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Contact

Dr Leila Luheshi

leila.luheshi@phgfoundation.org

Beating the bugs: the pathogen genomics revolution

The rapid development of low-cost whole genome sequencing technology is catalysing a transformation in the way clinical and public health microbiologists and epidemiologists can manage the threat of infectious diseases in the UK



Outbreak
epidemiology



Treatment
stratification



Surveillance



Antibiotic
stewardship



Novel threat
detection



Vaccine and
drug design

Infectious diseases are responsible for 7% of deaths in the UK per annum and 8% of all hospital bed days. It has been estimated that they cost the economy approximately £30 billion per annum.

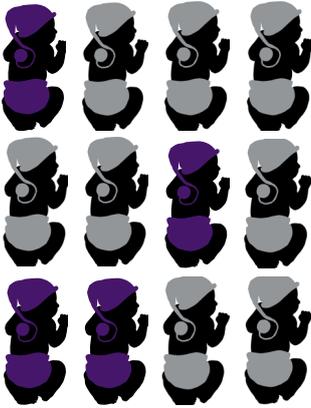
Whilst increased availability of vaccines and antibiotics have significantly reduced both mortality and morbidity associated with infectious disease in the UK over the past 50 years, the burden of these diseases remains high and our ability to combat them is under severe threat as bacteria and viruses mutate to evade both our vaccine-boosted immune systems and our antibiotics.

Overcoming this challenge will require:

- **More rapid and accurate diagnosis of infections**
- **More effective surveillance of infections** to prevent spread throughout our communities and hospitals
- **More targeted and effective use of antibiotics**

The pathogen genome revolution – faster, cheaper and more effective

The genome of a pathogen reveals (at the highest possible resolution) its identity and ancestry, the ways in which it infects us, and how it evades both antibiotic treatment and our own immune system. Furthermore, as the genomes of bacteria and viruses are between one thousand to one million times smaller than the human genome they can be sequenced and analysed more rapidly (in less than a day) and cheaply (for around £50 per genome) bringing the insights of pathogen genomics within reach of the budget and time frames in which clinical and public health microbiology services operate.



Tackling drug resistant tuberculosis

Current methods to determine the drug resistance profile of a TB infection can take more than a month to complete. Whole genome sequencing of TB promises to reduce this time to less than two weeks. This will mean patients get the right drugs sooner, improving their health and reducing the risk of further spread of the infection in the community.

Resolving an MRSA outbreak on a special care baby unit

Pathogen whole genome sequencing was used during a suspected outbreak of MRSA (methicillin-resistant *Staphylococcus aureus*) infections on a special care baby unit first to confirm that an outbreak was underway and then, in combination with epidemiological information, to identify a probable source of the infections enabling the infection control team to end the outbreak.

Why pathogen whole genome sequencing?

The effectiveness of the current standard techniques in both microbiology and virology, whilst satisfactory for many infections, is in some clinically important cases limited by the time and associated cost of performing iterative culture based analysis and molecular testing. Furthermore, the incomplete nature of the information about the organism that is obtained from these tests, and the associated difficulties in its interpretation, significantly limit its utility in clinical and public health decision making.

Introduction of whole genome sequencing of pathogens has the potential to improve the management of infectious diseases in the following ways:

- **Precision**
More precise identification of the bacteria or virus causing an infection improves the accuracy of outbreak investigation and effectiveness of infection control.
- **Sensitivity**
Pathogen genomics may enable the early detection of emerging drug resistant virus in HIV patients.
- **Speed**
For slow growing bacteria, such as *M. tuberculosis*, pathogen genomics enables faster detection of drug resistance than current culture methods.
- **Personalisation**
Genomic information can be useful in identifying which drugs will or will not be effective in treating an infection, enabling more effective personalisation of care.
- **Detecting novel threats**
Genomics are proving an important tool in improving detection and understanding of emerging infectious diseases such as Mers-CoV.

Why now is the right time to implement pathogen genomics in infectious disease management

- **A public policy priority**

The threat of spreading antimicrobial resistance, awareness that the next infectious disease pandemic could arise at any time, and the continued challenge posed by incidence of healthcare associated infections make the search to improve the way we manage infectious disease a national priority.

- **Translational research impact**

Strategic support for translational research has catalysed the development of pathogen whole genome sequencing and analysis techniques specifically designed to have applications in clinical and public health microbiology

- **Improved access to technology**

The cost of the hardware and reagents required to perform pathogen whole genome sequencing continues to fall, reducing a significant barrier to the implementation of genomics in the UK health system.

- **Patient benefit**

Early evidence from translational research studies suggests that judicious application of pathogen genomics could deliver significant patient benefits, particularly through reducing incidence of hospital acquired infections and more rapid and accurate targeting of infections with the most effective treatments.

Policy
priority

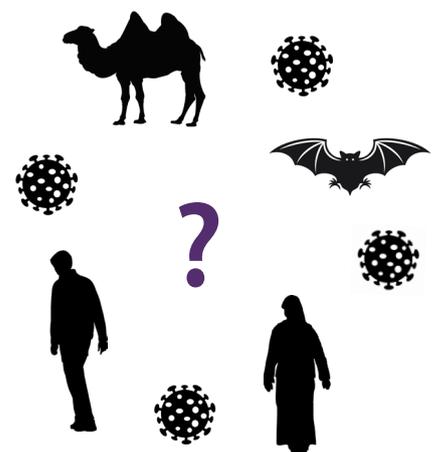
Translational
research
impact

Technology

Patient
benefit

Understanding the emergence and spread of Middle East Respiratory Syndrome (MERS)

Researchers and clinicians have worked together to rapidly sequence the whole genome of the virus (MERS-CoV) responsible for an ongoing outbreak of severe, often fatal, respiratory illness. Comparison of the MERS-CoV genome sequences from infected patients is enabling epidemiologists to better understand how the virus is being transmitted between people, and between animals and humans. This information is vital to support efforts to halt the spread of this potentially fatal disease.





The PHG Foundation is an independent health policy think-tank based in Cambridge, UK. Our mission is making science work for health.

Challenges ahead: translating pathogen genomics into practice

Whilst pathogen whole genome sequencing has the potential to transform parts of clinical and public health microbiology practice, there are many hurdles yet to be overcome before we can realise the benefits of this exciting new technology:

- **Prioritising the application of pathogen WGS in public health and clinical care**
It will be important to understand for which infectious diseases, and which infection control scenarios pathogen WGS will provide the most significant individual and population health benefits compared to continued use of existing microbiological techniques.
- **Harnessing the data**
The true benefits of pathogen WGS will only be fully realised if systems are built to curate, standardise and share both genomic data and associated metadata, enabling global surveillance, outbreak control and knowledge exchange.
- **Understanding the social impact**
Exploration of the ethical, legal and social impact of increasing the accuracy with which sources and transmitters of infections may be identified in the era of pathogen genomics will be required.
- **Establishing cost effectiveness**
Evaluation of pilot implementation programmes must be undertaken to determine whether the costs of introducing this new technology will be outweighed by the savings accruing from improved patient care and replacement of existing technologies.
- **Managing the technology transition**
The rapid pace of development in genome technology and analytics will require the design of flexible and agile laboratory and analytical capabilities in clinical and public health systems, that are able to maintain continuity of service (including backwards compatibility of data) whilst maximising the benefits of adopting the latest techniques.
- **Strengthening global cooperation**
Multinational and multi-agency collaboration, through initiatives such as the Global Microbial Identifier project, will be required to ensure that implementation of pathogen genomics in clinical and public health practice in the UK results in maximal benefit for the surveillance and control of globally significant infectious diseases.

To learn more about this project, see:
www.phgfoundation.org/project/id

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