Public Health England

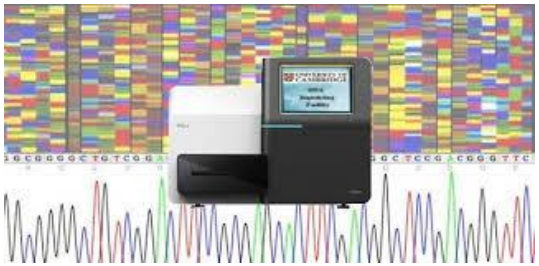
Genomics and its Impact on Diagnostic Microbiology

Rick Holliman
Lead Public Health Microbiologist for London

Public Health England

Outline

- **Where are we now?**
- **What is coming our way?**
- **How will things change?**
- **Where will we be?**



Public Health England

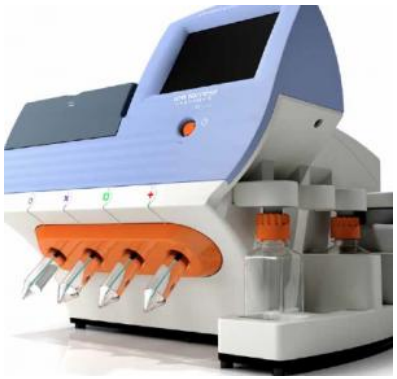
Current Clinical & Public Health Microbiology Practice

- **reactive**
- **extended TAT**
- **restricted profile**
- **most microbial tests have little direct impact on patient care**

Public Health England

Application of Genomics

- **identification of pathogens**
- **predicting susceptibility**
- **determining epidemiology**



Public Health England

First Wave Application

Pathogen	Identification	Susceptibility	Epidemiology
Mycobacteria	x	x	x
HIV		x	
HCV		x	
Clostridium difficile			x

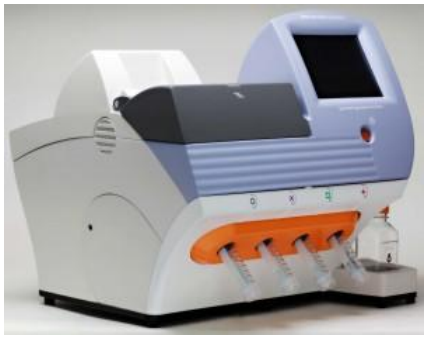
Public Health England

Second Wave Application ?

Pathogen	Identification	Susceptibility	Epidemiology
Legionella		x	x
Staph aureus (MSSA & MRSA)			x
Salmonella	x		x
Antimicrobial resistance		x	x

Public Health England

Impact of Genomics on Diagnostic Practice



- reduced TAT
- increased profile
- decreased costs
- enhanced safety
- nearer patient testing

Public Health England

Applying Genomics in Clinical Practice

- **select appropriate pathogens**
- **prioritise**
- **systematic deployment plan**
- **determine genomic diversity**
- **apply due diligence**
- **initial parallel testing**

  (phenotypic & genotypic)

Public Health England

Tools for Understanding the Genomic Stability of a Pathogen

- **re-sequencing a single sample (technical reproducibility)**
- **multiple samples from one individual at one time**
- **multiple samples from one individual over a period of time**
- **multiple samples from a point source outbreak**
- **multiple samples from the community**

Oxford Genomics Group

Public Health England

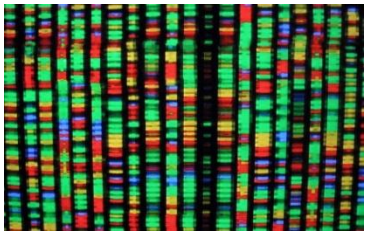
Genomic Stability Measures

Organism	SNP Rate (per year)
TB	<2
Clostridium difficile	<5
Pseudomonas aeruginosa	<10
Staph aureus	<20

Public Health England

Genomic Sequencing

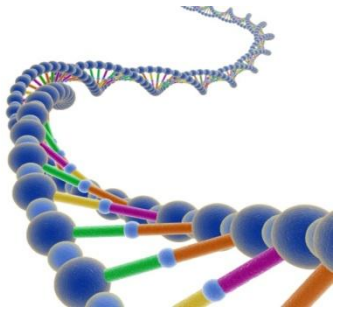
- **core genome**
- **parasitic elements - plasmids; phages**
- **accessory genome - gene variation/mutations**
- **gene pool – library of available mutations**



Public Health England

Hierarchal Genomic Sequencing

- **1 locus = 16s rRNA**
- **53 loci = rMLST**
- **>500 loci = whole genome sequencing MLST**
  - **- core genome**
  - **- core + accessory genome**



Public Health England

Question Driven Sequence Analysis

- **sequence only down to the level required**
- **Goldilocks principle applies**

- not too much

- not too little

- just right

Public Health England

Applying WGS in Clinical Practice

- **equipment**
- **IT links**
- **bioinformatics**
- **staff training**
- **assay validation – generic and specific**
- **local verification**
- **UKAS accreditation (addition to scope)**
- **IQA and EQA**
- **lead-in time with parallel testing (6-12 months?)**

Public Health England

Re-inventing the Wheel ?

- **collaboration with established local clinical services (clinical genetics, haem-onc etc)**
- **share staff, equipment, SOPs, validation, QA & accreditation**

Public Health England

Continuous Deployment

research lab

reference Lab

regional lab

diagnostic lab

NPT

Public Health England

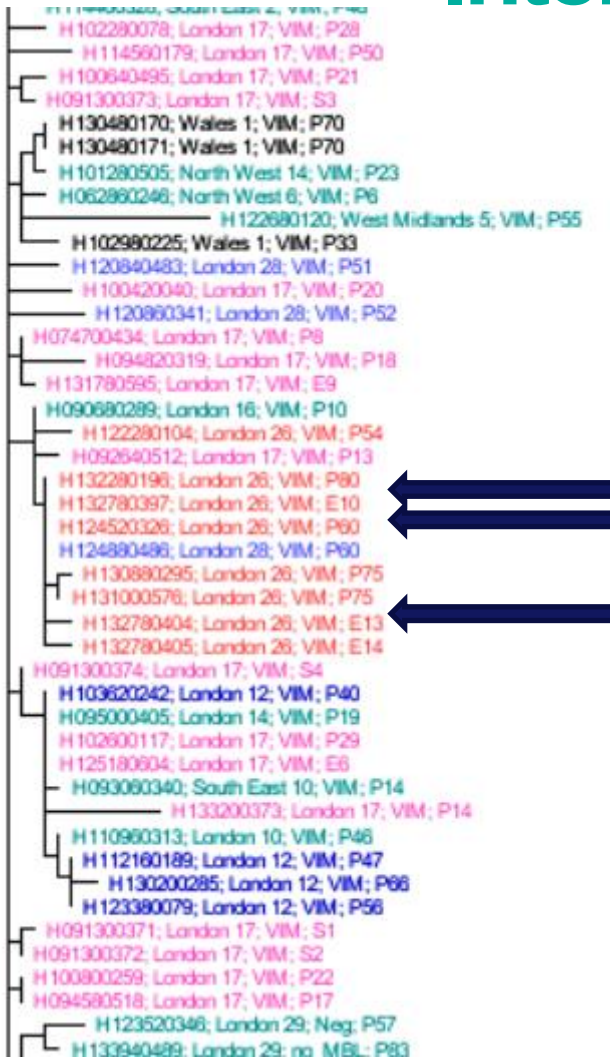
Impact on Routine & Specialist Diagnostic Microbiology

- **decreased TAT**
- **enhanced clinical impact**

- **altered staff skill mix**
- **altered working practice**

Public Health England

Informing Infection Control Interventions



site specific persistence

outbreak & transfer

sporadic

integrons & phages coding resistance to heavy metals disinfectants & detergents

Public Health England

But What About my Job?

- **altered working practices**
- **new skills & competencies**
- **data generation plus information synthesis**
- **heightened clinical profile**
- **enhanced employment opportunities through transferable skills**

Public Health England

Carpe Diem

- **due diligence**
- **risk aware - not risk adverse**

Public Health England

Required Development

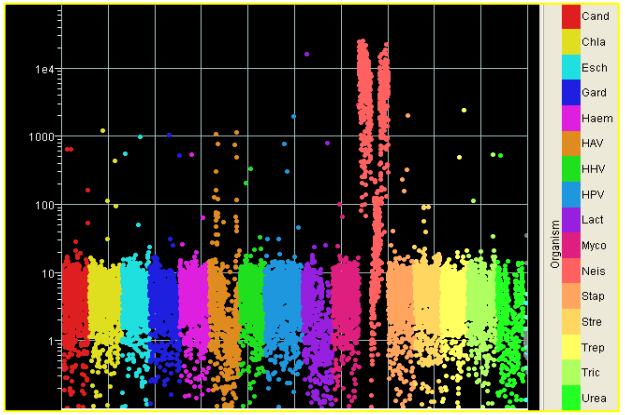
- **direct genomic investigation of clinical specimens (metagenomics)**
- **establish real time diagnosis**
- **inform effective antimicrobial stewardship**
- **guide immediate infection control interventions**

Public Health England

Not Only But Also – Other Technology

2nd generation proteomics

- **amino acid sequencing**
- **meta-proteomics**



syndromic micro-arrays & multiplex PCR

Public Health England

Summary

- **Current microbiology methods are slow, restricted and have limited direct clinical impact**
- **First wave genomics will be deployed within 6 months**
- **Genomics will have a profound impact on diagnostic, specialist and reference labs – but we will change rather than disappear**