Review

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Omics: Fulfilling the Promise

Omics approaches in food safety: fulfilling the promise?

Teresa M. Bergholz[1], Andrea I. Moreno Switt[2], and Martin Wiedmann[2]

[1] Department of Veterinary and Microbiological Sciences, North Dakota State University, Fargo, North Dakota, USA
[2] Department of Food Science, Cornell University, Ithaca, New York, USA

Genomics, transcriptomics, and proteomics are rapidly transforming our approaches to the detection, prevention, and treatment of foodborne pathogens. Microbial genome sequencing in particular has evolved from a research tool into an approach that can be used to characterize foodborne pathogen isolates as part of routine surveillance systems. Genome sequencing efforts will not only improve outbreak detection and source tracking, but will also create large amounts of foodborne pathogen genome sequence data, which will be available for data-mining efforts that could facilitate better source attribution and provide new insights into foodborne pathogen biology and transmission. Although practical uses and application of metagenomics, transcriptomics, and proteomics data and associated tools are less prominent, these tools are also starting to yield practical food safety solutions.

Food safety challenges are constantly changing and require new approaches and tools

Foodborne diseases caused by bacteria, viruses, and parasites cause considerable disease burden worldwide. For example, it has been estimated by the Centers for Disease Control and Prevention (CDC) that about 1 million foodborne illnesses caused by known pathogens or unspecified agents occur every week in the USA [1,2]; about 50–100 deaths per week are associated with these cases. With a US population of about 300 million, this translates into a 1 in 300 chance for a given individual to experience a foodborne illness episode in a given week. Although the US data are typically cited because the US CDC has been a leader in providing estimates of total foodborne illness rates, on a population basis foodborne illness rates and burdens are probably similar in many developed countries of North America and Europe. Data on foodborne illness burdens in many parts of the world, including many developing countries, are difficult to obtain. A World Health Organization (WHO) publication suggests that 2.2 million deaths due to diarrheal illnesses occur annually worldwide [3]; many of these illnesses are likely caused by microbes transmitted via food and/or water.

Although some advances in reducing specific foodborne illnesses have been made in parts of the world (e.g., listeriosis in the USA [4]), overall progress in reducing foodborne illnesses has been slow. Importantly, the use of molecular surveillance systems (in particular PulseNet [5]) has had a major impact by improving the ability to (i) detect foodborne disease outbreaks rapidly, leading to smaller outbreaks with fewer cases (e.g., [6]), and (ii) identify outbreak sources, thereby providing information on foodborne disease transmission routes that can be used to target industry and government efforts to control foodborne pathogen transmission. However, the use of molecular tools has also raised concerns: for example, rapid detection methods could potentially lead to a decrease in pathogen isolation, and this would subsequently reduce the ability to perform subtyping (due to a lack of pure isolates from human specimens or food samples); this issue could at least be partially addressed through (omics) methods that allow rapid detection and subtyping without a need for bacterial isolation. As detailed below, many omics tools have the potential to improve considerably our ability to prevent foodborne illness cases and outbreaks (Table 1). Full consideration of both the benefits and challenges associated with these tools is essential to ensure that these tools realize their full potential (Box 1).

Whole-genome sequencing (WGS) allows improved outbreak detection and could rapidly replace currently used subtyping methods

The use of WGS as a tool for subtyping foodborne pathogen isolates has considerable potential for improving our ability to detect foodborne disease outbreaks rapidly. Although currently used subtyping methods, in particularly pulsed-field gel electrophoresis (PFGE) and multiple-locus variable number tandem repeat analysis (MLVA), have provided valuable tools for the surveillance and detection of foodborne disease outbreaks [5,7], these methods have some shortcomings that can be overcome by WGS. For instance, for highly clonal pathogens, both PFGE and MLVA may provide limited discriminatory power [8]. WGS can overcome this issue because it provides substantially increased discrimination. Examples of bacterial pathogens where PFGE may not provide sufficient

Corresponding author: Wiedmann, M. (mw16@cornell.edu).
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Table 1. Selected omics techniques and examples of their application in food safety

Technique[a]	Examples of uses and applications in food safety
Genomics (genome sequencing)	Subtyping; characterization of new and emerging pathogens; identification of assay and therapeutic targets; characterization of transmission routes
Transcriptomics	Characterization of pathogen response to stress and antimicrobial treatments; new antimicrobial discovery
Proteomics	Characterization of pathogen response to stress and antimicrobial treatments; new antimicrobial discovery; characterization of host response to pathogens; identification of protein-based assay targets
Metabolomics	Characterization of pathogen response to stress, antimicrobial treatments, and different environments (including competitive microorganisms); characterization of host response to pathogens
Metagenomics	Detection of pathogens in mixed cultures, identification of transmission routes; identification of new non-culturable pathogens; characterization of bacterial diversity in the food chain and effect on pathogen diversity and presence
Synthetic biology	Construction of control strains for detection and validation studies; construction of antimicrobial producer strains to be used for biocontrol; construction of highly virulent and wide host-range bacteriophages for detection and biocontrol

[a]Techniques discussed here are not necessarily all covered in the text of this review.

discriminatory power include *Bacillus anthracis* and *Yersinia pestis* [9–11]. An early example of the increased discriminatory power of WGS is provided by the use of this tool to characterize *B. anthracis* isolates, including isolates linked to the 2001 bioterrorism incident in the USA [12]. More importantly, PFGE and MLVA often fail to provide appropriate discriminatory power for specific subtypes within a given pathogen species, such as for particular *Salmonella* serovars. For example, it has been well documented that PFGE shows limited discrimination among highly clonal serovars such as Enteritidis or Montevideo [13,14]. In addition, DNA-based subtyping methods [e.g., multilocus sequence typing (MLST)], may not always discriminate between closely related *Salmonella* serovars (e.g., Typhimurium and 4,5,12:i:– [15]). WGS, on the other hand, will be able to differentiate closely related *Salmonella* serovars; and further experimental work is necessary to develop approaches that allow reliable serovar prediction by WGS. Recent publications have specifically shown that WGS can provide substantially increased discriminatory power which can group isolates into epidemiologically relevant groups and can help with outbreak investigations. In two independent retrospective studies, a whole-genome single-nucleotide polymorphism (SNP) approach successfully discriminated *S.* Montevideo isolates linked to the 2009 outbreak (associated with spices) from non-outbreak strains with identical pulsotypes (based on PFGE with several enzymes, e.g., *Xba*I, *Bln*I, *Spe*I, *Sfi*I, and *Pac*I) [14,16]. Based on the rapid improvements of both sequencing technologies and bioinformatics pipelines, routine application of WGS for foodborne disease surveillance is highly feasible and will provide improved outbreak detection. The US CDC, for example, has implemented routine WGS of human *Listeria monocytogenes* isolates starting in 2013 (http://www.cdc.gov/media/releases/2013/p0604-listeria-poisoning.html). WGS will not only provide improved discriminatory power over PFGE, but also will provide the data needed to determine whether strains that differ by three or less bands in their PFGE pattern are closely related and share a recent common ancestor, suggesting a common source. For example, retrospective WGS of *L. monocytogenes* isolates that differed by three bands and were linked to a large human listeriosis outbreak in Canada in 2008 indicated that these isolates were closely related, and likely both were part of the outbreak [17].

In addition to providing improved subtyping, next-generation sequencing methods also provide an opportunity for rapid generation of whole-genome sequence data that can be used to develop assays to detect specific outbreak strains or new and emerging organisms for which no detection methods are available, as illustrated by the *Escherichia coli* O104:H4 outbreak in Europe in 2011. Whole-genome sequences for multiple isolates of the highly virulent O104:H4 strain responsible for this outbreak were generated within weeks of outbreak onset and the genomes were publicly deposited [18,19]. Availability of these genome sequences was followed by rapid development of real-time PCR assays that specifically detect the outbreak strain [20–22]. Software is available that allows rapid identification of molecular targets without the need for genome annotation [21], and will facilitate similar applications with other organisms in the future.

Next-generation sequencing methods have also been used for subtyping and detection of foodborne viruses.

Box 1. Outstanding questions

Outstanding questions on omics use:

- How long will it take to apply next-generation sequencing globally in foodborne outbreak investigations?
- Will developing countries be able to adopt next-generation sequencing widely for outbreak investigations?
- How will the application of omics in food safety affect the international food trade?
- Will industry stakeholders be willing to use omics methods to detect and control foodborne pathogens?
- Will industry and regulatory agencies approve the use of challenge strains, constructed using synthetic biology, in commercial processing facilities and in the field?

Outstanding research questions:

- Is it possible to genetically engineer phages to have the host specificity needed to allow highly specific detection of target organisms?
- Is it possible to develop fully synthetic phages for biocontrol and pathogen detection?
- Do foodborne pathogen populations show enough structure to allow reliable source tracking (i.e., are there distinct pathogen subtypes, as defined by WGS, in different regions)?
- Is it possible to develop appropriate sequencing techniques and bioinformatics tools to allow prediction of PFGE patterns from WGS data?
- Is it possible to predict effective chemical hurdles that control pathogen growth from transcriptomics and metabolomics data?

Several published studies [23–25] show how these tools can improve detection of virus-related outbreaks and tracking of virus transmission routes. For example, WGS of viral RNA from stool samples of patients implicated in a norovirus outbreak in a children's hospital provided improved subtype discrimination over sequencing of the capsid gene (region D), which represents the standard scheme for subtyping of noroviruses as implemented in CaliciNet (http://www.cdc.gov/norovirus/php/reporting.html); WGS data also facilitated implementation of successful control strategies in this outbreak [26]. For foodborne parasites, whole-genome sequencing has not yet been used as extensively as for bacterial and viral foodborne pathogens. Although genome sequences have been generated for several strains representing different parasites that can be transmitted via food and water (e.g., *Giardia lamblia*, *Cryptosporidium parvum*, and *Cryptosporidium hominis* [27–29]), application of WGS to support outbreak investigations has been limited. For both viral and parasitic foodborne disease outbreak investigation, next-generation sequencing methods are often used in a metagenomics approach where DNA or RNA extracted from patients or foods is sequenced to detect pathogen signatures, as discussed in the next section.

Examples of next-generation sequencing technologies that have been used to sequence foodborne pathogens include Ion Torrent [18], 454 pyrosequencing [14], PacBio [30], and Illumina [31]; in addition, combinations of technologies have also been used. WGS of a bacterial isolate can be performed for less than $100, which is competitive with other currently used subtyping methods (as detailed in http://www.cdc.gov/pulsenet/next-generation.html). Although WGS data will allow improved outbreak investigations, they cannot replace epidemiological investigations. Even when WGS approaches are used in outbreak investigations, concordance of subtyping and epidemiological data is essential for reliable identification of outbreaks and outbreak sources. Importantly, definition of a clear SNP cut-off that determines when two isolates are 'unrelated' (and thus are not involved in a transmission event) does not seem feasible. Instead, micro-evolutionary analyses can be used to determine the most likely time of a recent common ancestor of closely related isolates, and epidemiological data can then be used to help to define meaningful clusters of closely related isolates (as detailed in [32]). Recent identification of a hypermutator phenotype in isolates of methicillin-resistant *Staphylococcus aureus* involved in an outbreak [33] also shows a specific mechanism that may complicate interpretation of SNP differences, together with the fact that the mutation rates in natural populations of foodborne pathogens are typically unknown. In addition to the development of improved approaches for interpretation of SNP differences, further development of whole-genome sequence databases for foodborne pathogen isolates (including associated metadata) is also needed. Efforts developing these databases are underway at the Center for Genomic Epidemiology in Denmark (http://www.genomicepidemiology.org/index.html), and include projects such as the 100K Foodborne Pathogen Genome Project (http://100kgenome.vetmed.ucdavis.edu/index.cfm) as well as projects in other laboratories and organizations around the world.

Metagenomics tools provide a powerful approach to disease diagnostics and food safety testing, but will require a cautious approach to data analyses and communication

The term metagenomics refers to culture-independent analysis of the genetic material of microbial communities in a given environment [34]. The ability of next-generation sequencing to generate large amounts of DNA sequence data has considerably facilitated metagenomics studies, including of food-associated and intestinal microbes [35–38]. Specific applications of metagenomics in food safety include, among others, (i) the identification, from clinical specimens, of novel and non-culturable agents that cause foodborne disease [39], (ii) characterization of microbial communities (including pathogens and indicator organisms) in foods and food associated environments (e.g., processing plants), and (iii) characterization of animal and human intestinal microbiomes to allow the identification of microbiota that may protect against infection with foodborne pathogens.

Use of metagenomics approaches has been well documented to provide a valuable approach to detect and identify the causative agent of foodborne disease cases from clinical specimens. For example, Nakamura *et al.* [40] used metagenomics approaches to identify *Campylobacter jejuni* as the causative agent for a foodborne illness case that was not diagnosable by conventional microbiological culture. Briefly, metagenomic analyses showed that the DNA of *C. jejuni* was present in a fecal sample collected from a patient who experienced campylobacteriosis-like symptoms, but this DNA was not present in a fecal sample collected from the same patient 3 months following clearance of the infection, suggesting *C. jejuni* as the causative agent [40]. Viral metagenomics studies can similarly be used to identify novel or known viruses in humans [41]. Interestingly, a recent study in Japan illustrates how metagenomic approaches can identify novel parasitic pathogens that cause foodborne illness [42]. In this specific study, a combination of epidemiological investigations, metagenomic studies, and animal studies helped to identify the myxosporean parasite *Kudoa septempunctata* as the likely etiological agent responsible for several foodborne illness outbreaks associated with the consumption of a specific fish species (olive flounder; *Paralichthys olivaceus*).

Although there are many opportunities to use metagenomics tools to support detection of foodborne pathogens from foods and food-associated environments, most metagenomics studies on the detection of microbes in foods have focused on characterizing the microbial ecology and microbial successions during fermentations [43], for example of kimchi [44,45]. The opportunities for metagenomics approaches to improve foodborne pathogen detection are illustrated by a study that used metagenomics approaches to characterize the species composition associated with the tomato phyllosphere – both on the native plant and in the pre-enrichment and enrichment media used to isolate *Salmonella* [46]. This study was conducted because isolation of *Salmonella* from the tomato phyllosphere has previously proven challenging despite the fact that tomatoes have been implicated as the source of several human

salmonellosis outbreaks. Interestingly, this metagenomic study identified considerable growth of *Paenibacillus* spp. during enrichment; this is important because this organism may outcompete or even kill *Salmonella* during enrichment. In addition, sequences matching different *Salmonella* serovars were identified both from the uncultured samples as well as from different enrichments, suggesting the presence of *Salmonella* despite the fact that these samples were negative by both bacteriological analytical manual (BAM) methods and real-time PCR. Although these findings do support the possibility that *Paenibacillus* may have outcompeted *Salmonella* during enrichment, it is also possible that the detection of *Salmonella* DNA sequences is due to presence of dead *Salmonella* cells.

Although several publications thus support the potential for metagenomics applications in food safety, the use of metagenomics as a tool for the detection of foodborne pathogens in food-associated environments and foods still faces several challenges. For one, metagenome sequencing will detect DNA from both dead and alive organisms. Although DNA from dead cells may degrade over time, this still presents a challenge because samples may be classified as positive for a foodborne pathogen due to dead cells (e.g., for food samples tested after pasteurization or environmental samples tested after sanitation). This challenge could potentially be overcome by using metatranscriptomics approaches [47], but even there extended persistence of some mRNA species, after cell death, cannot always be excluded. An additional challenge is that both metagenomics and metatranscriptomics approaches will create massive sequence data sets linked to a given food or food-associated facility (e.g., processing facility or farm), and these are likely to contain at least some sequence data that can easily be misconstrued as indicating a food safety hazard (e.g., the presence of antimicrobial resistance genes or virulence genes). Because, at least in some countries, food safety testing data may have to be released, under specific circumstances, to lawyers or regulatory agencies, some facilities may be reluctant to use these tools out of fear that the data created could inadvertently (and incorrectly) implicate a facility as having evidence of pathogen presence in a food or environment. In addition, data from metagenomic studies of human specimens could potentially be linked to individuals because the data generated may also contain host sequence data that could potentially identify a patient. Both these potential issues may be addressed through initial filtering and removal of sequence data (e.g., human sequences). Future development of guidelines on the proper and ethical use of metagenomics data in food safety may nevertheless be necessary to encourage and facilitate the use of these potentially powerful tools.

Transcriptomics, proteomics, and metabolomics provide future opportunities to develop improved approaches to control foodborne pathogens from farm to table

With the aim of developing rational control strategies for foodborne pathogens in the food supply, there is a need to determine the physiological state of pathogens when present on foods. Modulation of gene and protein expression in response to stress indicates activation or repression of a specific physiological response, and this can be used to determine the physiological state of the pathogen under different conditions. Several studies over the past 10 years have assessed transcriptomes and/or proteomes of bacteria under conditions simulating those a pathogen may experience on a food; for example, the low water activity and low temperature that *E. coli* O157:H7 could encounter during beef carcass chilling [48]. Other recent studies have evaluated changes in gene expression of pathogens inoculated onto actual food products, such as *Salmonella* on cilantro and lettuce [49], *E. coli* O157:H7 on lettuce [50], and *L. monocytogenes* in milk [51]. Although all these studies assess different pathogens in different food matrices, all show increased expression of stress response genes, including the general stress response, the cell envelope stress response [50], and the oxidative stress response [51]. Activation of these stress responses while on foods has the potential to impact resistance or sensitivity of the pathogen to subsequent processing treatments; for example, the significant upregulation of genes involved in *E. coli* O157:H7 cell envelope stress response on lettuce could lead to increased resistance of the pathogen to decontamination treatments that damage the cell envelope.

In addition to understanding the physiological state of pathogens on foods, transcriptomics can be used to assess how microbes respond to physical, chemical, or biological food preservation treatments. In many cases it is known that a specific compound has an antimicrobial effect, but there is limited information about the effects of that antimicrobial at the molecular level. A characterization of the transcriptional response of *E. coli* O157:H7 to the antimicrobial cinnamaldehyde highlighted that the initial response of the pathogen was to activate the oxidative stress response and, after a relatively short period of time, was able to overcome the antimicrobial stress by converting cinnamaldehyde to cinnamic alcohol [52]. A characterization of the proteome of *S.* Enteriditis exposed to propionate determined that the DNA-binding protein Dps and the cell envelope stress response regulator CpxR played significant roles in the ability of the pathogen to survive the stress [53]. Food preservation treatments are typically used in combination, referred to as hurdle technology. Hurdle technology combines different preservation methods to inhibit microbial growth. Ideally, the hurdle components will exhibit synergy – meaning that the level of inhibition achieved by the combination of the growth inhibitors is greater than the sum of the levels of inhibition achieved by each inhibitor alone. Conversely, multiple hurdles could have antagonistic effects and lead to cross-protection, where bacterial adaptation to one hurdle reduces the effectiveness of sequential or concurrent hurdles. An understanding of the modes of action of these growth inhibitors enables us to understand how synergy works at a mechanistic level. For example, an investigation of changes in the transcriptome of *L. monocytogenes* exposed to commonly used growth inhibitors lactate and diacetate, both singly and in combination, suggests that the synergistic effect of these two organic acid salts is because the pathogen must shift fermentation pathways

to produce acetoin instead of lactate or acetate [54]. Production of acetoin prevents further acidification of the cytoplasm, but also results in less energy being produced, and this contributes to the reduced rate of growth of *L. monocytogenes* in the presence of these acids. In addition to providing mechanistic information on how bacteria are responding to control strategies, the data suggest that additional treatments that interfere with energy-generation processes could be used to reduce further the ability of *L. monocytogenes* to grow.

There is tremendous potential for transcriptomics and proteomics data to be utilized for rational development of new control strategies for foodborne pathogens. One promising approach is to use the information from these studies to identify new compounds that specifically interfere with pathways important for survival in foods. As an example, a recent study identified that the small molecule fluoro-phenyl-styrene-sulfonamide (FPSS) specifically inhibits the activation of the general stress response sigma factor, SigB, in *L. monocytogenes* [55]. If the general stress response is induced by *L. monocytogenes* in foods, compounds such as FPSS may be useful as an additional control measure to inhibit the general stress response and reduce survival of the pathogen. Transcriptomics data from foodborne pathogens under different environmental stresses have also been used to identify biomarkers related to specific resistance characteristics of the pathogen [56]. These data are proposed to be integrated into mathematical models to predict microbial behavior [57], also with the potential to improve control measures.

The combination of synthetic biology and omics approaches provides new opportunities to solve old food-safety problems

Although synthetic biology may not be considered an 'omics' technique *per se*, the tools associated with this emerging discipline may have some important applications in food safety. Synthetic biology is often defined as the application of engineering design principles to biology [58]. Synthetic biology can be used to design organisms or systems to produce biological compounds effectively, including for use in food [59], and thus represents a promising platform for the development and synthesis of new antimicrobial compounds, including compounds that could be used in foods, such as bacteriocins. For example, synthetic biology could be used to facilitate the synthesis of novel types of leaderless bacteriocins [60].

Although the generation of a completely synthetic microorganisms in 2010 [61] illustrates the potential for synthetic biology to break new ground, one does not need to look very far to see potential opportunities for use of custom-designed bacteria in food safety. For example, pathogen strains that have been constructed to contain unique deletions or signature sequences (e.g., strains expressing GFP) can be used as control strains in testing laboratories [62]; use of these types of control strains facilitates the detection of false positive laboratory results due to contamination with a laboratory control strain. Similarly, Murphy *et al.* [63] reported *S. enterica* and *L. monocytogenes* strains constructed to express GFP and associated real-time PCR assays for GFP detection, which, in combination, could be used as positive controls that are added to samples before enrichment, therefore monitoring for false negatives due to steps anywhere in the sample testing from enrichment to detection.

In the future, one could also envisage the use of specifically constructed bacterial mutant strains (or even fully synthetic bacteria) as challenge strains for in-plant process validation. Currently, validation of bacterial kill steps has to be performed either in Biosafety Level 2 (BSL-2) laboratories or processing facilities with pilot-scale equipment, or under experimental conditions (which does not reflect the in-plant conditions) or in plants, but using surrogate organisms (which do not necessarily have the same characteristics as the pathogenic target organisms) [64]. Although use of attenuated strains for validation studies has already been reported [65], in the future pathogen strains could potentially be constructed for validation studies to (i) be virulence-attenuated, and (ii) have deletions in appropriate genes to ensure that these strains are not detected with conventional or molecular methods. In addition, these strains could be fully characterized by both genome sequencing and transcriptomics studies to ensure absence of potential genes of concerns (e.g., antibiotic resistance genes) and stress-response systems equivalent to the parent strains. Although the use of these types of strains of course would need to be discussed and potentially approved by regulatory agencies before such efforts are undertaken, this provides an example of the type of new approaches to food safety that a combination of synthetic biology and genomics approaches could facilitate.

Synthetic biology, together with genomics, can also be used to design new phages that can be used for either pathogen detection or biocontrol. Genetically engineered phages have been constructed for pathogen detection (e.g., for detection of *B. anthracis* or *E. coli* O157:H7 [66–68]). Appropriate reporter phages (e.g., phages expressing luciferase or GFP) permit rapid detection of the target organisms from different matrices (e.g., clinical specimens or food samples), even though a short enrichment or resuscitation step may still be required. Phages have also been engineered to modify their virulence; for example, a lysozyme-inactivated GFP-labeled phage was constructed to detect viable and viable but non-culturable *E. coli* [68]. In addition, for biocontrol of *E. coli* O157:H7, non-lytic phages have been engineered to encode proteins that are lethal for the host cell (lethal transcriptional regulator); this engineered phage can kill *E. coli* without releasing phage progeny, and is therefore without causing potential ecological disturbance [69]. Because viable synthetic phages have already been constructed [70,71], it is likely that we will see use of synthetic phages to control and detect foodborne pathogens in the not too distant future.

The potential of combining omics methods and synthetic biology is also illustrated by new approaches that have been taken to address food contamination by aflatoxin, a cancer-inducing mycotoxin produced by *Aspergillus flavus* [72–75]. As of December 2013, approximately 20 genomes of *Aspergillus* strains have been sequenced and deposited in a database that contains these genomes and associated RNA-seq data (http://www.aspgd.org). These omics data have led to the identification of genes involved in aflatoxin

production and to the development and application of engineered atoxigenic *A. flavus* strains; these atoxigenic strains compete with toxigenic strains in the field, and thus reduce aflatoxin in food [74]. Although the examples provided here illustrate that synthetic biology presents considerable opportunities for improving food safety, there also is a need to define further potential risks (e.g., through horizontal gene transfer) that may be associated with the release and use of synthetic bacterial or fungal strains and phages in foods.

Concluding remarks

Although omics approaches are potentially on the verge of making major impact in some areas of microbial food safety, there are several areas where use of these approaches is still in its early stages. Adoption of next-generation sequencing as a common tool for outbreak detection and research in food microbiology will not only require investment in equipment but also in trained personnel (Box 1). To facilitate further use of these approaches efforts are needed to train scientists who can bridge food and public health microbiology, omics tools, and bioinformatics. Development of faster, less computationally intensive, and easier to use bioinformatics tools will also play a crucial role in facilitating further use of omics tools, and may be more important than the almost inevitable further improvements in sequencing technology. In addition, the development of appropriate legal frameworks for the use of omics data and results will also be important to facilitate industry and government use of these tools.

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