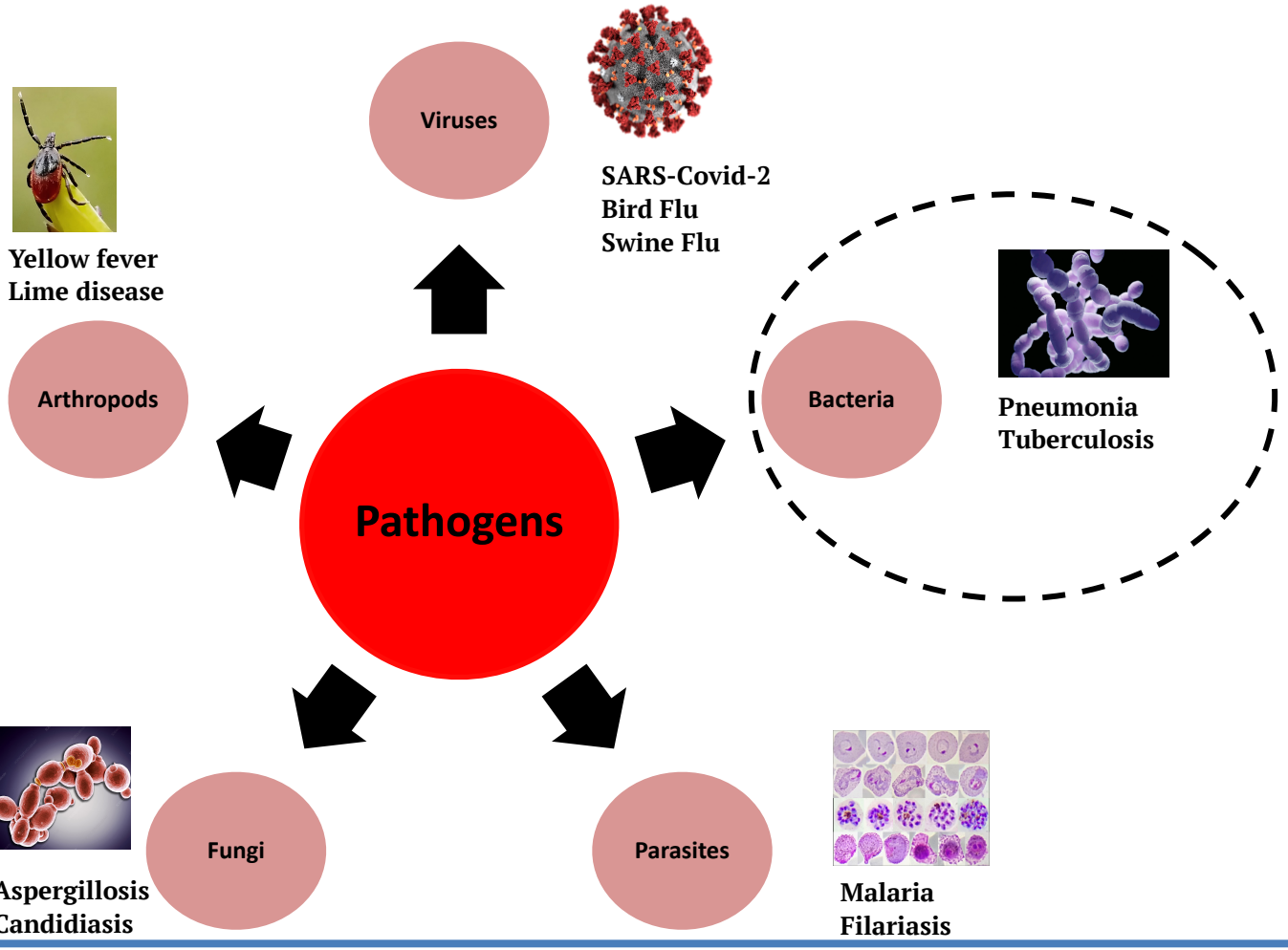
H3ABioNet
Pan African Bioinformatics Network for H3Africa

wellcome connecting science

Next Generation Sequencing
Bioinformatics Course 2021

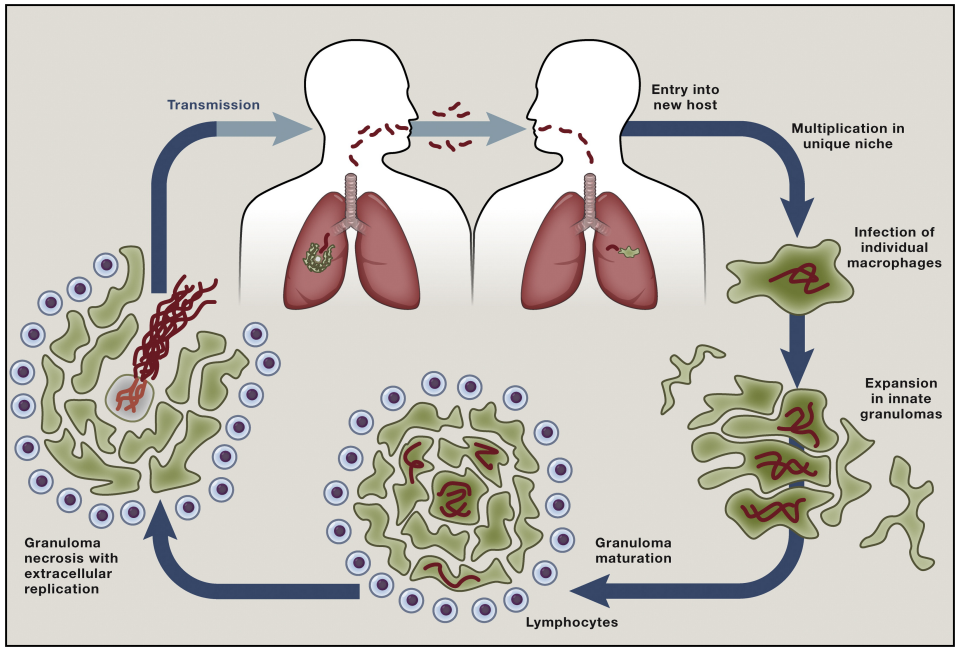
Module 6 – Pathogen variant calling

Pathogens



Mycobacterium tuberculosis

- Cause Tuberculosis in humans
- Primary source of transmission through aerosols produced during cough
- Diagnosis involves microscopy, GeneXpert
- Culturing takes weeks to months
- Phenotypic DST labour and time intensive
- Rapid methods for detecting resistance needed : WGS



Question: Investigating resistance in *M. tuberculosis*

What we know

- 4 isolates from patients with Tuberculosis in a region
- The rapid tests (GeneXpert) have revealed resistance to rifampicin
- WGS performed for all 4 isolates

Isolate	Drug	Resistance
MD001	Rifampicin	Resistant
MD002	Rifampicin	Resistant
MD012	Rifampicin	Resistant
MD024	Rifampicin	Sensitive

Questions we would investigate

- Detect genetic variants for resistance
- resistance to other anti-Tb drugs
- Are these related isolates (pairwise SNP difference)
- Understand their phylogenetic relationship

Resistance mechanisms: *M. tuberculosis*

Acquired genetic mutations confers resistance

Drug	Gene	Mutations
Rifampicin	*rpoB*	S450X, D435X
Streptomycin	*rpsL*	K43R
Isoniazid	*katG*	S315T
Fluoroquinolone	*gyrA*	D94X

Contents

- **Session1: Alignment to reference**
- **Session2: Variant calling and filtering**
- **Session3: Inferring genetic relatedness**
- **Session4: Summary of all the results**

Thank you