PulseNet on the High Wire

16th Annual PulseNet Update Meeting
8th Annual OutbreakNet Meeting
Atlanta, Georgia

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Disclaimers

- The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

- Use of trade names is for identification only and does not imply endorsement by the Centers for Disease Control and Prevention or by the U.S. Department of Health and Human Services.
Stone Mountain

Carving = 3 acres or ~12,000m²

Pres. Jefferson Davis
Gen. T. J. "Stonewall" Jackson
Gen. Robert E. Lee
Objectives

- After this talk, participants will:
  - Understand the challenges posed by emerging diagnostic techniques for foodborne laboratory-based surveillance
  - Know about new subtyping approaches being pursued by PulseNet
  - Describe possible scenarios for the future structure and functionality of PulseNet
Outline

- No Matter Where You Go, There You Are
- To Culture or Not to Culture; Is that the Question?
- Ability Will Never Catch Up with its Demand
- The Present is Now!
No Matter Where You Go, There You Are

Confucius / Buckaroo Banzai
So, Where Is PulseNet Now?

- >85 PulseNet participating laboratories in the US
- ~87 PulseNet International laboratories in six regions around the world

PulseNet Patterns, by Organism 1996-2011

- Nine standardized PFGE protocols
- Three standardized MLVA protocols

PulseNet National Database 2011
- "Isolates" uploaded to database: 60,234
- Total PFGE patterns submitted: 74,817

Long-term investment in next generation subtyping methods
PulseNet
- 245 Clusters Identified in CY2011
- 187 in FY2012 (as of 7/31/2012)
Where Were We Headed?

Next generation subtyping efforts

MLVA

SNP Analysis

CRISPR Analysis
Trends, Burden, and Attribution

Outbreak Detection

Control

Outbreak Investigation

FoodNet

- Distill Data
- Cluster analysis
- Correlate ‘next gen” data with historical profiles

Next Generation Subtyping Approach

Perform “Next Gen” Subtyping Locally
SNP Analysis
Array- and Luminex-based

Next (NOW) Generation Sequencing

1ST Generation Sequencing (Sanger)

OpGen
Whole Genome Mapping

Genome Sequence Scanning

Many Others…

Pathogenetix

Pacific Biosciences

Roche 454

Illumina (MiSeq)

LifeTech/Ion Torrent

Nanopore
To Culture or Not to Culture, Is that the Question?
Pathogen Specific Surveillance

- Physician/Patient
- Clinical Lab
- Public Health
- Case Reports
- Lab Reports
- Isolates
- Case Interviews
- Prevention/Control

Vet/Ag Labs

Physician/Patient

Clinical Lab

Lab Reports

Isolates

Case Interviews

Prevention/Control

Case Reports

Public Health
On a Need to Know Basis

“Private Health”

- Diagnose illness
- Guide therapy

Clinical Lab

- Lab Reports
- Rapid test
- Accurate test
- Control cost

Public Health

- Lab Reports
- Isolates

- Outbreak detection
  - Characterization
  - Subtyping
  - Susceptibility monitoring
- Limit transmission
- Control
- Monitor trends
- Informed policy development

That is the question!
Clinical Diagnostics Trending Toward “Culture-Independent” Tests

Enzyme Immunoassays

Amplification (molecular)

Mass Spectroscopy

Pathogens Included In The Panel

xTag GPP

MALDI-TOF S. Typhimurium (Proteins)

Sauer & Kliem, Nature Reviews Microbiology 8, 74-82 (January 2010)

Electro Spray Ionization (nucleic acids/PCR)
YOU'RE LATE, IT'S BEEN MOVED TO ANOTHER BUILDING AND YOU WERE SUPPOSED TO INTRODUCE THE SPEAKER

keynote:
UNDERSTANDING
ANXIETY
DREAMS
CIDT: Coping Mechanisms

- Status quo not an option
- Education/Awareness (a two-way street)
  - Culture-Independent Diagnostics Forum: Charting a Path for Public Health
    - First meeting held in April 2012 in Atlanta
    - Coordinated by CDC, APHL, CSTE
    - Attendees included regulatory, clinical, scientific, and industry experts
    - Outcomes
      - Formation of several workgroups
      - Relationships
      - Publications
      - Follow-up meetings
CIDT: Coping Mechanisms

- Guidelines and Recommendations
  - Work with medical industry to make new tests compatible with public health needs
  - Modify criteria for medical device licensure?
  - Make reflex culture reimbursable?
  - Modify State reporting rules
  - Develop isolate recovery capacity for PHLs
  - Sentinel culture-based surveillance?
CIDT: Coping Mechanisms

Technology

- **Intermediate-term:**
  - Next generation” approaches adaptable to a non-culture world
    - Characterization and subtyping

- **Longer-term:**
  - Evaluate platforms that specifically address CIDT issues
    - Next Gen Whole Genome Sequence Analysis
    - Metagenomics
CIDT: Opportunities

- Faster results
  - Improved exposure recall
  - Faster intervention
- More reported cases
- Better understanding of disease causation
  - Outbreaks of unknown etiology
- “Village” approach to adoption of new methods
- Increase the speed of diagnosis and reporting to public health
Ability Will Never Catch Up with its Demand

Confucius
Next gen subtyping tools must:

Lead to solutions that address our ability to:

- Enhance laboratory-base surveillance
- Loss of cultures/isolates to “CIDT”

Long-term approach:

- Next Generation Sequencing of Whole/Partial Genomes
- Metagenomics (“specimen sequencing”)
Path to the Future

Next Gen Sequencing:
- Complex
- Infrastructure
- Bioinformatics (bottleneck)
  - Expertise
  - Pipelines
  - Turn-key approaches
- Data quality (standardization)
- Data management, storage and security issues
- Data interpretation
- Data accessibility
It Takes a Village...
The Present Is Now!
Grater Genome Projects

- 250 STEC whole genome sequencing project
  - Reference of sequences
  - Diversity within and across STEC serotypes

- Metagenomics project
  - Stool samples

- Outbreak specific projects (*V. cholerae*, *Listeria*, *E. coli*, others)

- Collaborations with national and international groups

- 100K Foodborne Pathogen Genome Project

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FDA, UC Davis, Agilent Technologies and CDC to create publicly available food pathogen genome database

Genetic code sequencing of 100,000 food pathogens will provide roadmap to help identify causes of outbreaks

The U.S. Food and Drug Administration (FDA), the University of California, Davis, Agilent Technologies Inc., and the Centers for Disease Control and Prevention (CDC) announced today a collaboration to create a public database of 100,000 foodborne pathogen genomes to help speed identification of bacteria responsible for foodborne outbreaks.
Listeria Cantaloupe Outbreak

- Eight Listeria Isolates sent to Illumina and Life Tech/Ion Torrent for genome sequencing
- Strains represented four different outbreak patterns
- Results from sequence comparisons (based on SNPs) correlate with PFGE data
- First of a series of collaborations aimed at streamlining process
  - PHL friendly
Outbreak Detection

- Distill Data
- Cluster analysis
- “Deep drilling” analysis

Specimen, material or device

Next Gen Whole Genome Sequencing

PulseNet In The Clouds

Public?
Parallel Subtyping Universe

- Epidemiologic relevance
- Adaptable to a network like PulseNet
- Practical
- Cost effective
Forecasting the Future is Hard...

1. Atlanta, 8/27/2012 @8PM
   - Mon: 90°F, 65°F
   - Tue: 88°F, 71°F
   - Wed: 89°F, 72°F
   - Thu: 90°F, 72°F
   - Fri: 88°F, 72°F

2. Atlanta, 8/28/2012 @8PM
   - Tue: 83°F, 73°F
   - Wed: 84°F, 71°F
   - Thu: 85°F, 72°F
   - Fri: 86°F, 69°F
   - Sat: 87°F, 72°F

3. Atlanta, 8/28/2012 @10PM
   - Wed: 85°F, 72°F
   - Thu: 82°F, 72°F
   - Fri: 87°F, 70°F
   - Sat: 88°F, 72°F
   - Sun: 89°F, 73°F

4. Atlanta, 8/29/2012 @6AM
   - Wed: 86°F, 72°F
   - Thu: 85°F, 70°F
   - Fri: 86°F, 70°F
   - Sat: 87°F, 70°F
   - Sun: 88°F, 72°F
Technology, Next Generation or Otherwise, is Not a Substitute for Strong Epi
Life is on the Wire!
Karl Wallenda
Thank You!

For more information please contact Centers for Disease Control and Prevention
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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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