

Bioinformatics for Antimicrobial Resistance Research

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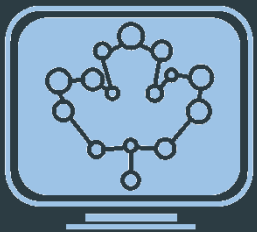
Agriculture and Agri-Food Canada

Lethbridge Research and Development Centre

One Health Summer Institute

June 16, 2021

Canada 



Goals of the workshop

- ▶ Overview of methods for bacterial genomics and molecular epidemiology
- ▶ Introduction to databases and tools for the analysis of antimicrobial resistance genes

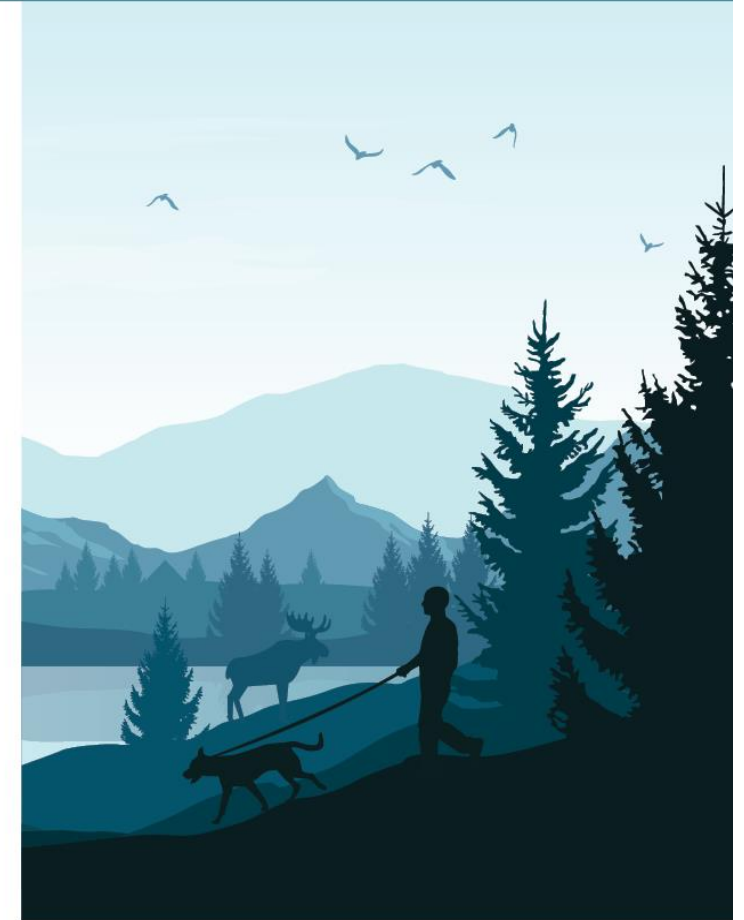
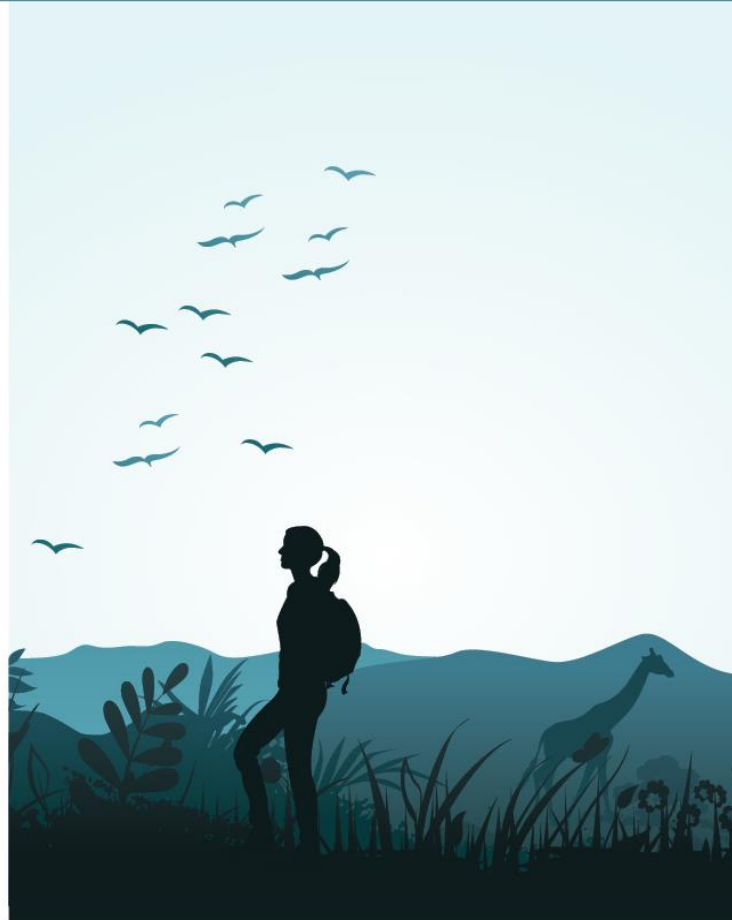
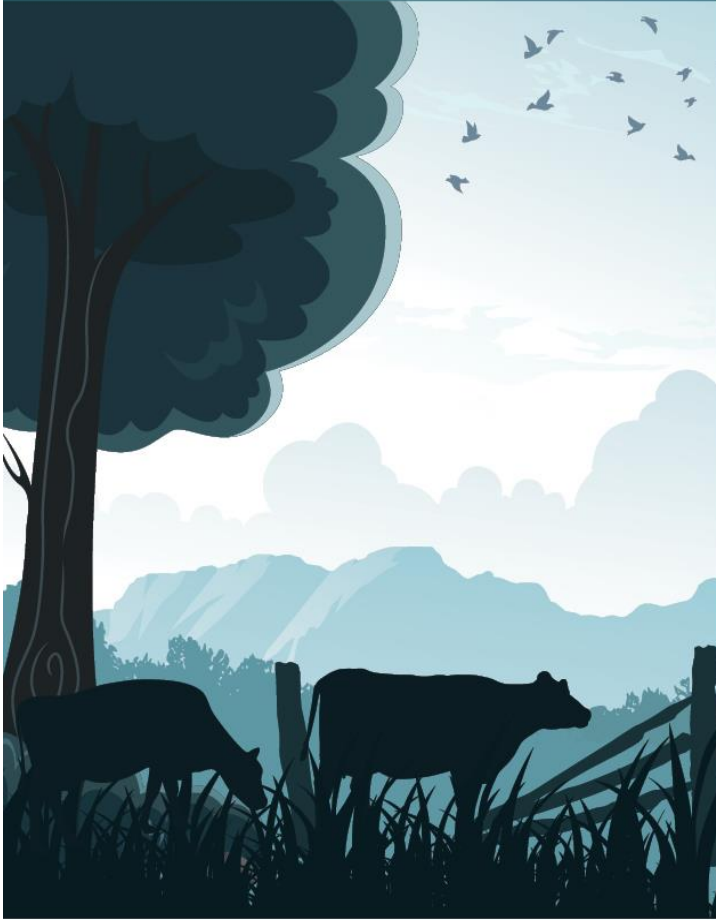
Introduction

- ▶ Head of the Bioinformatics Research Support Unit in a research and development centre of Agriculture and Agri-Food Canada (federal government)
- ▶ Located in Lethbridge, Alberta
- ▶ Distributed team of staff, students and collaborators (AB, BC, ON)
- ▶ Our unit is part of a national network of agriculture bioinformatics units
- ▶ I am a biologist who **applies** computational tools to address **research questions in Agriculture**
- ▶ Background:
 - ▶ Canadian Food Inspection Agency: research on foot-and-mouth disease virus
 - ▶ University of Lethbridge: analysis of One Health continuum metagenomics data
- ▶ We can do our own **experiments** with computational infrastructure
- ▶ Bioinformatics analysis is **driven by the research questions and study design**

ONE HEALTH



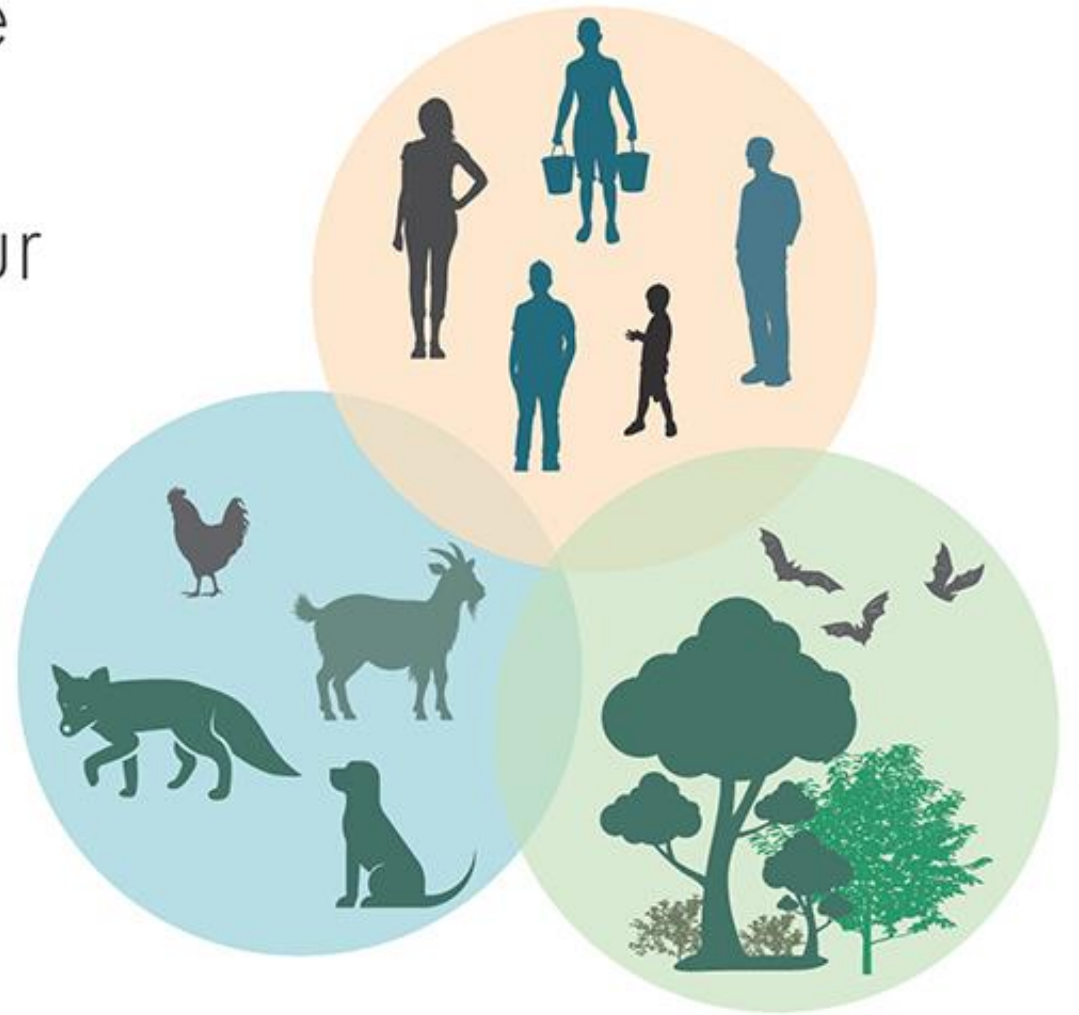
U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention



CONNECTING HUMAN, ANIMAL, AND ENVIRONMENTAL HEALTH

One Health is the idea that the health of people is connected to the health of animals and our shared environment.

When we protect **one**,
we help protect **all**.

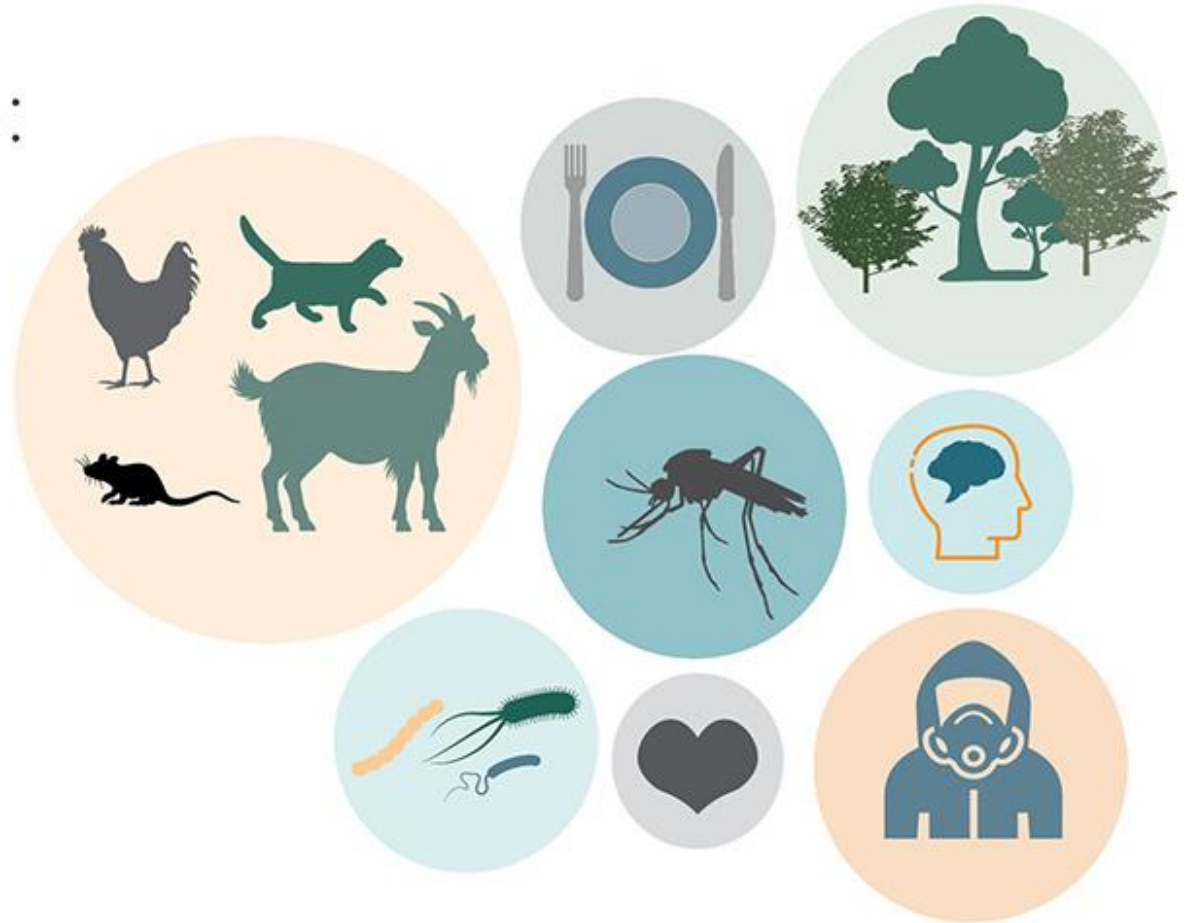


Did You Know?

One Health issues include:

- Zoonotic diseases
- Antibiotic resistance
- Food safety and security
- Vector-borne diseases
- Environmental health
- Chronic diseases
- Mental health
- Occupational health

...And more!



What do you study or want to study?

- What aspect of One Health do you work on?
- Are you focusing on a single pathogen? Or microbiomes / communities?
- Are you interested in presence/absence of pathogen? Or do you have other questions: AMR genes, virulence factors, genotyping?

Bacterial Typing

HTS for *in silico* typing and feature extraction to identify bacteria and provide brief characterization of known targets (i.e. ARG, virulence attributes)

Results from pathogenomic studies can reveal new genetic factors to develop/update current typing schemes and reference databases for additional feature extractions.

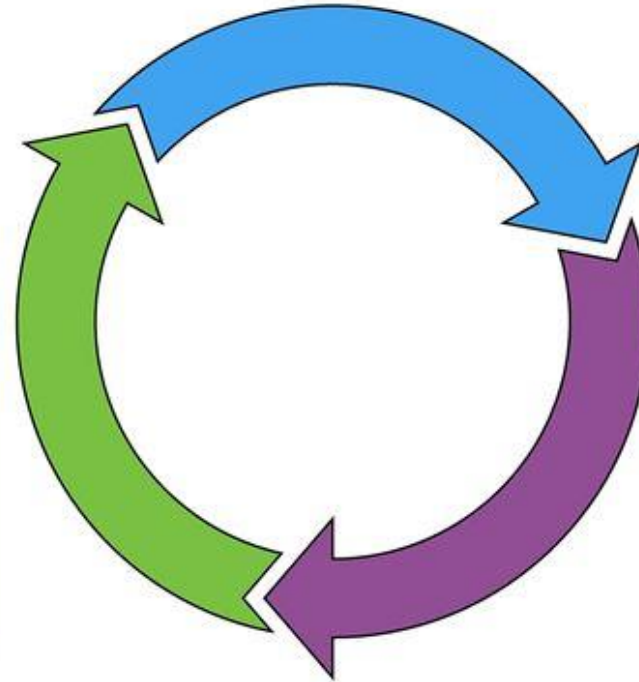
Pathogenomics

Utilizes HTS data in exploratory research to address larger questions. Expand dataset using global repositories and employ additional methods to progress research field (proteomics, transcriptomics, gene knockout experiments etc.)

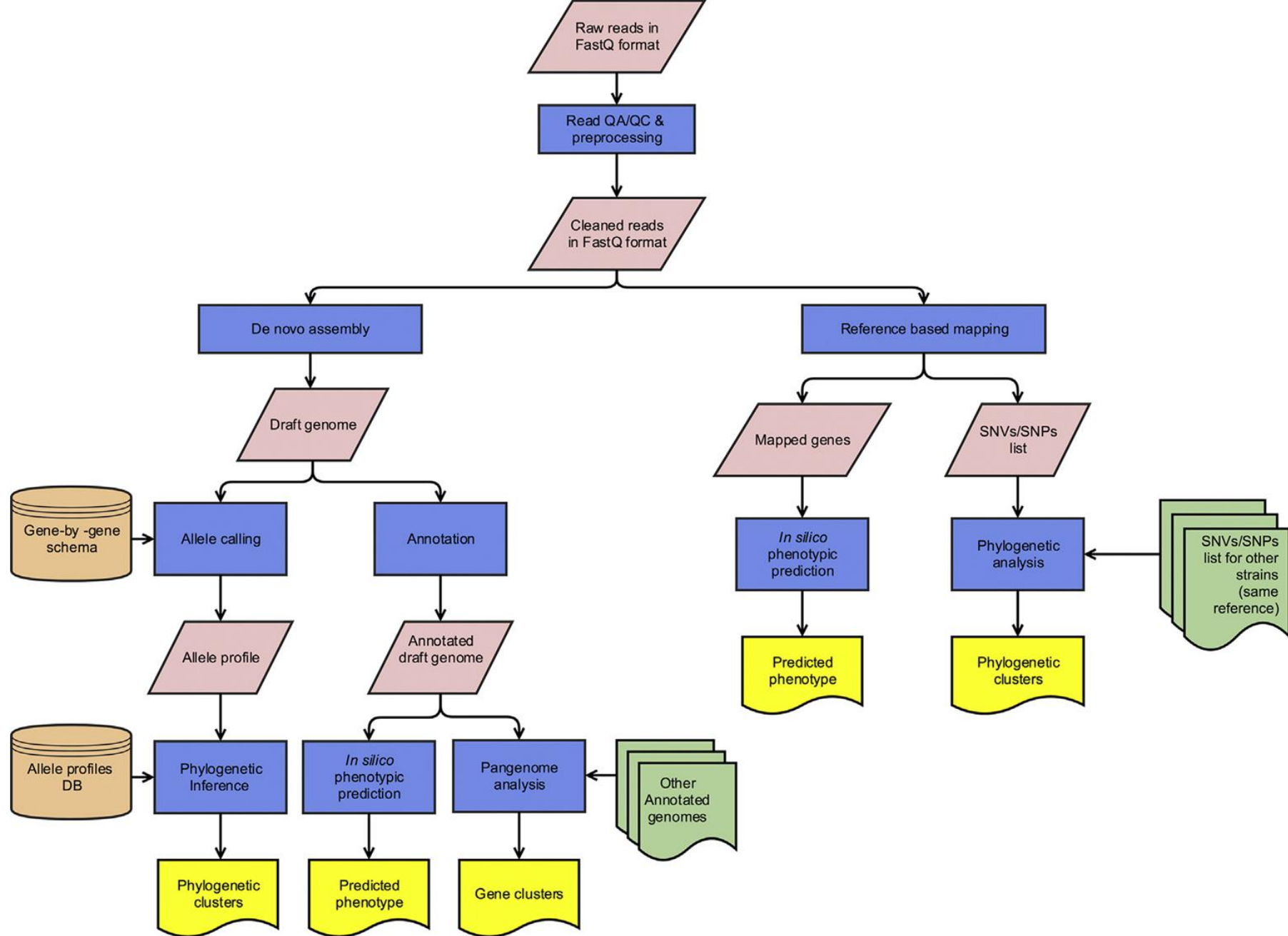
Bacterial typing informs isolate selection for comparison and provides genetic summary of known attributes relevant for outbreak investigations

Molecular Epidemiology

Applies HTS data to resolve outbreak investigations and molecular trends in the population (i.e. surveillance of ARG in circulating bacterial infections of a specific geographical region).



Molecular Epidemiology provides new comparative characteristics that may define novel genome(s) or populations requiring further research to understand.




Focusing on a single species

- Bacterial whole genome sequence analysis
- High resolution analysis of populations
- Molecular epidemiology
- Hundreds (or thousands) of isolates

[nature](#) > [scientific reports](#) > [articles](#) > [article](#)

Article | [Open Access](#) | [Published: 03 March 2020](#)

Surveillance of *Enterococcus spp.* reveals distinct species and antimicrobial resistance diversity across a One-Health continuum

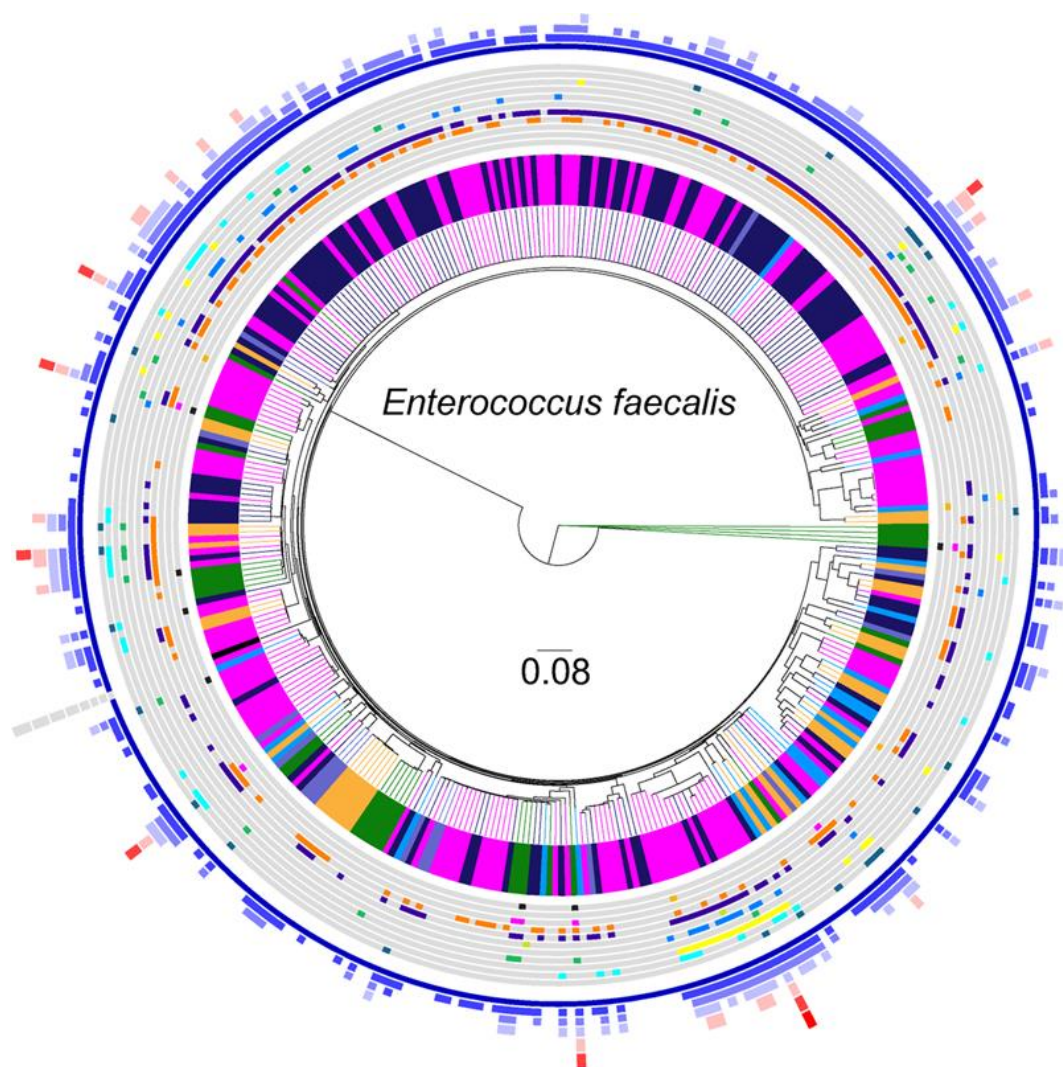
Rahat Zaheer, Shaun R. Cook, Ruth Barbieri, Noriko Goji, Andrew Cameron, Aaron Petkau, Rodrigo Ortega Polo, Lisa Tymensen, Courtney Stamm, Jiming Song, Sherry Hannon, Tineke Jones, Deirdre Church, Calvin W. Booker, Kingsley Amoako, Gary Van Domselaar, Ron R. Read & Tim A. McAllister 

Scientific Reports **10**, Article number: 3937 (2020) | [Cite this article](#)

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Enterococcus spp. study

- **Goal:** to compare hundreds of isolates from clinical and agricultural settings
- *De novo* assemblies of whole genome sequences
- Genome annotation
- **Antimicrobial resistance gene searches**
- Analysis of 500+ bacterial isolates



Inner ring

Isolate source

- Clinical (Non-sterile & Sterile)
- Urban wastewater
- Natural water sources
- Feedlot catchbasin
- Bovine feces
- Beef processing

Middle ring

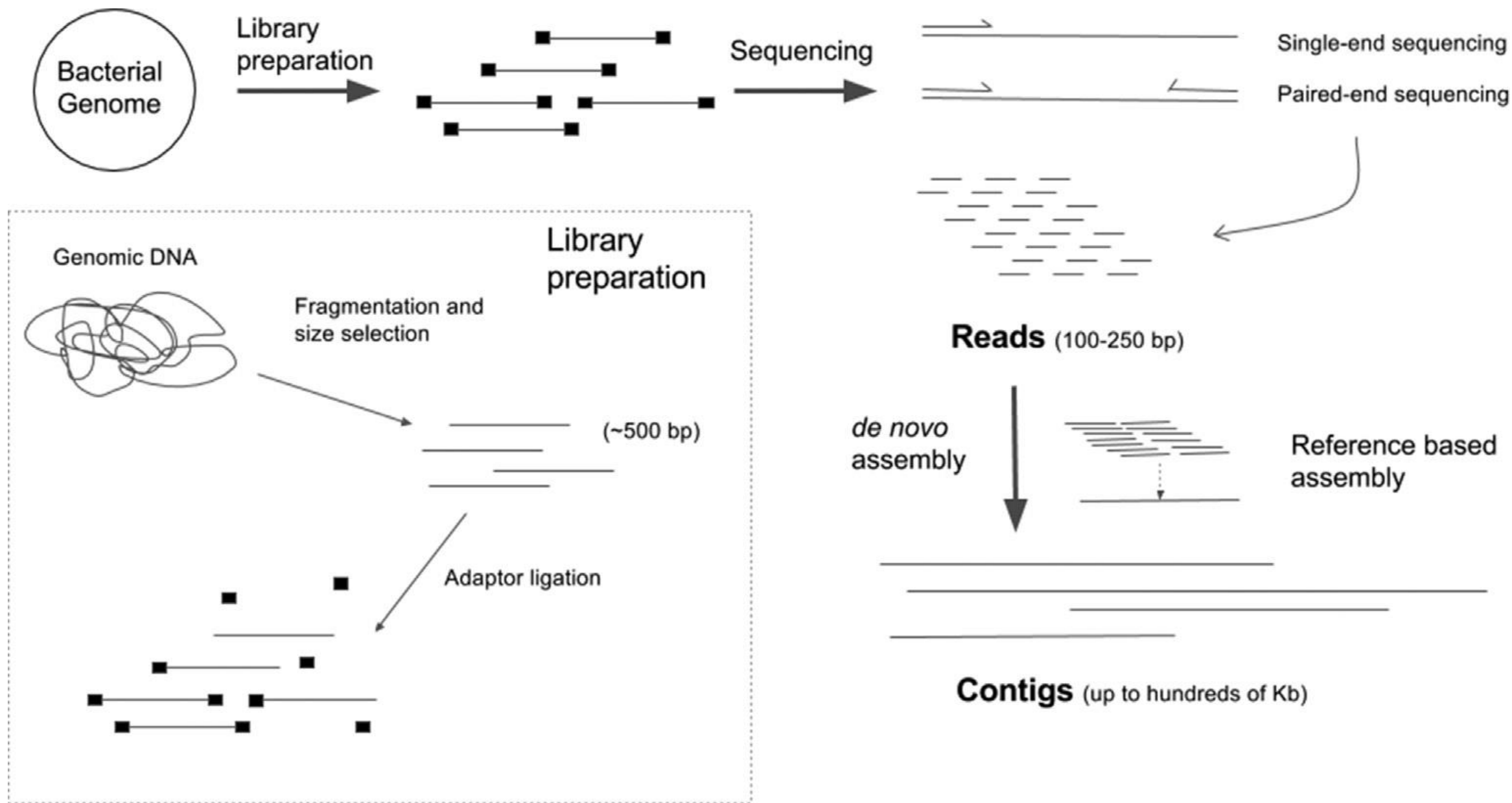
Phenotypic drug resistance

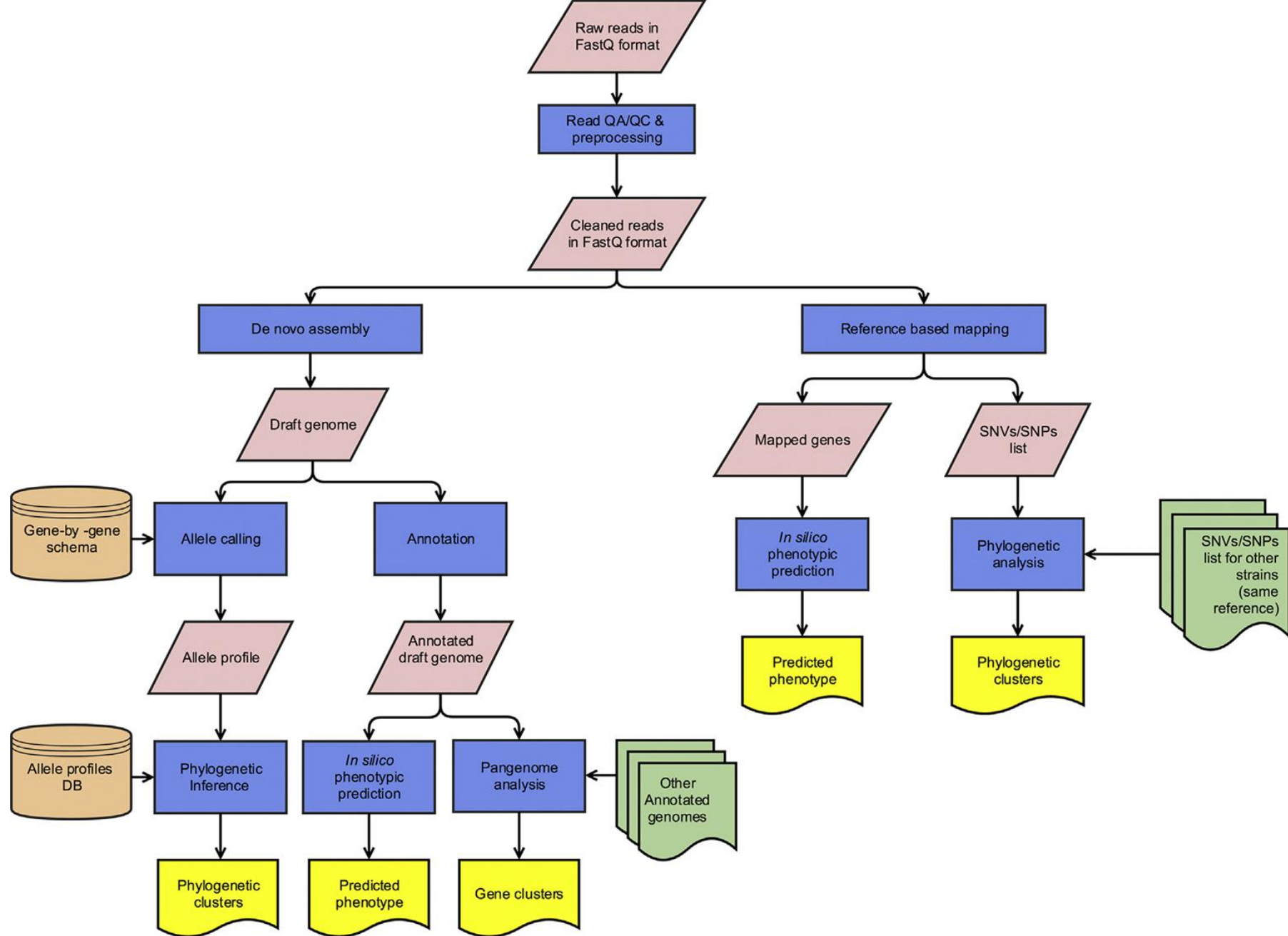
- Tigecycline
- Streptomycin
- Fluoroquinolones
- Linezolid
- Gentamicin
- Nitrofurantoin
- Erythromycin
- Tetracyclines
- β -lactam (penams)
- Teicoplanin
- Vancomycin

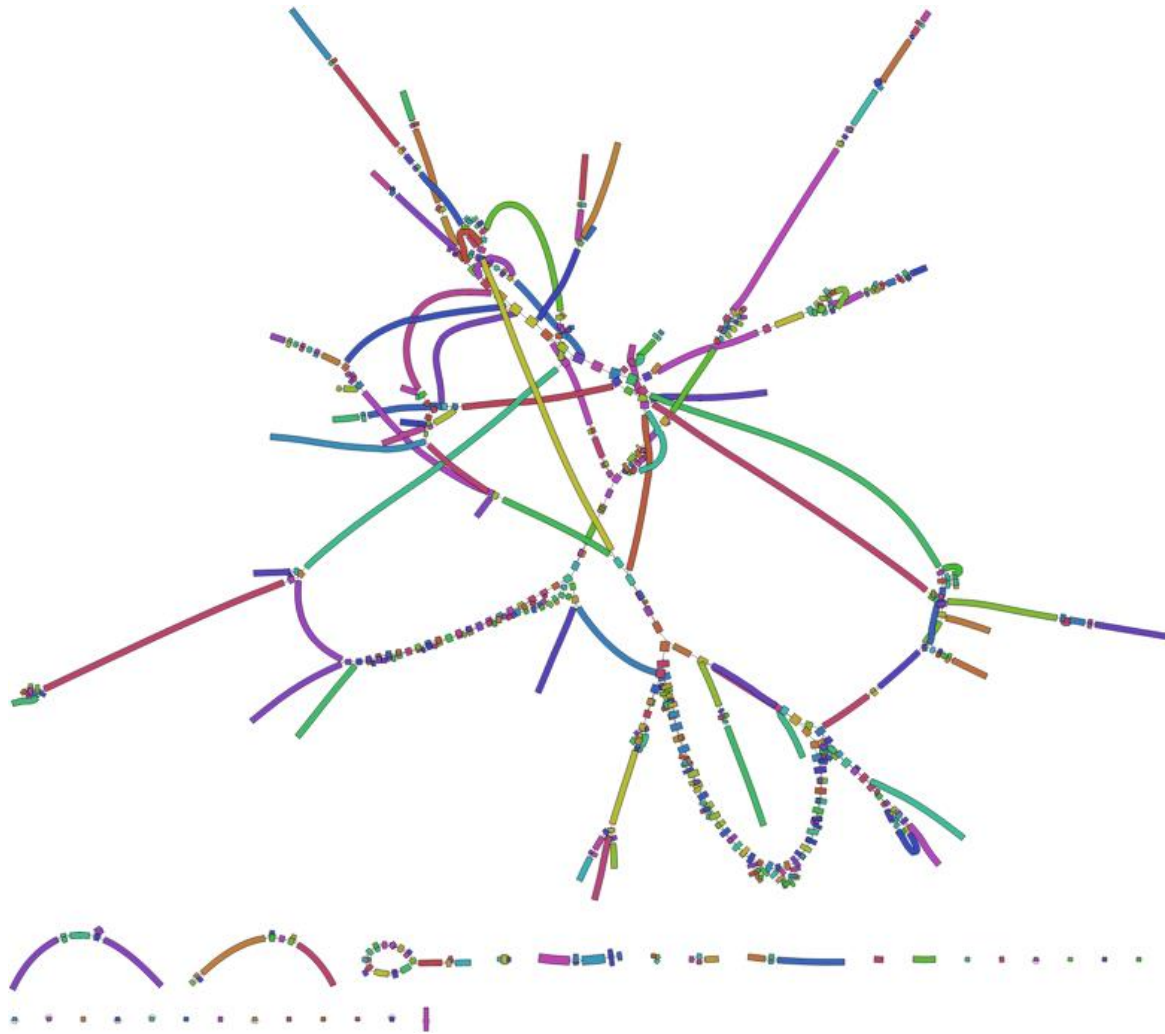
Outer ring

MDR

- Susceptible
- 1 drug
- 2 drugs
- 3 drugs
- 4 drugs
- 5 drugs
- 6 drugs
- 7 drugs







Visualization of draft assembly
of *Salmonella* genome with
Bandage software

Contigs compose an assembly
graph

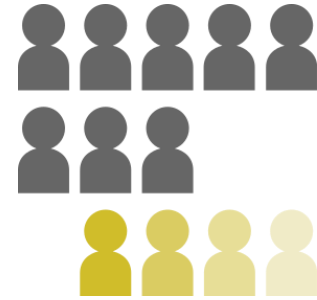
We can use this as a way to
assess assembly quality

Hands-on activities

1) Working with the CARD database

2) Using Galaxy to assemble a genome and explore the antimicrobial resistance genes

Thank you!



TlaaS

usegalaxy.eu

File and metatools

Get data: USCS, Uniprot
Send data: GenomeSpace Exporter
Convert

Genomics, HTS

Quality control: FastQC, MultiQC, Trim Galore!, etc
Alignment: BLAST, Diamond, etc
Mapping: Bowtie2, STAR, HISAT2, BWA, segemehl, etc
Assembly: Unicycler, SPades, Quast, etc
Transcriptomics: FeatureCounts, DESeq2, Trinity, Salmon, etc
RNA: LocARNA, RNAfold, RNAz, RNAplot, etc
Variant Calling: FreeBayes, Gemini, VCFTools, SnpEff, etc
Peak Calling: MACS2, Piranha, PEAChachu, etc
Epigenetics: Bismark, metilene, bwameth, MethylDackel, etc
deepTools, SAM Tools, HicExplorer, Picard, EMBOSS, etc

Text tools

Text manipulation
Filter and Sort
Join, Substract and Group
Statistics

Metagenomics

MetaPhlAn2, HUMAnN2, VSearch, ...
QIIME, Mothur
MEGAHIT, MetaSpades, ...

Annotation, ontologies

SortMeRNA, Aragorn, Roary, Prokka, Augustus, KOBAS, Glimmer, antiSMASH, etc

Proteomics, Metabolomics, Chemistry

OpenMS, PeptideShaker, SearchGUI, MADLIquant, etc
Jmol Editor, Docking, etc
OpenBabel, ChemFP, OMG, QED, etc

Training Infrastructure as a Service

<https://usegalaxy.eu/join-training/one-health2021/>

Private training queue will only be available during training period (today), but you can access data and history after the workshop

If you prefer you can also work with <https://usegalaxy.org/> as in the first day of the workshop. The tools are the same!

1. Access link

Galaxy Training Infrastructure as a Service

✔ Congratulations: you are successfully registered in **one-health2021**
[Return to Galaxy](#)

How It Works

We have deployed a dedicated compute node just for your training session to use. No one outside of your training has access to this machine. Completely transparently to you, all of the jobs that you run in Galaxy, during the period of the training event, will "prefer" to run on this machine. If there is no room on that machine, they will run on any other machine in our cluster with resources.

Training Infrastructure as a Service (TlaaS) licensed under the AGPLv3, running commit 061e459308e690a309fa918126c2731a072d49a6

2. Click on Return to Galaxy

Thank you!



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Agri-Food Canada

Agriculture et
Agroalimentaire Canada

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