Whole Genome Sequencing: The Future of Food Safety

The Listeria Whole Genome Sequencing Project is a collaborative effort by federal agencies to prevent infections caused by Listeria, a germ that can contaminate food. Listeria infections are rare, but almost always severe. Most patients are hospitalized and about one in five dies.

Improving the detection and investigation of outbreaks from Listeria
Solving Listeria outbreaks is difficult. Outbreaks are often small and hard to trace back to a food source because some patients may be too sick for interviews or cannot remember what they ate. Determining if the same strain of Listeria is making people sick, meaning it likely came from the same food source, requires intensive laboratory investigation.

The Listeria Whole Genome Sequencing Project:
- Began in 2013 as collaboration between CDC, U.S. Food and Drug Administration, U.S. Department of Agriculture, National Center for Biotechnology Information, and state and local health departments.
- Combines real-time whole genome sequencing and data about the foods patients ate to:
  - Detect more clusters of Listeria infections (listeriosis) that may represent an outbreak.
  - Solve more listeriosis outbreaks faster.
  - Link cases of listeriosis to a likely food source.
  - Identify new food sources of Listeria.

Linking epidemiologic and laboratory data
This project builds on PulseNet and the Listeria Initiative. Together, these investigation platforms help scientists detect outbreaks, determine who is getting sick, and identify contaminated foods.

What is PulseNet and how does it work?
- National laboratory network that collects information about Listeria (and other) germs isolated from patients, food, and the environment.
  - PulseNet uses pulsed-field gel electrophoresis (PFGE), a type of DNA “fingerprinting.”
  - Patients diagnosed with listeriosis submit a sample from blood or other tissue that scientists use to isolate and characterize the Listeria germ causing their illness.
  - The DNA fingerprint from each patient’s Listeria germ is compared with hundreds of other Listeria DNA fingerprints.
  - When PulseNet identifies a cluster of people with related Listeria germs, they notify epidemiologists, who begin an investigation to look for a common source of the illnesses.

What is the Listeria Initiative?
- National epidemiology system that collects reports of listeriosis in humans.
- Patients are interviewed about the foods they ate in the month before they got sick.
- When investigators identify a cluster of illnesses with a possible common source, they rapidly compare information on the foods eaten by patients in the cluster with foods eaten by listeriosis patients who are not part of the cluster.
  - This gives investigators important clues about possible sources and helps to solve outbreaks.
Using whole genome sequencing for enhanced surveillance

Whole genome sequencing provides investigators with a tool to:

- Identify outbreaks before they become large.
- Determine who is likely part of an outbreak and who is not.
- Help link illnesses to contaminated foods.

Whole genome sequencing can identify related illnesses that are not evident using PFGE alone. This method provides high-resolution genetic information about the type of *Listeria* germ causing illness. Sometimes genetically-related germs may have different PFGE patterns and distantly-related germs can have the same pattern.

All *Listeria* isolates from patients are sequenced at CDC or state laboratories. Whole genome sequencing is done at the same time as PFGE and is completed in as close to real-time as possible.

Assessing the first year of the *Listeria* Whole Genome Sequencing Project

Integrating whole genome sequencing with other *Listeria* surveillance activities has:

- Improved the detection of listeriosis clusters.
- Increased the number of solved outbreaks.
- Reduced the average cluster size.

The *Listeria* Whole Genome Sequencing Project has prevented illnesses and deaths from listeriosis. It helps investigators detect and solve outbreaks faster, so fewer people get sick.

In the first year of the project, one person’s listeriosis infection was linked to prepackaged lettuce. Before whole genome sequencing, it was almost impossible to make a link between contaminated food and only one sick person who was not part of an outbreak.

In December 2014, investigators identified caramel apples as the source of a large listeriosis outbreak. Whole genome sequencing identified the illnesses as a cluster one week faster than would have occurred with PFGE alone.

<table>
<thead>
<tr>
<th>Clusters detected</th>
<th>Outbreaks Solved</th>
<th>Average Cluster Size (# of cases)</th>
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</thead>
<tbody>
<tr>
<td>14</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>19</td>
<td>4</td>
<td>20</td>
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- Not using whole genome sequencing (September 2012-September 2013)
- Using whole genome sequencing (September 2013-September 2014)

Moving into the future

Whole genome sequencing cannot solve outbreaks alone but it has dramatically improved our ability to examine *Listeria* and other germs. Epidemiologic data are critical for outbreak investigations. Solving outbreaks caused by *Listeria* and other germs will improve with continued efforts to obtain important epidemiologic data, and to strengthen the link between epidemiologic and whole genome sequencing data.