Literature search: Tools to assess the pathogenicity of Nontuberculous Mycobacteria

Background information – Mechanisms of bacterial pathogenicity

The general steps of pathogenesis are: exposure, adhesion, invasion, infection and transmission. Bacteria use a plethora of mechanisms to do this (3).

Virulence factors contribute to execution of the previously mentioned steps. These virulence factors can be toxins, surface coats/capsules, surface receptors that bind to host cells, … (1). The presence of the virulence genes are of interest in these NTM genomes. That’s why virulence finder tools are of interest.

The virulence factors can be encoded on plasmids and bacteriophage DNA, as well as the chromosomal DNA (1). A plasmid is a small circular, dsDNA molecule that is distinct from a cell’s chromosomal DNA (2). Plasmids can contain genes that give the bacteria a genetic advantage thus can help overcome stressful situations (5). So when researching the pathogenicity, plasmids provide a lot of useful information about it. That is why plasmid finder tools are of interest.

Bacteriophages or phages are viruses that infect and replicate only in bacterial cells. There are two replication strategies that can happen: lytic or lysogenic. Lytic means it will introduce its genome in the host cell and use the host bacterium to assemble multiple copies of the phage. The bacterium dies to release the assembled phages. Lysogenic means that the genome will also be introduced in the bacterial cell genome. However, the bacterium will not die, but pass the incorporated genome of the phage on to daughter cells without killing them. The integrated phage genomes are called prophages (6). This is why (pro)phage finder tools are of interest.

One way of bacteria to spread virulence factors is by horizontal gene transfer (HGT). It is defined by the movement of genetic information between organisms, but not in a parent-offspring relationship (8). When the genetic information is incorporated into the genome of the recipient organism, it forms genomic islands. These islands are blocks of DNA that contain mobile genetic elements. The genomic islands are also referred to as pathogenicity islands since they often contain large blocks of virulence factors (4). This is why genomic island finder tools are of interest.

Transposon was mentioned regularly in literature when searching for bacterial pathogenicity.

From 7: “Transposons are a group of mobile genetic elements that are defined as a DNA sequence. Transposons can jump into different places of the genome; for this reason, they are called jumping genes.”

And

“Transposons are divided into two main groups: retrotransposons (class І) and DNA transposons (class ІІ). Retrotransposons are often found in eukaryotes. DNA transposons can be found in both eukaryotes and prokaryotes. The bacterial transposons belong to the DNA transposons and the Tn family, which are usually the carrier of additional genes for antibiotic resistance. Transposons can transfer from a plasmid to other plasmids or from a DNA chromosome to plasmid and vice versa that cause the transmission of antibiotic resistance genes in bacteria.”

Reference

1 - [Bacterial Pathogenesis - Medical Microbiology - NCBI Bookshelf (nih.gov)](https://www.ncbi.nlm.nih.gov/books/NBK8526/#:~:text=Pathogenic%20Mechanisms-,Bacterial%20Infectivity,that%20bind%20to%20host%20cells.)

2 - [plasmid / plasmids | Learn Science at Scitable (nature.com)](https://www.nature.com/scitable/definition/plasmid-plasmids-28/#:~:text=A%20plasmid%20is%20a%20small,advantages%2C%20such%20as%20antibiotic%20resistance.)

3 - [Summary of Microbial Mechanisms of Pathogenicity - LabXchange](https://www.labxchange.org/library/items/lb:LabXchange:c0dcc582-a76c-33a4-9d40-d2f7dd23200c:html:1?source=%2Flibrary%2Fbooks%2Fd16810cd-172e-4c2d-b82a-ba21e5dfbe0f#:~:text=Pathogens%20enter%20the%20body%20through,invasion%2C%20infection%2C%20and%20transmission.)

4 - [v078p00216.pdf (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1742320/pdf/v078p00216.pdf)

5 - [Bacterial DNA – the role of plasmids — Science Learning Hub](https://www.sciencelearn.org.nz/resources/1900-bacterial-dna-the-role-of-plasmids)

6 - [Bacteriophages - StatPearls - NCBI Bookshelf (nih.gov)](https://www.ncbi.nlm.nih.gov/books/NBK493185/)

7 - [Transposons: the agents of antibiotic resistance in bacteria - PubMed (nih.gov)](https://pubmed.ncbi.nlm.nih.gov/30113080/)

8 - [Horizontal Gene Transfer - PMC (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4536854/#:~:text=Horizontal%20gene%20transfer%20(HGT)%20is,offspring)%2C%20fueling%20pathogen%20evolution.)

Tools for detection of virulence factors

* VFDB = database for virulence factors (you can blast your sequences against the database and see if there are any hits with the virulence factors in the database)

Website: [VFDB - pathogenesis of Mycobacterium (mgc.ac.cn)](http://www.mgc.ac.cn/cgi-bin/VFs/genus.cgi?Genus=Mycobacterium)

Paper: [VFDB 2022: a general classification scheme for bacterial virulence factors | Nucleic Acids Research | Oxford Academic (oup.com)](https://academic.oup.com/nar/article/50/D1/D912/6446532?login=false)

* Virulence Searcher

Paper: [Virulence Searcher: a tool for searching raw genome sequences from bacterial genomes for putative virulence factors - Clinical Microbiology and Infection](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(14)62387-9/fulltext)

Website: /

Tools for detection of plasmids

* PlasmidFinder 2.0

Seems to be used regularly however I can’t find it anywhere

Paper: [Investigating Pathogenicity and Virulence of Staphylococcus pettenkoferi: An Emerging Pathogen - PMC (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8704685/)

GitHub: (no gitHub page)

Website: [cge.cbs.dtu.dk](https://cge.cbs.dtu.dk/services/PlasmidFinder/) (doesn’t work)

* plaSquid

Fairly new/not well known tool, does look interesting for this project

Paper: [Improved detection and classification of plasmids from circularized and fragmented assemblies | bioRxiv](https://www.biorxiv.org/content/10.1101/2022.08.04.502827v1.full)

GitHub: [mgimenez720/plaSquid: Nextflow pipeline for plasmid detection and classification from metagenomic data (github.com)](https://github.com/mgimenez720/plaSquid)

* plasmidID

Looks only possible on certain data.

Paper: /

GitHub: [BU-ISCIII/plasmidID: PlasmidID is a mapping-based, assembly-assisted plasmid identification tool that analyzes and gives graphic solution for plasmid identification. (github.com)](https://github.com/BU-ISCIII/plasmidID)

* SPAdes

I think this is only an assembler and not a plasmid finder.

Paper: [Plasmid detection and assembly in genomic and metagenomic data sets - PubMed (nih.gov)](https://pubmed.ncbi.nlm.nih.gov/31048319/)

GitHub: [ablab/spades: SPAdes Genome Assembler (github.com)](https://github.com/ablab/spades#plasmid)

* PlasForest

Uses a Random Forest classifier to identify plasmids in contigs and scaffold genomes. This is more of a machine learning approach.

Paper: [PlasForest: a homology-based random forest classifier for plasmid detection in genomic datasets | BMC Bioinformatics | Full Text (biomedcentral.com)](https://bmcbioinformatics.biomedcentral.com/articles/10.1186/s12859-021-04270-w)

GitHub: [leaemiliepradier/PlasForest: A random forest classifier to identify contigs of plasmid origin in contig and scaffold genomes (github.com)](https://github.com/leaemiliepradier/PlasForest)

Tools for detection of prophages

* PHASTER

Paper: [PHASTER: a better, faster version of the PHAST phage search tool - PMC (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4987931/)

Website: [PHASTER](https://phaster.ca/)

Tools for detection of genomic islands

* IslandViewer 4

Paper: [IslandViewer 4: expanded prediction of genomic islands for larger-scale datasets - PMC (nih.gov)](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5570257/)

Website: [Islandviewer 4 - Genomic Island Prediction and Genome Visualization Tool (sfu.ca)](https://www.pathogenomics.sfu.ca/islandviewer/)

Tools for detection of transposons

Might be good paper: [A benchmark of transposon insertion detection tools using real data | Mobile DNA | Full Text (biomedcentral.com)](https://mobilednajournal.biomedcentral.com/articles/10.1186/s13100-019-0197-9)

Extra

* PathogenFinder 1.1 (prediction of a bacteria’s pathogenicity towards human hosts)

Paper: [PathogenFinder - Distinguishing Friend from Foe Using Bacterial Whole Genome Sequence Data | PLOS ONE](https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0077302)

Website: [CGE Server (dtu.dk)](https://cge.food.dtu.dk/services/PathogenFinder/)