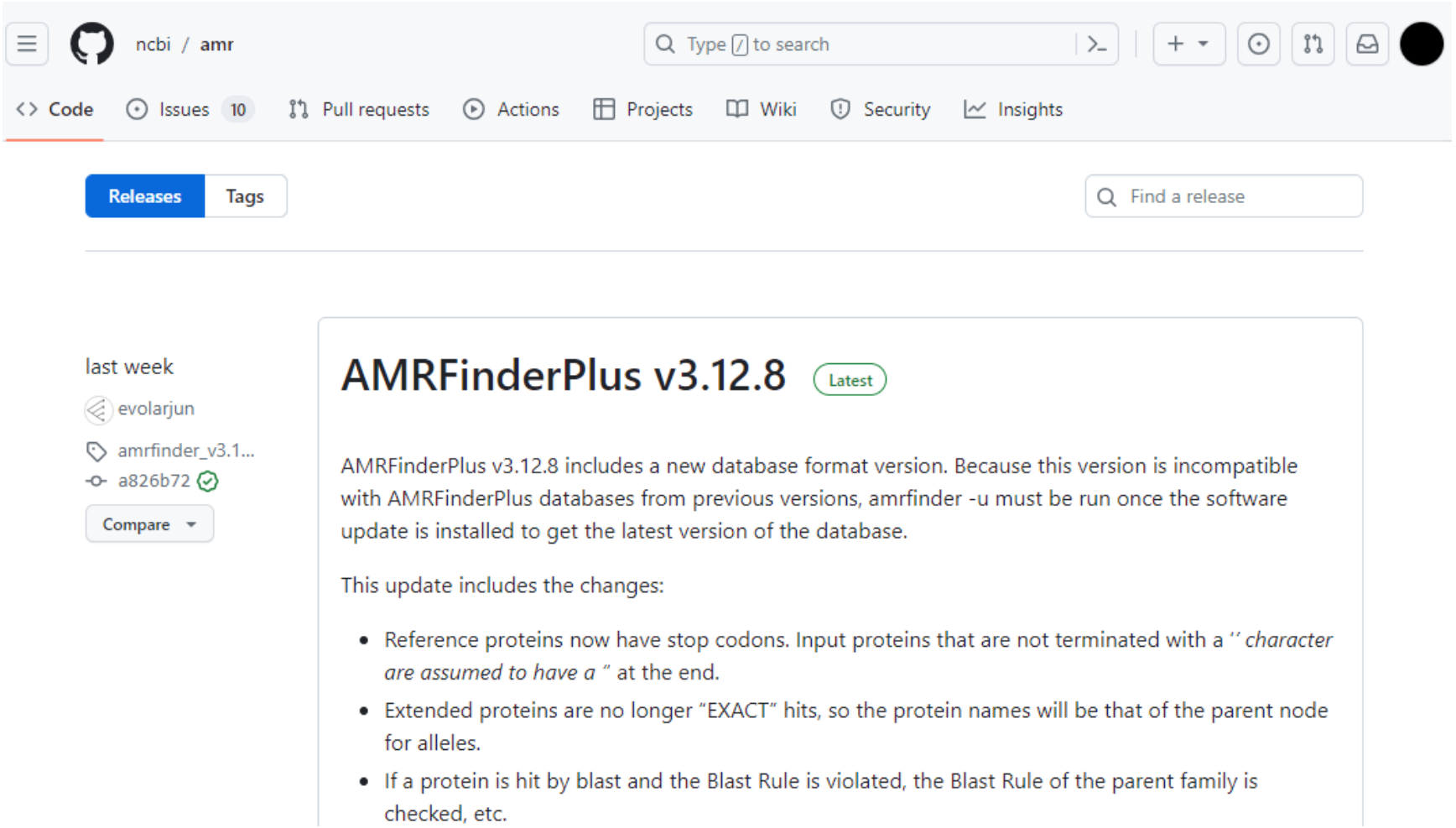
https://github.com/ncbi/amr/wiki

Issues/Questions



https://github.com/ncbi/amr/issues

History



https://github.com/ncbi/amr/releases

Database

Index of /pathogen/Antimicrobial_resistance/AMRFinderPlus/database/latest

Name	Last modified	Size
Parent Directory		-
allele_counts_by_year/	2024-02-05 11:11	-
AMR.LIB	2024-02-05 11:11	95M
AMRProt	2024-02-05 11:11	3.8M
AMRProt-mutation.tab	2024-02-05 11:11	139K
AMRProt-suppress	2024-02-05 11:11	608
AMRProt-susceptible.tab	2024-02-05 11:11	3.7K
AMR_CDS	2024-02-05 11:11	8.9M
AMR_DNA-Acinetobacter_baumannii	2024-02-05 11:11	303
AMR_DNA-Acinetobacter_baumannii.tab	2024-02-05 11:11	452
AMR_DNA-Campylobacter	2024-02-05 11:11	6.8K
AMR_DNA-Campylobacter.tab	2024-02-05 11:11	1.5K
AMR_DNA-Clostridioides_difficile	2024-02-05 11:11	2.9K
AMR_DNA-Clostridioides_difficile.tab	2024-02-05 11:11	295
AMR_DNA-Enterococcus_faecalis	2024-02-05 11:11	2.9K
AMR_DNA-Enterococcus_faecalis.tab	2024-02-05 11:11	390
AMR_DNA-Enterococcus_faecium	2024-02-05 11:11	2.9K
AMR_DNA-Enterococcus_faecium.tab	2024-02-05 11:11	388
AMR_DNA-Escherichia	2024-02-05 11:11	7.6K
AMR_DNA-Escherichia.tab	2024-02-05 11:11	7.5K
AMR_DNA-Klebsiella_oxytoca	2024-02-05 11:11	166
AMR_DNA-Klebsiella_oxytoca.tab	2024-02-05 11:11	726
AMR_DNA-Neisseria_gonorrhoeae	2024-02-05 11:11	5.9K
AMR_DNA-Neisseria_gonorrhoeae.tab	2024-02-05 11:11	2.2K
AMR_DNA-Salmonella	2024-02-05 11:11	1.6K
AMR_DNA-Salmonella.tab	2024-02-05 11:11	406
AMR_DNA-Staphylococcus_aureus	2024-02-05 11:11	3.3K
AMR_DNA-Staphylococcus_aureus.tab	2024-02-05 11:11	1.7K
AMR_DNA-Streptococcus_pneumoniae	2024-02-05 11:11	2.9K
AMR_DNA-Streptococcus_pneumoniae.tab	2024-02-05 11:11	825
ReferenceGeneCatalog.txt	2024-02-05 11:11	1.8M
ReferenceGeneHierarchy.txt	2024-02-05 11:11	1.0M
amr_targets.fa	2024-02-05 11:11	1.5M
changelog.txt	2024-02-05 11:11	1.4M
changes.txt	2024-02-05 11:11	1.4M
database_format_version.txt	2024-02-05 11:11	7
fam.tab	2024-02-05 11:11	302K
taxgroup.tab	2024-02-05 11:11	1.2K
version.txt	2024-02-05 11:11	13

https://ftp.ncbi.nlm.nih.gov/pathogen/Antimicrobial_resistance/AMRFinderPlus/database/latest/

Practice #2: AMRFinderPlus

Introduction to the exercise

practicals/manuals: AMR_practicals.docx

See: How to use this document

Conda environment with required software: CGEfinders and NCBItypers

Path to working folder: ~/BTG_2024

Path to assemblies: ~/BTG_2024/precomputed_data/day7/amr

Path to databases: ~/BTG_2024/data/databases

Path to output: ~/BTG_2024/amr/output

Path to precomputed output: ~/BTG_2024/precomputed_data/day7/amr

Introduction to the exercise (example)

Conda environment with required software: NCBItypers

Path to working folder: ~/BTG_2024/amr

Path to assemblies:
~/BTG_2024/precomputed_data/day7/amr/SRR27241771/SRR27241771.fasta

Path to databases: ~/BTG_2024/data/databases/amrfinderplus

Path to output: ~/BTG_2024/amr/output/SRR27241771/amrfinderplus_output.tsv

Path to precomputed output:
~/BTG_2024/precomputed_data/day7/amr/SRR27241771/amrfinderplus/output.tsv

Recap #2

SRR27241771 (Genes and point mutations)

Contig id	Start	Stop	Strand	Gene symbol	Scope	Element type	Class	Method	% Coverage of reference sequence	% Identity to reference sequence
SRR27241771_101/1	3911	4144	-	merE	plus	STRESS	MERCURY	BLASTX	100	96.15
SRR27241771_101/1	4144	4506	-	merD	plus	STRESS	MERCURY	BLASTX	100	90.08
SRR27241771_101/1	4527	6209	-	merA	plus	STRESS	MERCURY	BLASTX	100	93.23
SRR27241771_101/1	6995	7339	-	merT	plus	STRESS	MERCURY	BLASTX	99.14	99.13
SRR27241771_101/1	7429	7854	+	merR	plus	STRESS	MERCURY	BLASTX	98.61	92.96
SRR27241771_105/1	3191	4402	+	floR	core	AMR	PHENICOL	EXACTX	100	100
SRR27241771_113/1	47515	49704	+	sinH	plus	VIRULENCE	NA	EXACTX	100	100
SRR27241771_117/1	192	833	+	qnrB6	core	AMR	QUINOLONE	ALLELEX	100	100
SRR27241771_15/1	19613	20143	-	sodC1	plus	VIRULENCE	NA	BLASTX	100	99.44
SRR27241771_27/1	81	923	-	aadA16	core	AMR	AMINOGLYCOSIDE	EXACTX	100	100
SRR27241771_27/1	1107	1577	-	dfrA27	core	AMR	TRIMETHOPRIM	EXACTX	100	100
SRR27241771_27/1	3639	4088	-	arr-3	core	AMR	RIFAMYCIN	EXACTX	100	100
SRR27241771_37/1	537	1394	-	blaTEM-1	core	AMR	BETA-LACTAM	ALLELEX	100	100
SRR27241771_42/1	18124	18699	-	terD	plus	STRESS	TELLURIUM	BLASTX	100	95.31
SRR27241771_42/1	18751	19788	-	terC	plus	STRESS	TELLURIUM	BLASTX	100	90.46
SRR27241771_42/1	19814	20266	-	terB	plus	STRESS	TELLURIUM	BLASTX	100	90.73
SRR27241771_42/1	21449	22027	-	terZ	plus	STRESS	TELLURIUM	EXACTX	100	100
SRR27241771_42/1	28598	29062	+	terW	plus	STRESS	TELLURIUM	EXACTX	100	100
SRR27241771_47/1	4968	5870	-	mph(A)	core	AMR	MACROLIDE	EXACTX	100	100
SRR27241771_53/1	7	843	-	sul1	core	AMR	SULFONAMIDE	EXACTX	100	100
SRR27241771_53/1	840	1184	-	qacEdelta1	core	STRESS	QUATERNARY AMMONIUM	ALLELEX	100	100
SRR27241771_63/1	23575	24036	-	golS	plus	STRESS	GOLD	EXACTX	100	100
SRR27241771_63/1	24051	26336	-	golT	plus	STRESS	COPPER/GOLD	BLASTX	100	99.74
SRR27241771_63/1	26613	27836	+	mdsA	plus	AMR	EFFLUX	BLASTX	100	98.04
SRR27241771_63/1	27836	31000	+	mdsB	plus	AMR	EFFLUX	EXACTX	100	100
SRR27241771_69/1	11799	12980	-	emrD	plus	AMR	EFFLUX	BLASTX	100	92.64
SRR27241771_72/1	1424	2626	-	tet(B)	core	AMR	TETRACYCLINE	EXACTX	100	100

SRR27241772 (Genes and point mutations)

Contig id	Start	Stop	Strand	Gene symbol	Scope	Element type	Class	Method	% Coverage of reference sequence	% Identity to reference sequence
SRR27241772_100/1	1	561	+	aadA2	core	AMR	AMINOGLYCOSIDE	PARTIAL_CONTIG_ENDX	71.1	100
SRR27241772_100/1	728	1072	+	qacEdelta1	core	STRESS	QUATERNARY AMMONIUM	ALLELEX	100	100
SRR27241772_100/1	1069	1905	+	sul1	core	AMR	SULFONAMIDE	EXACTX	100	100
SRR27241772_100/1	7222	7806	-	mph(A)	core	AMR	MACROLIDE	PARTIAL_CONTIG_ENDX	64.78	100
SRR27241772_101/1	85573	87762	+	sinH	plus	VIRULENCE	NA	BLASTX	100	98.77
SRR27241772_106/1	12719	13900	-	emrD	plus	AMR	EFFLUX	BLASTX	100	92.89
SRR27241772_107/1	5690	5803	+	astA	plus	VIRULENCE	NA	BLASTX	100	97.37
SRR27241772_109/1	9063	11108	+	ireA	plus	VIRULENCE	NA	BLASTX	100	99.85
SRR27241772_113/1	204	1460	+	cmlA1	core	AMR	PHENICOL	EXACTX	100	100
SRR27241772_113/1	1556	2344	+	aadA1	core	AMR	AMINOGLYCOSIDE	EXACTX	100	100
SRR27241772_113/1	2517	2846	+	qacL	core	STRESS	QUATERNARY AMMONIUM	EXACTX	100	100
SRR27241772_113/1	4032	4820	-	sul3	core	AMR	SULFONAMIDE	EXACTX	100	100
SRR27241772_21/1	6553	7014	-	golS	plus	STRESS	GOLD	BLASTX	100	99.35
SRR27241772_21/1	7029	9314	-	golT	plus	STRESS	COPPER/GOLD	BLASTX	100	99.48
SRR27241772_21/1	9591	10814	+	mdsA	plus	AMR	EFFLUX	BLASTX	100	98.28
SRR27241772_21/1	10814	13978	+	mdsB	plus	AMR	EFFLUX	BLASTX	100	99.53
SRR27241772_44/1	3269	4480	+	floR	core	AMR	PHENICOL	BLASTX	100	99.75
SRR27241772_44/1	5086	6282	-	tet(A)	core	AMR	TETRACYCLINE	BLASTX	100	99.75
SRR27241772_44/1	7624	8454	-	aph(6)-Id	core	AMR	AMINOGLYCOSIDE	BLASTX	99.64	100
SRR27241772_44/1	8457	9257	-	aph(3'')-Ib	core	AMR	AMINOGLYCOSIDE	EXACTX	100	100
SRR27241772_44/1	9321	10133	-	sul2	core	AMR	SULFONAMIDE	EXACTX	100	100
SRR27241772_47/1	171835	174468	+	gyrA_D87G	core	AMR	QUINOLONE/TRICLOSAN	POINTX	100	99.77
SRR27241772_47/1	171835	174468	+	gyrA_S83F	core	AMR	QUINOLONE/TRICLOSAN	POINTX	100	99.77
SRR27241772_53/1	45066	47321	-	parC_S80I	core	AMR	QUINOLONE	POINTX	100	99.6
SRR27241772_63/1	254	1126	+	blaCTX-M-15	core	AMR	BETA-LACTAM	ALLELEX	100	100
SRR27241772_68/1	118	930	-	aph(3')-Ia	core	AMR	AMINOGLYCOSIDE	EXACTX	100	100
SRR27241772_7/1	617	1111	-	dfrA12	core	AMR	TRIMETHOPRIM	EXACTX	100	100

Resources

Tool	Item	Links
ResFinder	Online server	http://genepi.food.dtu.dk/resfinder
	Original paper	https://pubmed.ncbi.nlm.nih.gov/22782487/
	Database repository	https://bitbucket.org/genomicepidemiology/resfinder_db/src/master/
	Tool repository	https://bitbucket.org/genomicepidemiology/resfinder/src/master/
	Tool documentation	https://cge.food.dtu.dk/services/ResFinder/instructions.php

Tool	Item	Links
PointFinder	Online server	N/A
	Original paper	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5890747/
	Database repository	https://bitbucket.org/genomicepidemiology/pointfinder_db/src/master/
	Tool repository	https://bitbucket.org/genomicepidemiology/pointfinder/src/master/
	Tool documentation	N/A

Tool	Item	Links
AMRFinderPlus	Online server	N/A
	Original paper	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6811410/
	Database repository	https://ftp.ncbi.nlm.nih.gov/pathogen/Antimicrobial_resistance/AMRFinderPlus/database/3.11/2023-11-15.1/
	Tool repository	https://github.com/ncbi/amr
	Tool documentation	https://github.com/ncbi/amr/wiki

Acknowledgements

The creation of this training material was commissioned by ECDC to Statens Serum Institut (SSI) Danish Technical University (DTU) with the direct involvement of Egle Kudirkiene (SSI) and Karen Loaiza Conza (SSI)