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MAGICAL MICROBIOLOGY.

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NGS is an important tool for both disease management in clinical settings and genomic surveillance in the public health sector, but complex workflows and limited resources have hampered its more widespread adoption. Dr Shaun Yang, a pioneer in translational NGS, discusses the benefits of this approach, and how easy-to-use automation solutions are opening the door to implementation of NGS in settings requiring rapid turnaround times.

Advanced NGS technologies and pathogen-focused bioinformatics have the potential to address unmet clinical needs in the diagnosis and treatment of challenging infectious diseases. Combining microbial whole genome sequencing with metagenomics represents a state-of-the-art solution for pathogen identification, as well as providing a robust and highly sensitive method for real-time genomic surveillance to enable the early detection of novel pathogens and antimicrobial resistance (AMR) mechanisms in the community. This approach can also be used in outbreak investigation, emerging pathogen characterization and AMR monitoring, generating actionable information to guide infection prevention and treatment optimization. Dr Shaun Yang is an Associate Professor of Pathology and Laboratory Medicine, Associate Medical Director, and Director of the Molecular Microbiology and Pathogen Genomics Laboratory, and commented: “NGS is an example of how the use of new technologies can help solve unmet medical needs. Recent advances are now enabling the identification of many pathogens that could not otherwise be classified correctly, as well as characterization of virulence and pathogenicity, and determination of antimicrobial resistance profiles. This can directly impact patient care by providing critical information to help clinical decisions regarding diagnosis, treatment and disease monitoring.”

Shaun continued: “My laboratory was one of the first sites in the USA – and probably the world – to apply real-time NGS to the diagnosis, treatment and prevention of infectious diseases. We first integrated commercially available, validated tests into our routine workflows about five years ago, and continually evaluate and validate new technologies that could provide additional information to help guide the treatment of challenging cases of infectious disease. It’s something we’ve pioneered very successfully, positioning ourselves as a model for other laboratories in the field. The data we generate is also tremendously helpful for infection prevention; if one case becomes two, then three, we start to see a pattern and can connect the dots immediately, helping to prevent its spread.”



“NGS is also important for real-time surveillance of pathogens circulating in the community,” said Shaun. “Unnecessary or inappropriate use of antibiotics contributes significantly to AMR. If a patient is hospitalized due to an invasive infection caused by a drug-resistant pathogen, NGS gives us real-time information that is not only valuable from the individual patient perspective, but also provides critical drug surveillance data regarding pathogens in the community, which is extremely valuable from a public health standpoint. We have previously identified a New Delhi metallo- β -lactamase-producing *Pseudomonas aeruginosa* circulating in the community and have a large database of carbapenemase-producing Enterobacterales that our bioinformaticians plan to use to establish the prevalence of resistance genes in the population, correlating this data with phenotypic resistance patterns. This information will allow us to provide hospitals with guidance about the likelihood of a patient with a specific pathogen having resistance to one or multiple antibiotics. In the future, it may even be possible to use AI for disease prediction and tracking resistance patterns to guide treatment on a population level. This would pave the way for a new paradigm of clinical microbiology, which is revolutionary.”

Powerful NGS and bioinformatics approaches have the capability to transform clinical microbiology, moving from culturing techniques that simply establish the presence of Gram-positive or -negative bacteria, to technologies that can determine subspecies and resistance genes. Unfortunately, clinical microbiology labs have been slow to adopt these NGS approaches. Shaun explained why, and how, the challenges can be overcome: “The complexity of the workflow is a major issue preventing clinical labs from implementing NGS.



These labs are driven by a need for high productivity and fast turnaround times, while NGS is lengthy and labor intensive. It takes a technician two or three days to process as few as 20 samples for NGS, compared to 1,000 urine cultures in one week, which is clearly not cost effective. When combined with staff shortages and an increasing number of tests, this leads to a bottleneck, and hence we needed to automate the process.”

“As a clinical microbiology lab, our considerations for NGS automation in the lab are performance, ease of use, and cost of operation,” Shaun continued. “The primary consideration for an automation workflow is the need to consistently generate libraries and data quality similar to a validated manual workflow from a variety of sample types. The secondary consideration is the ease of use. Given our lack of automation expertise, the preference is for a plug and play system that does not require extensive training and enables more of the staff to use the system, rather than relying on a few well training users. This led us to evaluate Tecan’s MagicPrep™ NGS system, a fully automated benchtop platform that generates NGS libraries in a one-step process.”



“We compared the performance of MagicPrep to the current manual method, evaluating 35 pathogens isolated from clinical samples, including 28 bacteria and 7 fungi. The quantity and quality of the prepared libraries and sequences were assessed, and we demonstrated 100 percent concordance in the final microbial identification.¹ We also conducted workflow analyses, reproducibility studies and cost feasibility assessments. The MagicPrep NGS System allows for approximately 5.5 hours of continuous walk-away time, and objective workflow analysis demonstrated the potential for consolidation of the wet lab processes toward a more streamlined NGS workflow, with a single day of dedicated personnel staffing.”

“With respect to instrument operation and maintenance, the MagicPrep NGS is a batched, closed-system instrument with preprogrammed protocols using Illumina-compatible reagents. The operator simply inputs their parameters – input DNA and amplification cycles – and the instrument is immediately ready for use, allowing rapid adoption into existing workflows. Moreover, the MagicPrep NGS has a small footprint and minimal space requirements and requires no routine maintenance from the manufacturer. Together, these features ensure ease of implementation and scalability to accommodate the specific needs of a laboratory,” Shaun concluded.

1) Caldera, JR et al. Performance Evaluation of a Commercial Automated Library Preparation System for Clinical Microbial Whole-Genome Sequencing Assays. J Mol Diagn, 2024, DOI:https://doi.org/10.1016/j.jmoldx.2024.05.006.

The opinions expressed in this article are solely those of Dr. Shaun Yang and does not represent endorsement or promotion of this product by his employer.

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