Pathogen and antimicrobial resistance surveillance in Ugandan HIV positive adults with pneumonia

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Introduction

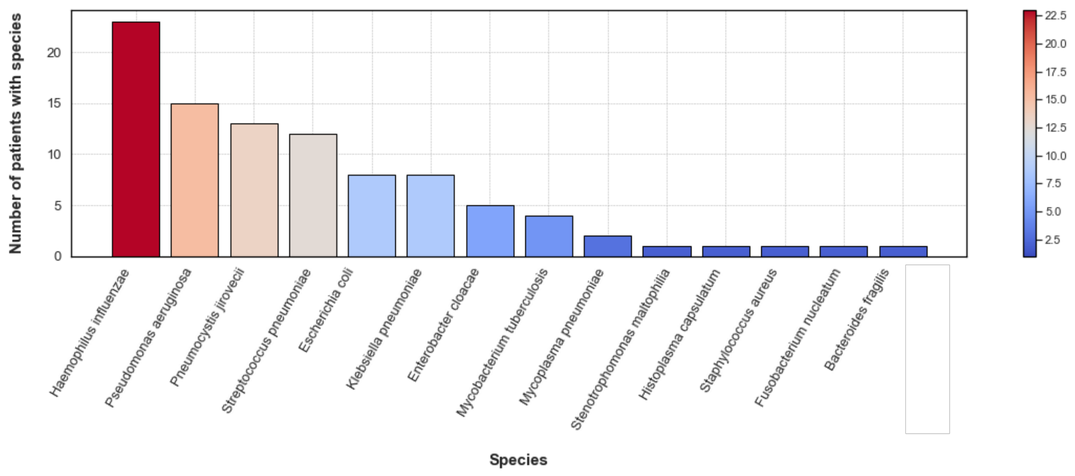
- Lower respiratory tract infections are the top cause of infectious disease-related deaths in the world.
- The causative pathogen is detectable in only 38% of adults with community acquired pneumonia.
- Time to diagnosis of pathogen is directly correctly with mortality.
- The widespread use of broad-spectrum empiric treatment contributes to the proliferation of antimicrobial resistance.
- Next Generation Sequencing could offer potential for early identification.

Methods

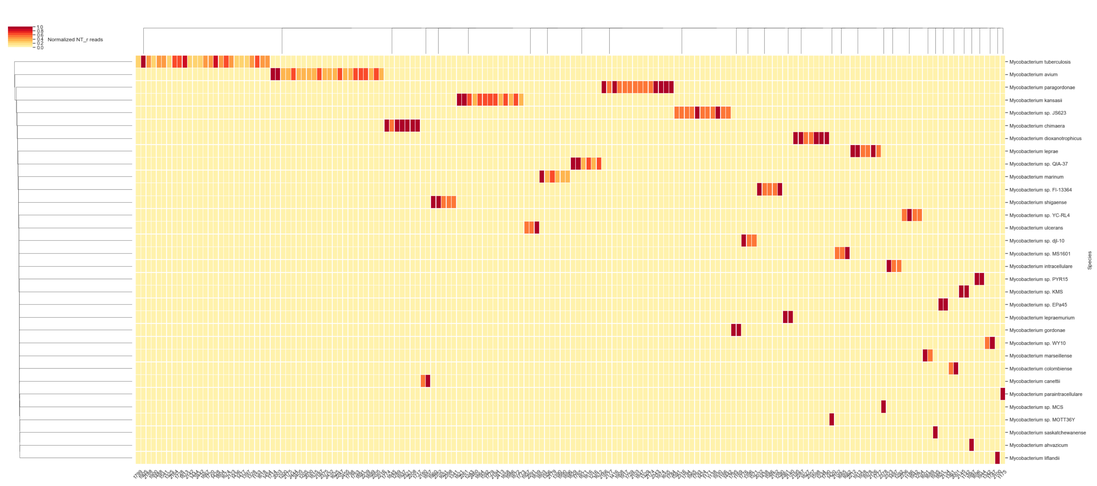
- RNA-seq from tracheal aspirates of 217 HIV+ pneumonia patients in Kampala, Uganda.
- Rules-Based Method identification of contributory pathogens using microbial abundance.
- Identified polymicrobial infections and assessed levels of opportunistic pathogens.
- Compared virus abundance between patients with CD4 counts > 200 versus < 200.
- Compared *Pneumocystis jiroveci* RNA-seq abundance (NT_r) to bronchioalveolar lavage (BAL) Giemsa stain.

Results

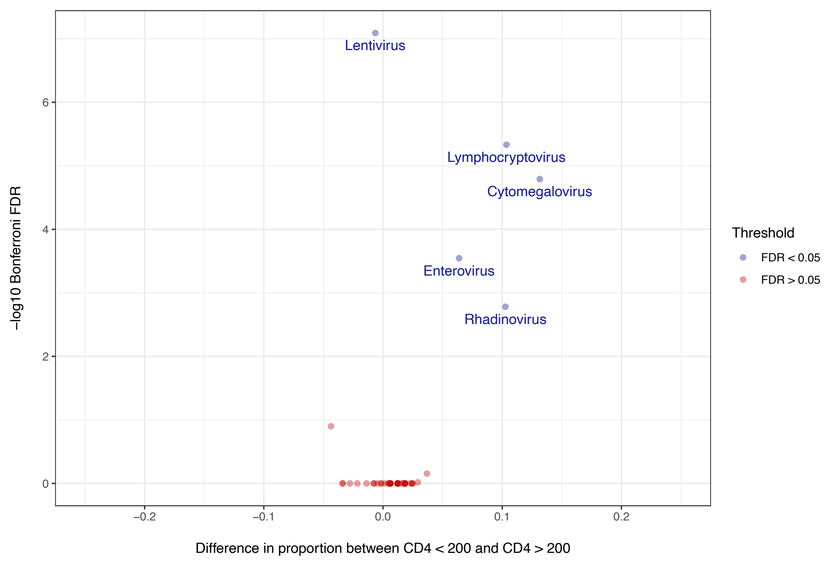
Bacterial and Fungal Pathogens



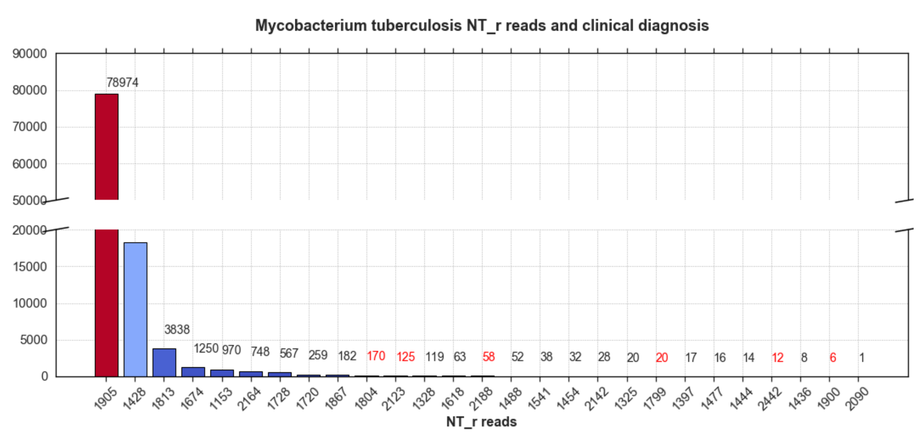
Mycobacterium Reads



Differentially Abundant Viruses in CD4 > 200 versus < 200



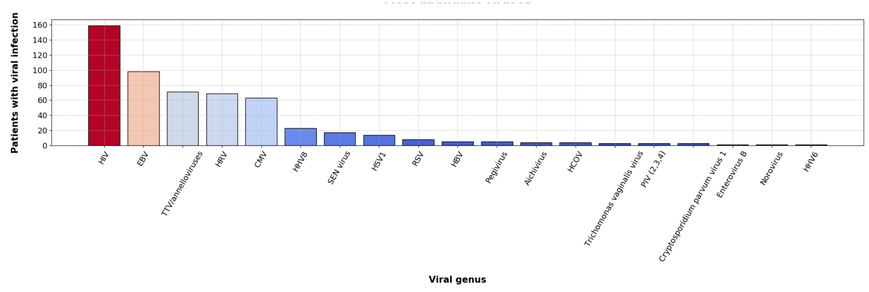
Threshold for active *Mycobacterium tuberculosis*



Pneumocystis jiroveci abundance

NT_r	BAL Giemsa	CD4 count
3,647,678	Positive	34
2,881,902	Positive	20
2,185,844	Positive	8
2,089,646	Positive	16
1,576,064	Positive	19
285,672	Positive	15
122,658	Positive	31
106,404	→ Negative	151
83,298	→ Negative	9
11,240	Positive	3
2,406	Negative	30
1,560	Negative	103
1,220	Negative	5
1,126	Negative	40
200	Negative	29
178	Negative	N/A
162	Negative	146
124	Negative	55

Viral Pathogens



Selected Patient Adjudications

	Pathogen 1	Pathogen 2	Pathogen 3	Pathogen 4
Patient 1153	Rhinovirus C	Mycobacterium tuberculosis	Pseudomonas aeruginosa	Haemophilus influenzae
Patient 1342	Human coronavirus HKU1	Streptococcus pneumoniae		
Patient 1714	Toxoplasma gondii			

Conclusions

- Apparent high number of *Pseudomonas aeruginosa* cases, an etiology not covered by the current ceftriaxone empiric treatment.
- RNA-seq identified 2 patients with high abundance of *Pneumocystis jiroveci* that had negative Giemsa stain.

References

1. Langelier C, Kalantar KL, Moazed F, et al. Integrating host response and unbiased microbe detection for lower respiratory tract infection diagnosis in critically ill adults. Proc Natl Acad Sci U S A. 2018;115(52):E12353–E12362.

2. World Health Organization (2017) The top 10 causes of death. Available at www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death. Accessed October, 1, 2018.