Advanced Molecular Detection and Epidemiology

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The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Impact of incorporating whole genome sequencing (WGS)

Role of epidemiological data in interpretation of WGS data

Potential use of Advanced Molecular Detection technology in infection control
What is Advanced Molecular Detection (AMD)?
Advanced Molecular Detection (AMD)

- Impact public health
  - Investigate outbreaks
  - Understand antibiotic resistance
  - Diagnose new pathogens
  - Identify control points

- New technologies
  - Next generation sequencing platforms
  - Supercomputers
Pulsed-Field Gel Electrophoresis (PFGE): Strengths

- Universal subtyping method
- Reproducible
- Outbreaks
  - Flag disseminated foodborne outbreaks (space, time)
  - Identify isolates that are likely to have come from a common source

http://www.cdc.gov/pulsenet/pathogens/protocol-images.html#pfge
Pulsed-Field Gel Electrophoresis (PFGE): Limitations

- Relatedness is not a true phylogenetic measure
  - Related isolates may have different PFGE pattern
  - Unrelated isolates may have same PFGE pattern
- Cannot discriminate between epidemiologically unrelated isolates
- Information only at the cut sites

PFGE  WGS
Whole Genome Sequencing (WGS): Strengths

- High resolution sequence data
- Information at every point in the genome
  - True phylogenetic relatedness
  - Transmission path
  - Identify control points
Impact of Next Generation Sequencing
Impact of Next Generation Sequencing

- Challenges
  - Data overload
  - Interpretation
Integration of Epidemiology and WGS
Mycobacterium tuberculosis Outbreak

Gardy et al. NEJM 2011; 364:730-739. 24 Feb 2011
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Mycobacterium tuberculosis Outbreak

- Identified transmission pathways
- Revealed socioenvironmental factor that led to outbreaks

Gardy et al. NEJM 2011; 364:730-739. 24 Feb 2011
Healthcare-associated infection
Denver, Colorado - 2012

- 8 patients in a single acute care hospital
- Carbapenem-resistant *Klebsiella pneumoniae* producing New Delhi Metallo-Beta-Lactamase (NDM)
- Laboratory typing
  - Pulsed-field gel electrophoresis (PFGE)
  - Whole genome sequencing (WGS)

Whole Genome Sequencing

Denver, Colorado - 2012

- Identified 3 areas where improvements in infection control were needed

Infection Control and Prevention
Standard Infection Prevention Strategies

- **Standard Precautions**
  - Hand hygiene
  - Personal Protective Equipment
  - Respiratory hygiene
  - Medication safety
  - Injection safety
  - Environmental/equipment cleaning and disinfection

- **Transmission-based Precautions**
  - Contact Precautions (e.g., CDI)
  - Droplet Precautions (e.g., respiratory viruses)
  - Airborne Precautions (e.g., TB, measles)

- **Antibiotic Stewardship**
On any given day, about 1 in 25 hospital patients has at least one healthcare-associated infection (HAI)
One in every 9 patients who gets a healthcare-associated infection will die during their hospitalization.

- Vital to continue progress in healthcare epi and implementation research
Protective Role of the Microbiota
Microbiome Disruption Indices (MDI)

- CDC working to develop
- Standardized criteria
- Characterize major human microbiomes
  - Lower intestinal microbiome
Causal Pathway from Health to Disease

Normal microbiome: Resistant to colonization

Disrupted microbiome: Susceptible to colonization

Colonization with MDRO

Overgrowth and dominance

Infection and Potential for transmission

Antibiotics

Exposure to MDRO

Normal microbiome restored
Causal Pathway from Health to Disease

Normal microbiome: Resistant to colonization

Normal microbiome restored

Disrupted microbiome: Susceptible to colonization

Exposure to MDRO

Colonization with MDRO

Overgrowth and dominance

Infection and Potential for transmission

Halpin, et al. 2016 AJIC
Causal Pathway from Health to Disease

- Normal microbiome: Resistant to colonization
- Disrupted microbiome: Susceptible to colonization
- Colonization with MDRO
- Overgrowth and dominance
- Infection and Potential for transmission

Antibiotics → Exposure to MDRO → Colonization with MDRO → Overgrowth and dominance → Infection

Normal microbiome restored
Potential MDI

- Potential MDIs
  - Compositional diversity
  - Species richness
  - Presence/absence of protective species
  - Resistome
  - Functional status – metagenomics, metabolomics
Uses for MDIs

- Monitor microbiome
  - When to take remedial action (e.g., fecal microbiota transplant)
  - Antibiotic stewardship/selection
  - Infection control decisions
    - Isolation precautions for when at increased risk for transmitting (colonized, dominated)
    - Reverse isolation precautions for those at high risk for colonization (disrupted)
Uses for MDIs

- Prepare for future FDA-approved microbiome remediation therapies
  - e.g., FMT, synthetic stool, advanced/designer probiotics

- Communicate disruptive potential of drugs, including antibiotics
  - Rating system to gauge relative risks of different agents
  - MDIs determined during approval process and included in package insert
Wrap Up

- Using WGS has already had a substantial impact on our ability to investigate outbreaks

- Collect timely and accurate epi data is crucial

- Interpret WGS in the context of available epi data
Thank you

For more information, contact CDC
1-800-CDC-INFO (232-4636)

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Antibiotic Resistance Threat Report

- 18 antibiotic resistant pathogens
  - >2 million infections
  - ~23,000 deaths
  - Billions in excess medical costs

- Half are healthcare-associated infections

- Vital to continue progress in healthcare epidemiology and implementation research
Pulsed-Field Gel Electrophoresis (PFGE): Strengths

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Denver, Colorado - 2012

Whole Genome Sequencing
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