

Genomic investigation unmask evidence of transmission across *Mycobacterium abscessus* cystic fibrosis patients

S Alateah, C Peters, DJ Dhasmana, K Pettigrew, R Fallon, A-L Seagar, DJ Sloan, IF Laurensen, M Holden, SH Gillespie

Background

Mycobacterium abscessus (*Mabs*) is a critical respiratory pathogen in Cystic Fibrosis (CF), with significant challenges in diagnosis and treatment. Recent whole genome sequencing (WGS) studies have challenged the assumption that acquisition in CF is primarily from soil and water systems¹. We sought to investigate potential transmission of *Mabs* within and between CF centres through WGS analysis of CF isolates from the Scottish Mycobacteria Reference Laboratory.

Methods

64 isolates were recovered and sequenced from CF samples positive for *Mabs* between 2008 and 2016. Multilocus sequence typing (MLST), and phylogenetic analysis based on core genome Single Nucleotide Polymorphisms (SNPs) was used to identify dominant circulating clones. Probable transmission clusters were defined by <20 SNPs between isolates, as suggested by previous studies. This work was carried out as part of a public health investigation.

Results

MLST analysis of the 64 confirmed *Mabs* isolates demonstrated the following: 8 strain types (ST) associated with *Mabs* subspecies *abscessus*, including ST9 (n=18), ST24 (12), ST5 (7), ST26 (4), ST21 (3), and ST10 (2); 11 identified as subspecies *massiliense* associated with ST4 (4), ST6 (3), ST7 (2) and ST3 (2); 4 identified as subspecies *bolletti*.

Phylogenomic analysis provided higher resolution and identified significant relatedness between and within clonal complexes. The most prevalent subspecies *abscessus* clone was ST9, of which 16 isolates were distinguished by <20 SNPs, 12 of which from one hospital region. Five of the ST9 isolates were indistinguishable at the SNP level, and yet originated from different Health Board regions and different hospitals. ST5, ST24 and ST26 also contained isolates distinguished by <20 SNPs and originated from several geographically distinct regions.

Conclusion

WGS has provided strong evidence of the circulation of dominant clones between and within CF centres across geographically diverse settings over an 8-year period. The high genomic relatedness provides strong evidence of transmission between CF patients, even though the precise mechanisms of transmission remain uncertain. Further studies are underway to understand the mechanism of transmission in this clinical context.

1. Bryant, J. M., Grogono, D. M., Rodriguez-Rincon, D., Everall, I., Brown, K. P., Moreno, P., ... Floto, R. A. (2016). Emergence and spread of a human-transmissible multidrug-resistant nontuberculous mycobacterium. *Science (New York, N.Y.)*, *354*(6313), 751–757.
<https://doi.org/10.1126/science.aaf8156>