New rapid test diagnoses pneumonia and other lower respiratory infections

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Themoula Charalampous, a researcher on the study. Credit: Quadram Institute

Scientists at UEA and the Quadram Institute have developed a new, rapid way of diagnosing lower respiratory tract infections that could improve patient care and control the spread of antimicrobial resistance.

Lower respiratory infections, such as pneumonia, account for around 3 million deaths worldwide each year, and can be caused by a variety of different microbes.

Current diagnostic methods rely on growing bacteria from patient samples, but this takes two to three days and may still not identify the cause. During this time, patients are given broad spectrum antibiotics, which may not work if the infection is caused by a resistant pathogen and could trigger side-effects. This can also drive the development of antimicrobial resistance.

Dr. Justin O"Grady from UEA's Norwich Medical School and his team at the Quadram Institute have successfully developed a clinical metagenomics test to precisely identify the bacterial causes of lower respiratory infections.

Clinical metagenomics uses modern sequencing technology to study all the genetic material in a patient sample and identify the pathogens present. It can also identify genes that make the pathogens resistant to particular antibiotics.

The new method, developed with colleagues at the Norfolk and Norwich University Hospital and the Earlham Institute, reduces the time to diagnose the precise causes of infection to just six hours.

This allows rapid treatment with targeted antibiotics, resulting in improved patient outcomes whilst reducing the use of broad-spectrum antibiotics and helping in the fight against antimicrobial resistance.

Dr. O"Grady said: "Clinical metagenomics has the promise to revolutionise the diagnosis of infectious diseases, and our study describes the first rapid affordable and accurate clinical metagenomic test that could readily be used on a routine basis in a clinical setting."

The study, published in the journal *Nature Biotechnology*, overcomes some of the hurdles that have to date held back the widespread deployment of clinical metagenomics.

The method incorporates a step that rapidly and efficiently removes human genetic material from the sample provided by the patient, thereby leaving mainly pathogen DNA for sequencing. Funding for the study came from the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the National Institute for Health Research.

Themoula Charalampous, from UEA's Norwich Medical School, said: "Respiratory samples are difficult to work with because they are mainly comprised of human genetic material. Removing this makes detecting the pathogens easier and reduces the sequencing cost and time."

The researchers worked with Oxford Nanopore Technologies, using their portable MinION sequencing device that facilitated real-time sequencing data generation and analysis. This reduces time-to-result from days to hours.

The pilot method was tested on 40 samples from patients with suspected lower respiratory infections. The team then refined the test to improve its sensitivity and reduce the time from sample to result to six hours and

tested on a further 41 respiratory samples.

Dr. Gemma Kay, from UEA's Norwich Medical School, said: "The pipeline that we've developed in this study produces data that can be used not only for clinical diagnostics but for public health applications such as outbreak detection and hospital infection control."

The protocol is now being assessed in a larger multi-site clinical trial to evaluate its performance for the diagnosis of hospital acquired pneumonia.

"Nanopore metagenomics enables rapid clinical diagnosis of bacterial lower respiratory infection" is published in *Nature Biotechnology* on June 24, 2019.

More information: Themoula Charalampous et al. Nanopore metagenomics enables rapid clinical diagnosis of bacterial lower respiratory infection, *Nature Biotechnology* (2019). DOI: 10.1038/s41587-019-0156-5

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