Outbreak Investigations and Whole Genome Sequencing

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Outline

• Role of FDA in Foodborne Outbreak investigations

• Whole Genome Sequencing (WGS) impact on outbreak investigations (Traditional and Retrospective)

• Examples of whole genome sequencing (WGS) in recent outbreak investigations

• Challenges and opportunities posed by WGS for foodborne outbreak investigations
Role of FDA in Foodborne Outbreak Investigations

• FDA’s role during outbreak investigations includes:
  – Traceback of suspected foods to their source
  – Food and environmental testing
  – Product and regulatory actions
  – Trace-forward (if needed)
  – Environmental assessments of farm or production facilities
  – Public communications
• Manages surveillance, response, and analysis activities related to incidents of illness linked to FDA-regulated human food, cosmetics, and dietary supplements

• Designed to streamline and strengthen FDA’s efforts to:
  – Detect
  – Investigate
  – Respond
  – Evaluate
  – Apply Lessons Learned
Solid lines represent lines of communication that occur for nearly every CORE outbreak; dotted lines are established for specific situations.
Identifying an Outbreak Vehicle: Lines of Evidence

Three types of evidence used:

- **Epidemiologic**: association between illness and food exposure
- **Traceback**: suspected food item links back to a common source of contamination
- **Microbiologic/laboratory**: pathogen found in the food, farm or facility

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How FDA uses WGS in Foodborne Outbreak Investigations

- **Traditional outbreak investigation** - FDA performs WGS on all outbreak-related samples to confirm epidemiologic links between cases and a suspect food item.

- **Retrospective outbreak investigations** - FDA uses WGS to identify links between FDA product or environmental isolates and clinical isolates (potential).
  - Compare FDA and state-generated sequences for food/environmental isolates with CDC and state-generated sequences for clinical isolates

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Outbreak of *Salmonella* Typhimurium Infections Linked to Coconut, 2018
**Salmonella Typhimurium Infections Linked to Coconut, 2018**

- On Jan 23, 2018, CDC notifies CORE Signals that:
  - *Salmonella* Typhimurium illnesses from six states
  - There was no definite epidemiological signal (bulk bin food products)

- States and FDA collected 23 samples from case patients home, retail outlets and distributors

- Open consumer samples of Brand A dried coconut slices revealed the presence of *Salmonella* Typhimurium
Salmonella Typhimurium Infections Linked to Coconut, 2018

WGS assisted in confirming the vehicle from multiple leads

0-2 SNPs difference
Informational Traceback and Inspections

- POS A
- Distributor A
- Distributor /Importer A
- Manufacturer A

- POS B-1
- POS B-2
- POS B-3
- POS B-4

- Distributer B
- Importer B
- Distributer C
- Manufacturer B
- Manufacturer C
Communications and Product Actions

- Outbreak posts
- Posted retail locations that received recalled bulk product
- Voluntary recall
- Import Alert
Salmonella Multiple Serotypes Infections Linked to Papaya, 2017

TRADITIONAL OUTBREAK EXAMPLE # 2
Salmonella Multiple Serotypes Infections Linked to Papaya, 2017

- *Salmonella* Anatum outbreak from March 2017
  - Papaya suspected as vehicle based on case exposures but TB did not converge, no sampling

- Subsequent sampling of imported papayas in August 2017 yielded a positive sample matching the old cluster by PFGE and WGS

- Confirmed papaya as the source of the outbreak AND demonstrated the contamination was an ongoing issue over multiple months
Salmonella Multiple Serotypes Infections Linked to Papaya, 2017

WGS contributes to further defining investigations—combining investigations/clusters
Outbreak of *Listeria monocytogenes* illnesses linked to ice-cream, 2015

**RETROSPECTIVE OUTBREAK EXAMPLE**
Listeria monocytogenes illnesses linked to ice-cream, 2015

- Feb 2015: South Carolina found LM in Company A ice cream products (7 PFGE patterns!)
- Samples collected by Texas from production facility also found LM in “scoops” produced on same line (different PFGE pattern). PFGE of scoops sample matched 2 KS cases.
- 3 additional KS cases - occurred between Jan 2014-2015 but were different PFGE patterns than the scoops ice cream
**Listeria monocytogenes illnesses linked to ice-cream, 2015**

- CDC and KS initiate epidemiologic investigation at hospital
- April 2015: WGS shows KS patient isolates are highly related to >100 ice cream isolates from TX facility
- Epi investigation confirms 4/5 patients regularly consumed milkshakes before illness onset
- Traceback determines hospital used Company A scoops to make milkshakes
Listeria monocytogenes illnesses linked to ice-cream, 2015

- Additional product samples from Company A Oklahoma facility were highly related to five additional cases.
- Company A subsequently initiated nationwide recall (all products, all production facilities) on April 21, 2015.
- Production halted in multiple facilities, corrective actions initiated.

WGS analysis by Enteric Diseases Laboratory Branch, CDC.
Advantages/Challenges of WGS

• Greater confidence in isolate relatedness
  – Breaks PFGE clusters apart, brings together different patterns

• Use of WGS for foodborne outbreak detection and response can result in:
  – Identification of more clusters, smaller case counts
  – Shift in temporal boundaries of an outbreak
  – Improved targeting of resources
  – Enhanced foodborne illness attribution
Advantages/Challenges of WGS

• Integration: Transition from PFGE to WGS in current outbreak detection and response platforms and procedures

• Interpretation: How close is close enough? What does relatedness mean?

• Communication: How do we communicate WGS results to different audiences (firms, lawyers, publicly)?
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