Molecular Mug Shots Make Catching Foodborne Pathogens Easier

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Source: BioScience, 62(12) : 1093

Published By: American Institute of Biological Sciences

URL: https://doi.org/10.1525/bio.2012.62.12.15

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They sicken millions of people in the United States each year, put almost 60,000 in hospitals, and kill more than 1300. It is the job of food detectives at the US Food and Drug Administration (FDA), the US Centers for Disease Control and Prevention (CDC), and the US Department of Agriculture (USDA) to find out which foodborne pathogens are responsible and trace the culprits back to their source.

This is no easy task. In the billions of years that they have been on Earth, ubiquitous microbes like *Salmonella*, among the most pervasive foodborne pathogens around, learned to adapt to almost anything nature can throw at them by commandeering survival genes from their microbial mates and rapidly evolving into new strains.

But science is evolving as well. New molecular methods such as next-generation sequencing (NGS), coupled with advanced informatics analysis, enable researchers to rapidly identify contaminating pathogens at every step in the food chain—from farms and slaughterhouses to transport, processing facilities, and supermarkets—according to Bart Weimer from the School of Veterinary Medicine at the University of California, Davis (UC Davis). "NGS is not only providing solutions to what we used to think were insurmountable challenges, it's allowing us to collect and analyze complete genome sequences from multiple bacteria in just a few days rather than a week or more," adds the FDA's Marc W. Allard.

This summer, in an unprecedented collaboration, UC Davis; the FDA's Food Safety Division in College Park, Maryland; and Agilent Technologies in Santa Clara, California, launched the 100K Foodborne Pathogen Genome Sequencing Project. Together, using the most advanced technologies, they are helping the world's public health community create a single global genomic database of 100,000 or more outbreak organisms.

Other agencies involved include the CDC, the USDA, and the National Center for Biotechnology Information, along with food oversight groups in Canada, China, Denmark, France, Germany, Japan, Mexico, the Netherlands, New Zealand, Portugal, Sweden, and the United Kingdom—a veritable Interpol of global public health policing. "We need all the [microbial] isolates we can get to better source track contaminants in the complex international food system," says Allard, who urges laboratories around the world to contribute samples. The FDA has already donated more than 500 *Salmonella* whole-genome draft sequences to the project.

In addition to *Salmonella*, the bacteria of greatest interest to the world's food detectives are *Shigella*, *Camplylobacter*, *Listeria*, *Vibrios*, and toxin-producing *Escherichia coli* such as *E. coli* 0104:H4 and *E. coli* 0157:H7. Foodborne viral and parasitic pathogens will also have their genetic material made available for global sharing.

FDA scientists, working in conjunction with the United Kingdom's Food and Environment Research Agency, recently helped validate the usefulness of NGS by successfully tracking a major outbreak of food poisoning caused by *Salmonella enterica* subspecies Montevideo back to its source. Globally, one or another of the 2500 known strains of *S. enterica* account for an estimated 1.3 billion cases of food poisoning annually, and the Montevideo variety is on the FDA's top 10 most wanted list.

In 2009 and 2010, a Montevideo subspecies of *S. enterica* found lurking in red and black pepper used to make Italian-style spiced meats infected more than 240 people in 38 states and the District of Columbia. This particular *Salmonella* confounded conventional epidemiologic traceback methods; however, by shotgun sequencing genomes of *S. enterica* subtype Montevideo from ingredient suppliers, infected patients, and samples from a variety of unrelated sources and analyzing them all with robotic genomic sequencers, the FDA researchers not only securely tied the infecting strain to pepper, they further discovered that it came from a drain in the New England processing plant that had produced the product.

As important as it is to find the exact source of an outbreak, what most impresses Allard, the study's lead investigator, is that NGS revealed a domestic origin for the *Salmonella* strain causing the food poisoning. This underscores the technique's ability to detect subtle genotypic differences, which is essential to the traceback of bacterial pathogens as they emerge in the food supply, he explains.

"The food chain is facing some very big challenges… and with world population projections and the growth of megacities, we could move toward increased megafarming," worries Weimer. "The 100K project will inform [us] about emerging pathogen adaption and [increased] antibiotic resistance that such intensive farming brings while we figure out what to do." UC Davis expects to deposit 1500 genomes into the project during its first year.

Lance Price from Translational Genomics in Flagstaff, Arizona, agrees that NGS will revolutionize how we investigate foodborne infections but cautions that the data will be only as good as the samples and metadata collected. A strong proponent of genomic epidemiology, Price notes that "the United States is currently far from implementing a truly robust and integrated surveillance program for foodborne pathogens, especially in terms of antibiotic resistance."

For more information, visit *http://100kgenome.vetmed.ucdavis.edu*.

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doi:10.1525/bio.2012.62.12.15