Food Safety magazine

A Silver Lining of the Pandemic: Whole-Genome Sequencing and Food Safety

The benefits of whole-genome sequencing are far ranging

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With the coronavirus disease 2019 (COVID-19) pandemic, whole-genome sequencing (WGS) has proven once again to be an efficient tool for outbreak investigations. The first sequence of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was published on January 10, 2020.[1] WGS was continuously used to investigate the virus's genetic variants and their spread, to understand the impacts of mutations, and to monitor emerging lineages.[2] The sequenced data and relevant information have been made available on open-source platforms, leading to scientific collaboration and accelerating research on the virus.

A prominent example of such collaboration is the "Nextstrain" project[3] with its online platform, which has enabled scientists to upload real-time data and facilitated further scientific analyses. While interpretations of the information on such platforms may have been used for decision making,[4] one of the most redeeming values of the open platform is that it connects scientists to the general public, as this is a scientific communication tool with effective visuals.[5] This confirms the importance of securing an enabling environment for global WGS data sharing, which was discussed extensively at a meeting convened by the Food and Agriculture Organization of the United Nations (FAO) in 2016.[6] The scope of the meeting was on WGS applications, particularly for food safety management, which deals with various types of pathogenic microbes.

Greater Detail and Precision Available through WGS

Zooming out and taking a broader perspective, WGS benefits are particularly visible in microbiology: WGS provides rapid identification and characterization of microorganisms with a level of precision that no tool has ever reached before. Through WGS, specific novel antibiotic targets (resistance genotypes) are being identified in the area of antimicrobial resistance (AMR) studies. It is a significant stepping-stone because more focused surveillance and more targeted diagnostics and drug development are made possible by identifying them and correlating them to the observed phenotypes.[7]

The level of detail provided by WGS makes it possible to refine case definitions precisely, which in turn allows for faster investigation of outbreak clusters, thus preventing additional cases of diseases sooner. For example, in 2014, a multinational *Salmonella* outbreak investigation was conducted in Europe where WGS was used to identify the root cause, and the data collected pointed to some egg farms in a specific location. While WGS was essential in the investigation, it was the international data-sharing efforts that made the investigation successful and conclusive.[8] Another example is the outbreak investigation of *Listeria* linked to enoki mushrooms in Canada where the specific sequence of the *Listeria* strain was internationally shared, resulting in successfully tracing the multinational food safety outbreak and the rapid recall of the affected products.[9]

Expanding Availability of WGS beyond Wealthy Nations

In the last several decades, consumer concern for chemical additives, residues, and contamination in food has grown due to both acute and chronic impacts on human health. While this is a legitimate threat, the reality is that the impact of microbiological contamination in food—caused by pathogenic bacteria, viruses, and parasites—is much larger. Worldwide, it kills an estimated 420,000 people and makes about 600 million people fall ill every year.[10] Meanwhile, the verified effectiveness of WGS has provided a number of countries with increasing confidence in investigating food safety outbreaks.[11]

As of 2021, WGS has been employed for regulatory purposes in the area of food safety by more than 20 countries.[12] However, most of these are high-income countries, and it has been a challenge for many low- and middle-income countries (LMICs) to fully benefit from WGS. Establishing microbiological laboratories that can test every single type of foodborne pathogen requires economic resources and technical capacities. Although it would require a substantial initial investment, WGS offers a strategic option, given its wide applicability for multiple pathogens, which could ultimately be cost effective.[8]

It is critical for the international community to develop a collective understanding of the global benefits of data sharing in tackling public health problems such as the current pandemic and food safety issues. The perceived state of urgency of pathogenic microbial contamination in food is not the same as that for SARS-CoV-2; however, open discussions held by various international communities confirmed the fact that global data sharing is not only effective but also essential to understand, mitigate, and manage microbiological food safety risks the same way it is doing for COVID-19.

For COVID-19, a number of SARS-CoV-2 sequences are now available online notwithstanding issues linked to the legal ownership, privacy laws, and the possible lack of trust on the ultimate use of the data. A driving force that led to the open data sharing of the coronavirus genome data was the call from scientists "for the rapid response against the biggest health threat to humankind in a very, very long time."[13] This will aid them in accelerating research to fight the virus and contribute to managing the effects of the pandemic through informed public health decisions.

The issues of privacy, ownership, and intellectual property rights would probably be raised if WGS data were shared for food safety purposes, and concerted international efforts would be necessary to address them. To share the benefits of genetic resources in a fair and equitable way, the Nagoya Protocol[14] was adopted in 2011 and entered into force in 2014; as of March 2021, it has been ratified by 130 parties.[15] The protocol and other relevant international instruments are expected to address the concerns over global sharing of WGS data with future revisions.

In 2018, a focus group study conducted by FAO identified a remarkable scientific status in LMICs: Scientists are confident about the use of WGS as they confirmed the existence of the relevant scientific capacity to use the technology in their countries. However, the main challenge is connected to government allocations of sufficient financial/human resources to introduce WGS.[16] While various technical capacities still need to be improved, policy makers and government officials also would need a good understanding of how WGS works.[17] Because of the pandemic, terminology such as "genes," "genome," "strains," "variants," and "sequencing" has become familiar to many nonexperts; thus, the timing is ripe to delve into considerations of expanding the use of scientific approaches in policy making.

WGS in Kenya: Successfully Pinpointing Disease Hot Spots

A collaborative effort captured in a concise case study illustrates the benefits of the technology and has caught the attention of policy makers. For 15 years, a research institute in Kenya conducted basic microbiological detection for selected pathogenic foodborne bacteria. Recently, the institute started collaborating with various government agencies to engage in this initiative and utilize WGS, sharing the data obtained openly among them. As a result, WGS demonstrated its strong ability to cluster the cases and was deemed successful in mapping disease hot spots, where the existing empiric treatment regimens could be revised and high-risk foods identified during outbreaks. The Kenyan government became more willing to consider investing in food safety and outbreak investigations, and there is a renewed interest by government ministries to analyze microbial food contamination and AMR in priority pathogens along the food-chain continuum.[8]

It is important to raise government authorities' awareness of WGS because the technology is becoming more accessible and affordable. Over the last decade, the cost of sequencing has sharply dropped and is expected to decrease even more in the future. The latest sequencing equipment is extremely sophisticated, and its simplified setup has made the sequencing process like an easy-to-follow recipe.[18] However, it has further highlighted the fundamental challenges of proper collection and use of the data. While anyone can be trained to mechanically run the sequencer, the handling of the big data it produces, analysis and interpretation, and the appropriate use of the conclusions in real-life decision making are still a major aspect of food safety management. Thus, bioinformatics, which transforms data into actionable information, has become a key expertise in employing WGS. While there are multiple reliable open-source bioinformatics tools and apps available for WGS data analysis at almost no cost, such tools can easily become a black box for those who lack a basic understanding of bioinformatics. To employ WGS and use the outputs for food safety management, it is important to have a skilled professional who can validate the parameters used for the bioinformatics.

In many countries, especially LMICs, bioinformatics is not a subject that university students can major in, nor is it part of the curriculum. This modern discipline could be a candidate for better inclusion in postsecondary education programs. It takes considerable time to groom a knowledgeable and experienced bioinformatician who has the necessary understanding in informatics, programming, and technologies. For food safety applications, it is critical for bioinformaticians to fully understand what output microbiologists would need from the data analyses and how this output can best be translated into actionable information. It would thus require the knowledge and expertise of more than one person to complete the WGS analyses that can be used for food safety management.

However, it is unfortunately a common practice in many LMICs that scientists in microbiology or virology are also tasked with most of the work on bioinformatics. Without having the discipline of bioinformatics evolving into a profession at a national level, WGS cannot achieve its optimal usefulness, and the quality of interpretations of the data will be limited. Given the changes at the global level, a periodic review of educational curricula is recommended for the authorities so that the selection of disciplines can include modern topics like bioinformatics. Otherwise, younger generations will not have the optimal skill sets to compete successfully in this job market when they are ready to work in 10 years or so.

Training to Fill the WGS Expertise Gap

To fill the current gap and to build the needed capacities in LMICs, several international communities have provided a number of technical trainings. FAO partners with two nonprofit bodies, namely the Global Microbial Identifier (GMI) and PulseNet International, and supports their initiatives to provide technical WGS training to scientists and government officials in LMICs. GMI organizes regular hands-on trainings on the latest compact sequencing machines and provides interlaboratory performance tests to facilitate harmonization and standardization in WGS and data analysis. In 2019, GMI supported bioinformatics training sessions for LMICs with the open-source bioinformatics tools developed by a public university that partners with GMI. PulseNet International uses its global laboratory networks to provide general guidance on how WGS can be used in the area of food safety. The pandemic has created various "new normals," and one of them is a greater comfort with remote learning and working. With this trend and more advanced technologies like virtual reality, the international science community can help further the scientists and government authorities in LMICs to improve their capacities on WGS for food safety.

The merit of globally shared WGS data is not limited to the data availability itself. WGS works on the basis of identifying homologies or similarities between newly obtained sequences and those stored in reference databases. Therefore, without a variety set of globally available sequenced data, WGS's biggest benefit—the ability to match and identify the exact sequences—won't be realized in full. For this very reason, strengthening the relevant capacities in LMICs will not only benefit LMICs but also contribute to the global good, given that food systems are global, with enormous amounts of food traded around the world.

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References

1. **Wu, F., et al. 2020. "A New Coronavirus Associated with Human Respiratory Disease in China."** ***Nature*** **579: 265–269.**
2. **European Centre for Disease Prevention and Control. 2020. Technical note: Sequencing of SARS-CoV-2.**
3. **https://nextstrain.org/.**
4. **Oude Munnink, B.B., et al. 2020. "Rapid SARS-CoV-2 Whole-Genome Sequencing and Analysis for Informed Public Health Decision-Making in the Netherlands."** ***Nat Med*** **26: 1405–1410.**
5. **Hadfield, J., et al. 2018. "Nextstrain: Real-Time Tracking of Pathogen Evolution."** ***Bioinformatics*** **34(23): 4121–4123.**
6. **http://www.fao.org/3/a-i6582e.pdf.**
7. **https://www.frontiersin.org/articles/10.3389/fpubh.2019.00242/full.**
8. **http://www.fao.org/3/i5619e/i5619e.pdf.**

9. **https://www.inspection.gc.ca/chronicle-360/science-and-innovation/sharing-bacterial-dna-data-helps-solve-internation/eng/1614737830950/1614737831200.**
10. **https://www.who.int/health-topics/food-safety.**
11. **http://www.fao.org/3/i5790e/i5790e.pdf.**
12. **At the end of 2016, countries that had adopted WGS for food and waterborne diseases were: Australia, Austria, Belgium, Canada, China, the Czech Republic, Denmark, Finland, France, Germany, Iceland, Ireland, Italy, Luxembourg, the Netherlands, Norway, Poland, Slovenia, Sweden, the United Kingdom, and the United States.**
13. **https://www.nature.com/articles/d41586-021-00305-7.**
14. **The full title of the protocol is "the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity."**
15. **https://www.cbd.int/abs/nagoya-protocol/signatories/.**
16. **Apruzzese, I., et al. 2019. "Investing in Food Safety for Developing Countries: Opportunities and Challenges in Applying Whole-Genome Sequencing for Food Safety Management."** ***Foodborne Pathogens and Disease*** **16(7): 463–473.**
17. **Healy, M.J., et al. 2016. "Regulatory Bioinformatics for Food and Drug Safety."** ***Regul Toxicol Pharmacol*** **80: 342–347.**
18. **Giani, A.M., G.R. Gallo, L. Gianfranceschi, and G. Formenti. 2020. "Long Walk to Genomics: History and Current Approaches to Genome Sequencing and Assembly."** ***Comput Struct Biotechnol*** **J 18: 9-19.**

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SIDEBAR

FAO Resources

FAO. 2021. International Treaty on Plant Genetic Resources for Food and Agriculture.

http://www.fao.org/plant-treaty/overview/en/

FAO. 2021. Whole-Genome Sequencing and Food Safety.

http://www.fao.org/food-safety/scientific-advice/crosscutting-and-emerging-issues/wgs/en/

FAO. 2021. Food Safety and Quality.

http://www.fao.org/food-safety/background/en/

FAO. 2020. Global Community Meeting of the FAO GM Foods Platform. Towards Effective Risk-Based GM Food Safety Assessment and Regulatory Management. Meeting Report. Rome.

https://doi.org/10.4060/ca8945en

FAO. 2016. Technical Meeting on the Impact of Whole-Genome Sequencing on Food Safety Management: Poster Abstracts.

http://www.fao.org/3/a-bl427e.pdf

FAO. 2016. Final Meeting Report: Technical Meeting on the Impact of Whole-Genome Sequencing on Food Safety Management: Within a One Health Approach.

http://www.fao.org/3/a-i6582e.pdf

FAO. 2016. Technical Background Paper: Applications of Whole-Genome Sequencing in Food Safety Management.

http://www.fao.org/3/i5619e/i5619e.pdf

FAO. 2016. Meeting Report: Side Event on Whole-Genome Sequencing and Food Safety. Joint FAO/WHO/OIE; Side Event of the 39th Codex Alimentarius Commission, FAO Headquarters, Rome.

http://www.fao.org/3/bp080e/bp080e.pdf

FAO. 2016. Meeting Report: Application of Genome Sequencing for Sustainable Agriculture and Food Security. Side Event of the 25th Session of the Committee on Agriculture (COAG).

http://www.fao.org/3/bq675e/bq675e.pdf

FAO. 2016. Highlights: Whole Genome Sequencing for Food Safety.

http://www.fao.org/3/i5790e/i5790e.pdf

FAO. 2015. Workshop Proceedings: Drafting the Technical Paper on Applications of Whole-Genome Sequencing for Food Safety Management. Food and Agriculture Organization of the United Nations in Collaboration with World Health Organization (WHO).

http://www.fao.org/3/bl207e/bl207e.pdf

Tay, M.Y.F., et al. 2019. "Whole-Genome Sequencing Analysis of Nontyphoidal Salmonella enterica of Chicken Meat and Human Origin Under Surveillance in Sri Lanka." Foodborne Pathogens and Disease 16(7): 531–537.

Nanyang Technological University. 2016. Report of the INFOSAN Meeting on Regional Perspectives of Food Science: New Science for Food Safety: Supporting Food Chain Transparency for Improved Health.

https://fr.slideshare.net/LeeGheeSeow/new-science-for-food-safety-supporting-food-chain-transparency-for-improved-health-75462556

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