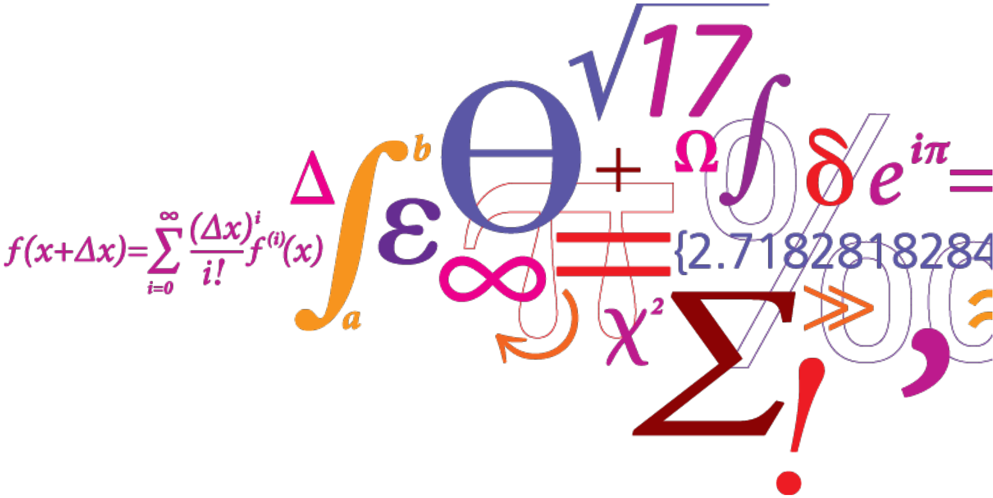
PathogenFinder

Johanne Ahrenfeldt
PhD Student
johah@cbs.dtu.dk



Who am I

Johanne Ahrenfeldt

johah@cbs.dtu.dk

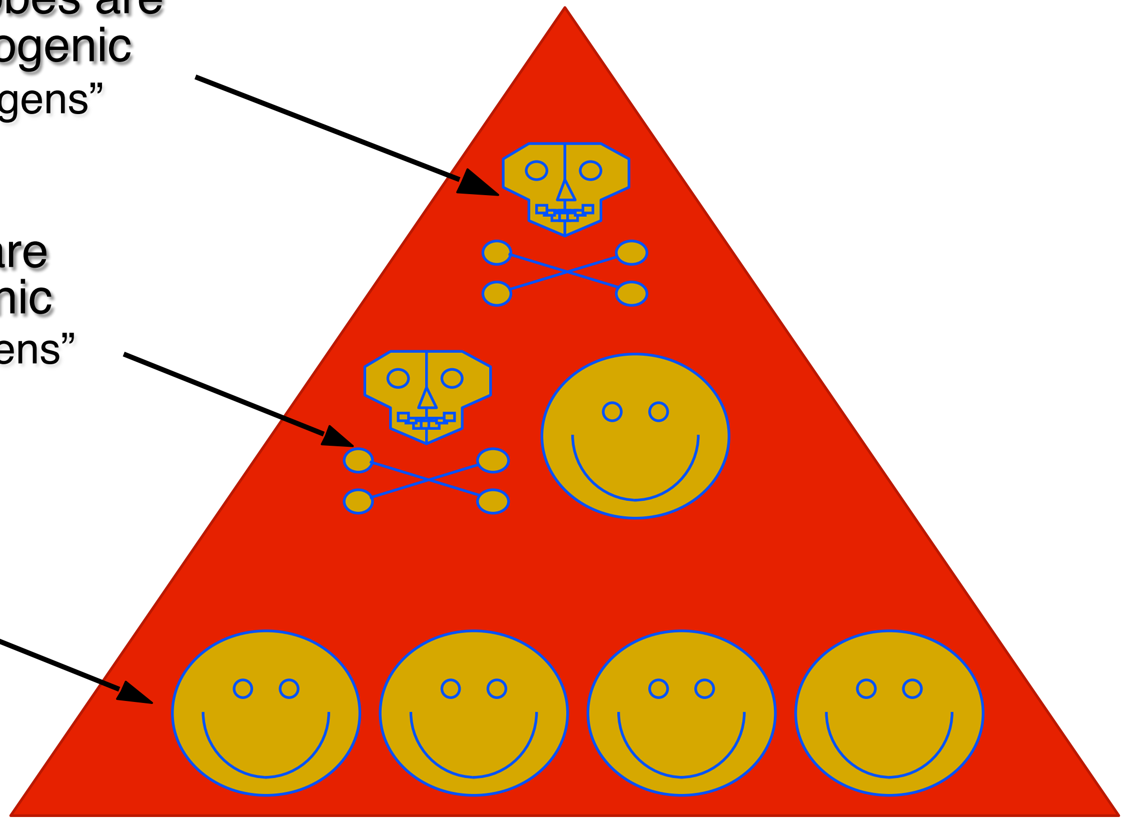
- PhD student in Genomic Epidemiology
- Graduate engineer in Bioinformatics and Systems Biology from DTU – 2014
- Mainly work with Whole Genome based Phylogeny

Bacterial pathogenecity and virulence

- **Pathogenicity.** This is the potential capacity of certain species of microbes to cause an infectious process.

- **Virulence.** signifies the degree of pathogenicity of the given strain. Virulence, therefore, is an index of the qualitative individual nature of the pathogenic microorganism.

Microbes and humans



Very few microbes are always pathogenic
"Strict pathogens"

Many microbes are potentially pathogenic
"Opportunistic pathogens"

Most microbes are never pathogenic
"Non-pathogenic"

Student activation

- Give an example on a strict pathogen

- Give an example on an opportunistic pathogen

- Give an example on a non-pathogen

How do we know that a given pathogen causes a specific disease?

- Koch's postulates
  - the pathogen must be present in every case of the disease
  - the pathogen must be isolated from the diseased host & grown in pure culture
  - the specific disease must be reproduced when a pure culture of the pathogen is inoculated into a healthy susceptible host
  - the pathogen must be recoverable from the experimentally infected host

Use 2 minutes to discuss in small groups how you would conquer the island.

Include:

- **How to get on to and how to stay on the island**

Back-paddle, throw an anchor, use a rope, swim from the boat (might require more than one swimmer!!)

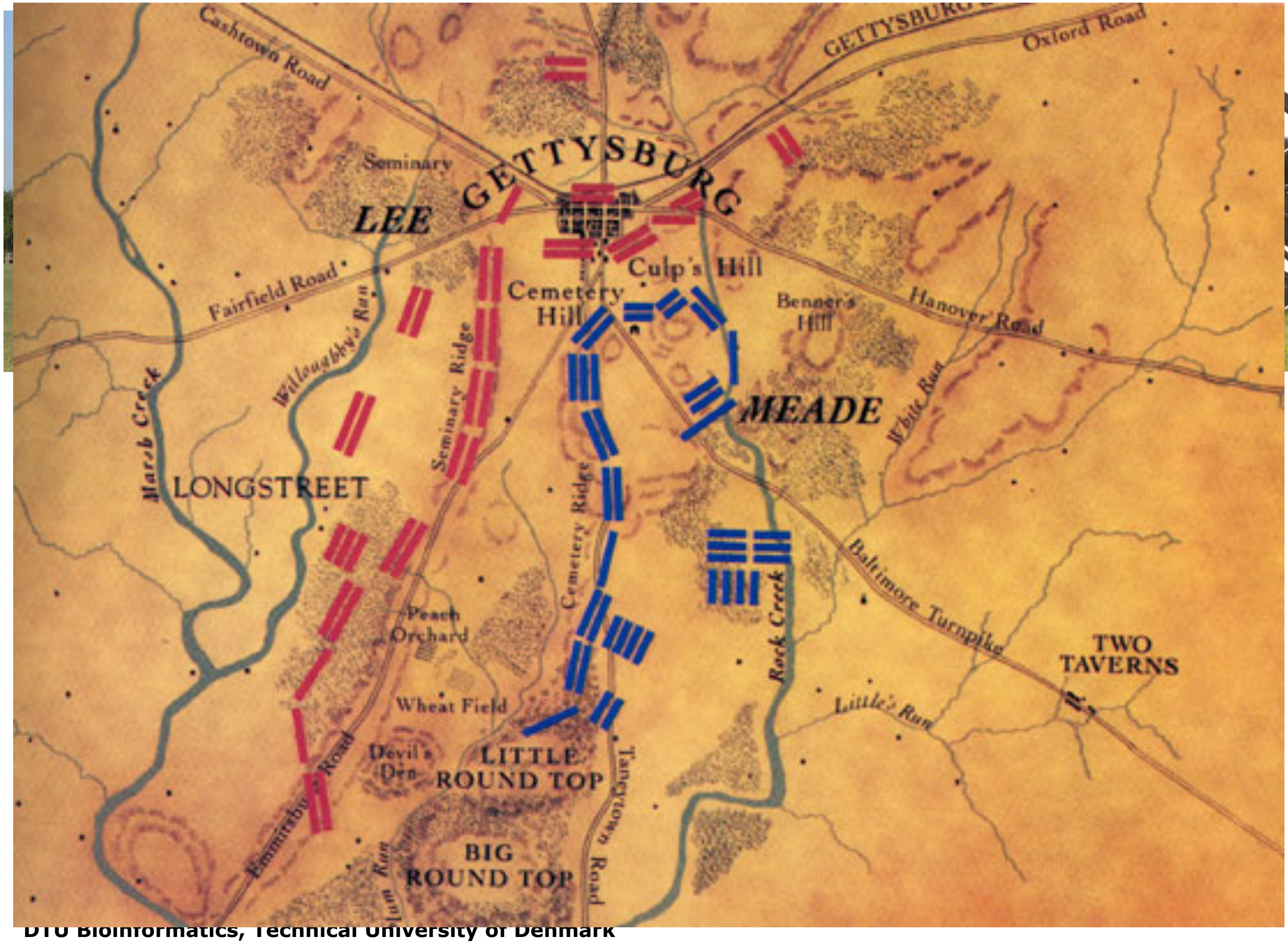
- **How to avoid being detected by the island defense**

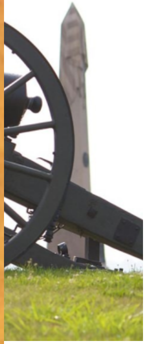
Camouflage, hide, dig-in, costume

- **How to eliminate the island defense**

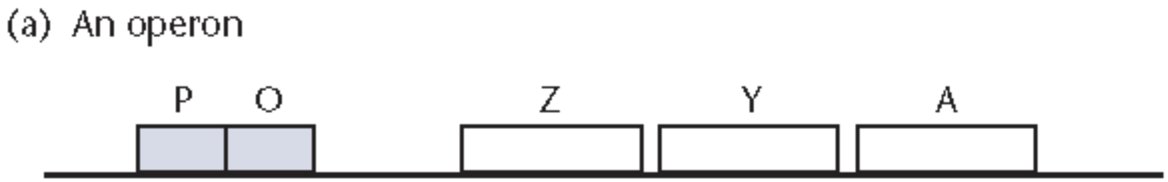
Poison, weapon, scare to perform suicide

Coordinated attack





Gene regulation – A tool for a coordinated attack



Purpose

The main purpose of PathogenFinder is to predict the pathogenecity of a given bacteria, based on the whole genome sequence or the proteome.

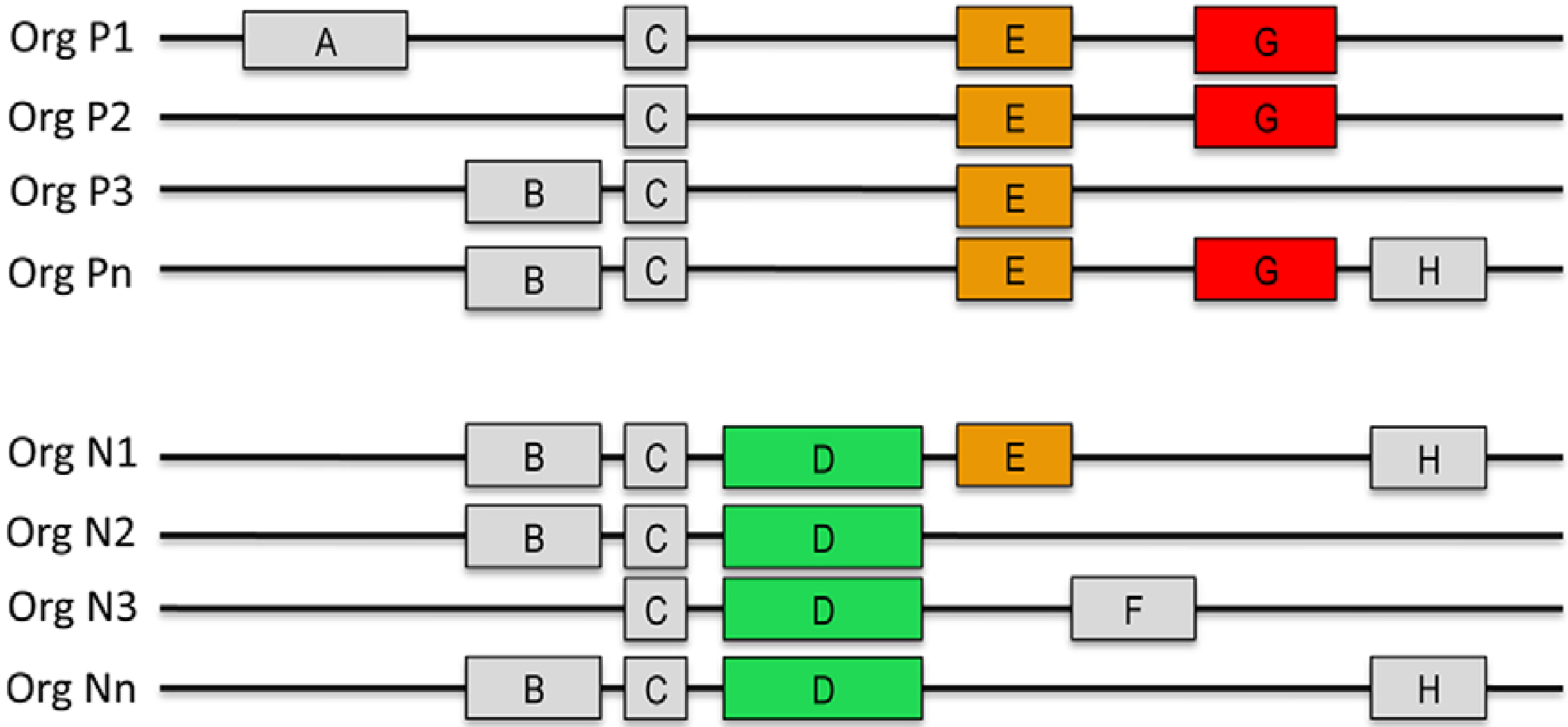
Method

- PathogenFinder identifies and divides the genes after protein families

- The genes are the clustered using CD-hit

- After clustering it is determined whether a group of genes is more pathogenic or non-pathogenic

Pathogenic gene families



Pathogenic gene families

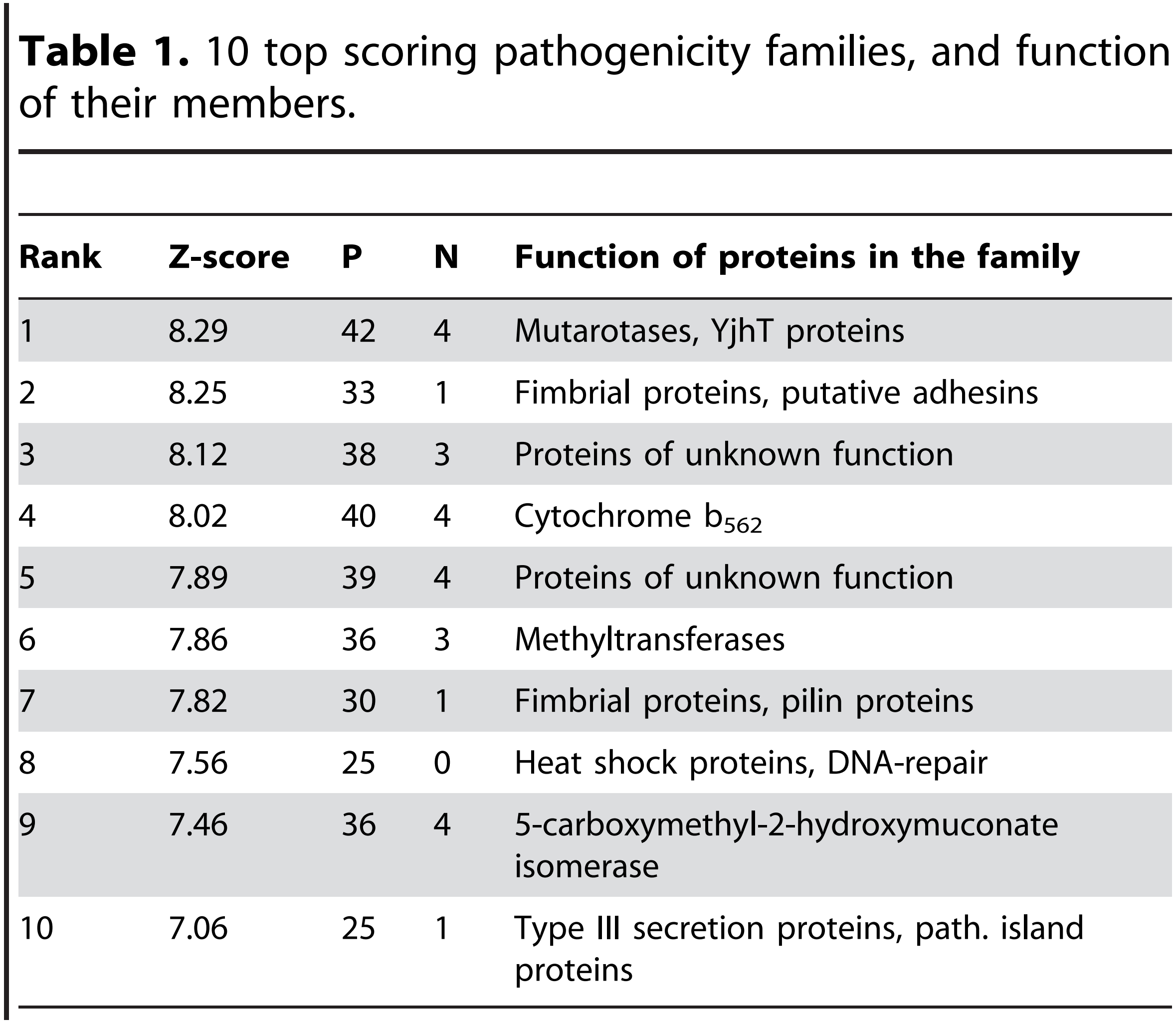


Table 1. 10 top scoring pathogenicity families, and function of their members.

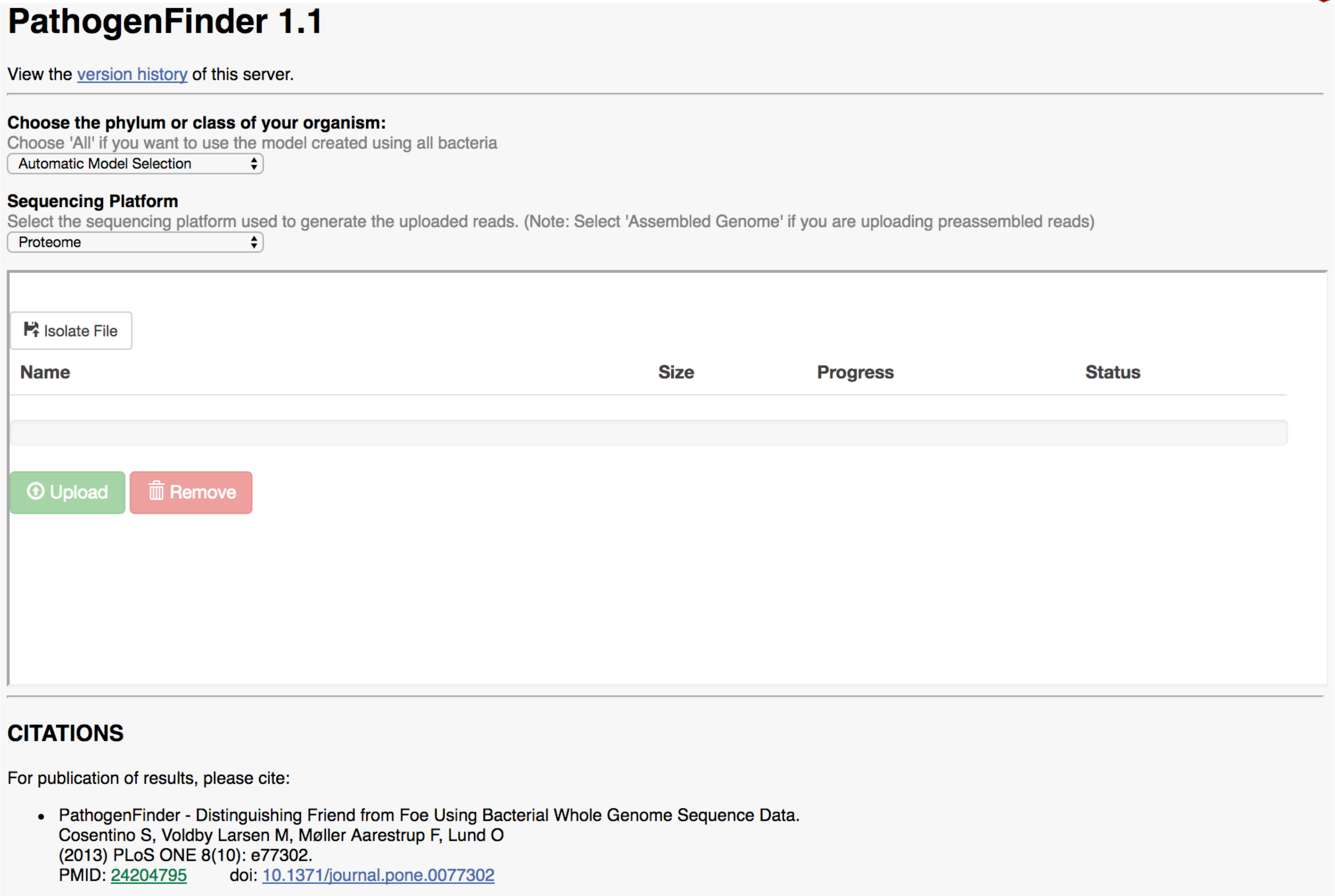
Rank	Z-score	P	N	Function of proteins in the family
1	8.29	42	4	Mutarotases, YjhT proteins
2	8.25	33	1	Fimbrial proteins, putative adhesins
3	8.12	38	3	Proteins of unknown function
4	8.02	40	4	Cytochrome b_{562}
5	7.89	39	4	Proteins of unknown function
6	7.86	36	3	Methyltransferases
7	7.82	30	1	Fimbrial proteins, pilin proteins
8	7.56	25	0	Heat shock proteins, DNA-repair
9	7.46	36	4	5-carboxymethyl-2-hydroxymuconate isomerase
10	7.06	25	1	Type III secretion proteins, path. island proteins

Predicting pathogenicity

The following 4 steps describe the process that leads to the prediction:

I	Compare the input proteins to the PathogenFinder Database of protein families
II	Filter hits based on the identity threshold
III	Calculate final score summing the Z values associated to the matched PFs
IV	Compare the final score to the model’s Zthr threshold and give the final prediction

https://cge.cbs.dtu.dk/services/PathogenFinder/



PathogenFinder 1.1

View the version history of this server.

Choose the phylum or class of your organism:
Choose 'All' if you want to use the model created using all bacteria
Automatic Model Selection

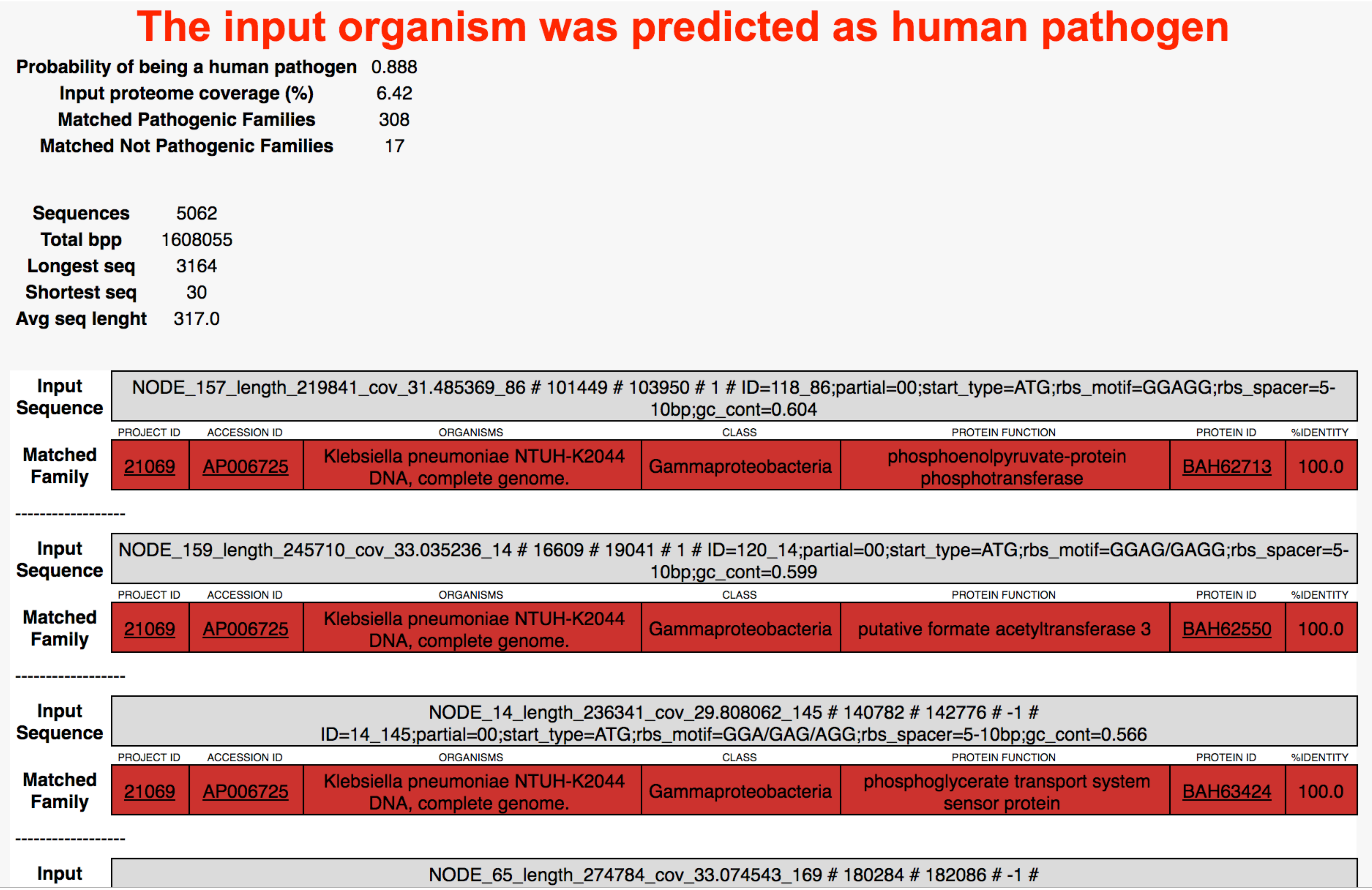
Sequencing Platform
Select the sequencing platform used to generate the uploaded reads. (Note: Select 'Assembled Genome' if you are uploading preassembled reads)
Proteome

CITATIONS

For publication of results, please cite:

- PathogenFinder - Distinguishing Friend from Foe Using Bacterial Whole Genome Sequence Data.
  Cosentino S, Voldby Larsen M, Møller Aarestrup F, Lund O
  (2013) PLoS ONE 8(10): e77302.
  PMID: 24204795 doi: 10.1371/journal.pone.0077302

Results



The input organism was predicted as human pathogen

Probability of being a human pathogen	0.888
Input proteome coverage (%)	6.42
Matched Pathogenic Families	308
Matched Not Pathogenic Families	17

Sequences	5062
Total bpp	1608055
Longest seq	3164
Shortest seq	30
Avg seq lenght	317.0

Input Sequence NODE_157_length_219841_cov_31.485369_86 # 101449 # 103950 # 1 # ID=118_86;partial=00;start_type=ATG;rbs_motif=GGAGG;rbs_spacer=5-10bp;gc_cont=0.604

	PROJECT ID	ACCESSION ID	ORGANISMS	CLASS	PROTEIN FUNCTION	PROTEIN ID	%IDENTITY
Matched Family	21069	AP006725	Klebsiella pneumoniae NTUH-K2044 DNA, complete genome.	Gammaproteobacteria	phosphoenolpyruvate-protein phosphotransferase	BAH62713	100.0

Input Sequence NODE_159_length_245710_cov_33.035236_14 # 16609 # 19041 # 1 # ID=120_14;partial=00;start_type=ATG;rbs_motif=GGAG/GAGG;rbs_spacer=5-10bp;gc_cont=0.599

	PROJECT ID	ACCESSION ID	ORGANISMS	CLASS	PROTEIN FUNCTION	PROTEIN ID	%IDENTITY
Matched Family	21069	AP006725	Klebsiella pneumoniae NTUH-K2044 DNA, complete genome.	Gammaproteobacteria	putative formate acetyltransferase 3	BAH62550	100.0

Input Sequence NODE_14_length_236341_cov_29.808062_145 # 140782 # 142776 # -1 # ID=14_145;partial=00;start_type=ATG;rbs_motif=GGA/GAG/AGG;rbs_spacer=5-10bp;gc_cont=0.566

	PROJECT ID	ACCESSION ID	ORGANISMS	CLASS	PROTEIN FUNCTION	PROTEIN ID	%IDENTITY
Matched Family	21069	AP006725	Klebsiella pneumoniae NTUH-K2044 DNA, complete genome.	Gammaproteobacteria	phosphoglycerate transport system sensor protein	BAH63424	100.0

Input NODE_65_length_274784_cov_33.074543_169 # 180284 # 182086 # -1 #