March 2016

Authors
Dr Chris Rands
leila.luheshi@phgfoundation.org

Delivering an effective infectious disease genomics service

Infectious diseases remain a significant burden in all nations but particularly in middle and low income countries, where resulting rates of mortality and morbidity may be higher and the economic impact greater. New infectious disease genomics technologies *could* help alleviate the disease burden where traditional approaches are insufficient, but what components are needed to deliver an effective infectious disease genomics service?

Infectious disease genomics technologies services will only perform optimally if they are setup with all the components essential to an effective clinical service.

- Infectious disease genomics is the application of next generation sequencing (NGS) technologies to the genomes of harmful microorganisms (pathogens), such as certain bacteria or viruses that cause communicable diseases
- The medical applications of infectious disease genomics include diagnosing the presence of infections, tracking infectious disease outbreaks, and determining antimicrobial drug resistance
- Genomics should only be employed when alternative approaches are insufficient
- Components needed to deliver an effective, efficient and safe infectious disease genomics service include: data generation, data processing, data access, defined standards, service configuration, service evaluation and strategic collaboration
- Anticipated health outcomes from implementing infectious disease genomics services will not be achieved if these components are ignored

The recent Ebola outbreak in West Africa highlighted the importance of rapidly and accurately detecting novel infectious disease threats, and the global shortage of effective antibiotics is a major global health concern.

What is infectious disease genomics?

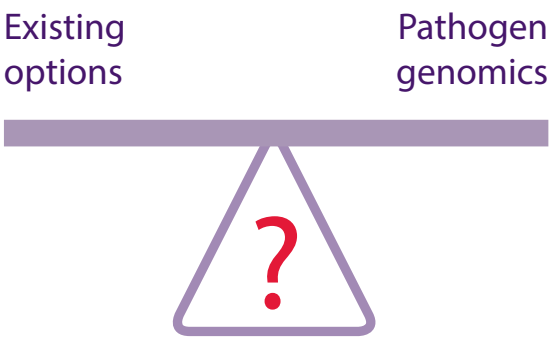
Infectious disease genomics, or pathogen genomics, is the application of next generation sequencing (NGS) technologies to the genomes of harmful microorganisms (pathogens), such as certain bacteria or viruses that cause communicable diseases. NGS covers those genomic technologies that permit the rapid parallel sequencing of DNA, including products produced by Illumina, Oxford Nanopore Technologies, Ion Torrent and Pacific Biosciences. NGS permits both whole genome sequencing and targeted sequencing approaches.

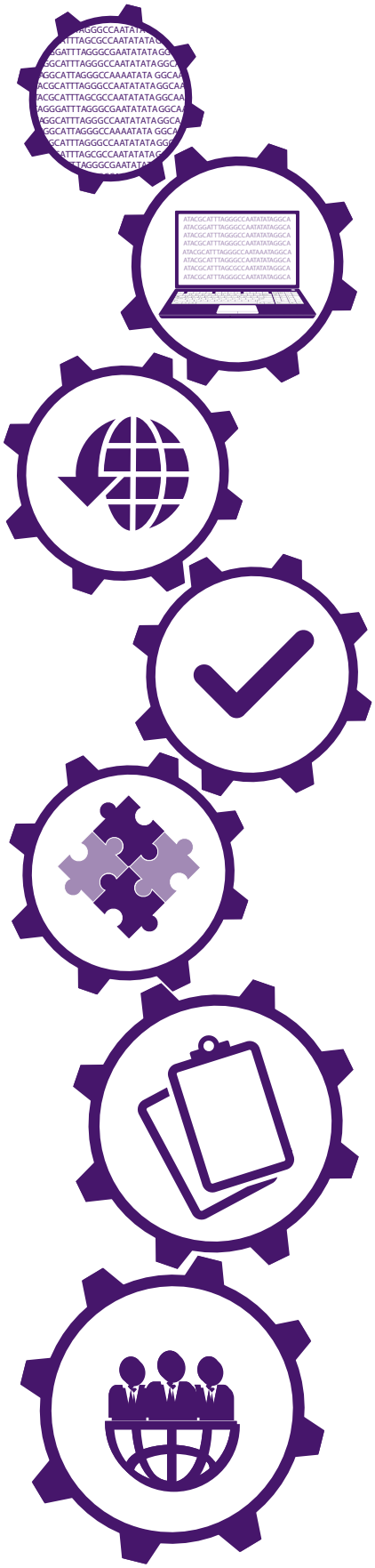
What are the medical applications?

Downstream (bioinformatic) analyses of NGS data derived from pathogen genomes has multiple possible clinical and public health applications, including: diagnosing the presence of infections, tracking infectious disease outbreaks, and determining antimicrobial drug resistance. Such utility can be critical, for example, the recent Ebola outbreak in West Africa highlighted the importance of rapidly and accurately detecting novel infectious disease threats [1], and the global shortage of effective antibiotics is a major global health concern [2].

Is genomics the best option for tackling the infectious disease burden?

Infectious disease genomics has many potential health applications, but there are alternative methods for diagnosing infections that are cheaper and easier, such as microscope-based approaches or methods that detect immune molecules produced by the pathogen. Genomics should only be employed when alternative approaches are insufficient. Other diagnostic methods may be lacking in the sense that they are too slow, cumbersome, inaccurate, unable to track outbreaks at high resolution, or unable to accurately determine antibiotic resistance, but context and pathogen-specific evaluation is required to determine when this is the case.





How to deliver an effective, efficient and safe infectious disease genomics services?

There are multiple general health system requirements for setting-up and maintaining a successful infectious disease genomics service at a national or regional level. Some of these features are listed below, drawing on **recommendations** from a recent PHG Foundation strategic **review** for implementing clinical and public health infectious disease genomics into the UK health service.

Data generation

Technologies to obtain clinical samples, extract DNA and prepare it for sequencing, and NGS machines, along with staff to operate the equipment.

Data processing

Computational resources and informatics infrastructure for data analysis and storage, and training of bioinformatics workforce with appropriate quantitative analytic skills (R26, R28, R27, R29).

Data access

Mechanisms to put curated raw sequence data with minimal metadata in the public domain and to securely and accessibly share sensitive data with relevant scientists and clinicians (R17, R18, R19, R20, R23, R24, R25, R34).

Defined standards

Standards, ideally applied at a national or international level, for the quality and format of data, in addition to minimum standards and benchmarks for methods, and standardised descriptive genomic, clinical and epidemiological terms and nomenclature (R30, R31, R32).

Service configuration

Defined pathways for each test from sequencing to clinical reporting and mechanisms to prioritise developments in laboratories that already provide extensive microbiology services, initially due to economies of scale, while also ensuring equity of access to services (R3, R4, R6).

Service evaluation

Mechanisms to evaluate (and ultimately accredit) the validity and utility of the service and each type of test, and health economic analyses to evaluate cost-effectiveness (R7, R8, R9, R35).

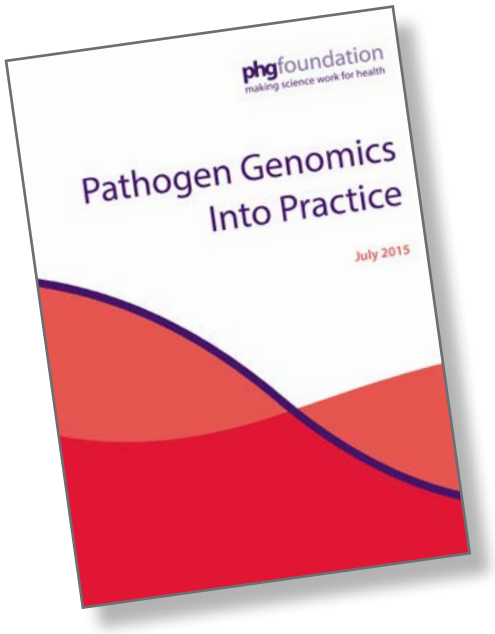
Strategic collaboration

Mechanisms to encourage human, animal and environmental health agencies, in addition to private sector stakeholders, to work together in a coordinated collaborative framework (R1, R12, R15).

What will infectious disease genomics services look like in the future?

Infectious disease genomics services could help tackle the infectious disease burden in many contexts, but there are components - from data infrastructure to coordinated clinical and academic expertise - that are required for a comprehensive pathogen genomics informed clinical microbiology service. Those health systems considering the development and implementation of such new services will need to pay attention to ensuring all these components are in place, otherwise the anticipated health outcomes will not be achieved.

The way in which these services are delivered in the medium to long term may change, for instance **metagenomics** can permit rapid culture-free detection of multiple unspecified pathogens [3]. Portable sequencers can potentially offer near 'real-time' mobile genomic epidemiology during disease outbreaks [4], and may help democratise sequencing by moving from a model where genomic services are centralised, to one where local, point-of-care genomic diagnostics are available. Nonetheless, substantial strategic planning, coordination and investment will be needed to successfully implement promising infectious disease genomic technologies sustainably throughout local health systems.



References

1. Perkins MD. *et al.* Nat Biotechnol, 33(5): p. 464-9. (2015). 2. Shallcross LJ. *et al.* Philos Trans R Soc Lond B Biol Sci, 370(1670): p. 20140082 (2015). 3. Pallen M.J. Parasitology, 141(14):p.1856-62. 4. Gardy J. *et al.* *Genome Biology,* (16):p.155 (2015).

The PHG Foundation report Pathogen Genomics Into Practice, along with a summary the roadmap to successful implementation of genomics policy services can be downloaded free from:

www.phgfoundation.org

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