

What Is the Real Impact?

Experts share their opinion on the value of fully automated NGS results in a single day

At this year's Association for Molecular Pathology meeting in Baltimore, Thermo Fisher Scientific launched the Ion Torrent™ Genexus™ System, a first-of-its-kind, fully integrated, next-generation sequencing (NGS) platform. The system, for research use only, features an automated specimen-to-report workflow that delivers results economically in a single day and holds the potential to advance precision medicine. Its unprecedented turnaround time – as low as 14 hours to final results – making speed the quintessence of the system*. That speed, along with a fully automated workflow and the ability to return data with only minimal sample input, provides a cost-effective turnkey solution that may ultimately broaden NGS adoption to local and community hospital pathology labs in the future.

Luca Quagliata, Global Head of Medical Affairs at Thermo Fisher Scientific, asked NGS expert users for their thoughts on the newly launched Ion Torrent™ Genexus™ System and how obtaining a complete tumor sample molecular profile within a single day might impact precision medicine in the future. Nicola Normanno of the Department of Translational Research, INT-Fondazione Pascale, Naples, Italy, has longstanding expertise in molecular testing, especially in the context of clinical trial-associated transitional research. His reaction to the system: "I was really impressed by the Ion Torrent™ Genexus™ System for a number of reasons. The first is that it's very easy to use. Even a person with low experience could load it in an extremely simple way,

and it's very difficult to make a mistake because the system will alert you if there is an error."

Was the instrument intuitive? Approachable?

Jose Luis Costa, Clinical Researcher at the Ipatimup Center and an Affiliated Professor at the Department of Pathology, University of Porto Faculty of Medicine, Portugal, was an early tester of the Ion Torrent™ Genexus™ System. He says, "The instrument is extremely intuitive. I would say that it is even childproof, so anyone – even without any expertise – can just plug in the instrument and start working with it. All the instructions are fairly simple to follow. The instrument tells you exactly what to do, step by step. So you don't really need to prepare in advance to work with it. In fact, the only thing you need is a pipette to transfer the samples into the system."

What kind of advantage would such a system bring to your laboratory? Costa says, "What the Ion Torrent™ Genexus™ System brings to the laboratory is more time for people to do things other than just jam in processing samples for NGS testing. As well, because the system goes from sample to final report with little to no intervention, no errors are introduced in the process. This offers great performance robustness along with high reproducibility. So, to wrap it up, time and robustness are area where we have major advantages, I would say."

What are the main barriers to NGS adoption in smaller laboratories? Costa says, "The barriers to NGS adoption are the same as for larger laboratories. The difference is the resources to overcome them. In a nutshell, I think it's the expertise that is needed, from both a molecular biology and a bioinformatics standpoint, including result interpretation. Also, the cost related to both the instruments and

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the sequencing itself forces the need to batch a lot of samples to be cost-efficient in running samples. Usually, small laboratories do not have enough samples to be cost-efficient – sometimes, even large laboratories don't! The Ion Torrent™ Genexus™ System offers a solution to all these barriers."

How does the Ion Torrent™ Genexus™ System help overcome those barriers? Costa says, "The way the Ion Torrent™ Genexus™ System overcomes these barriers is essentially by tackling all these different aspects. The expertise needed to run it is essentially none, because it's a fully automated system. The machine does everything, including providing a full annotated report for final interpretation. Notably, you no longer need to batch samples. In principle, you can run the system with a single sample! But it is when you have just a handful that it becomes extremely cost-efficient. When I think of costs – not just the reagents, but time needed to process samples – that is a major component."

So labs that don't have any experience with NGS can use the Ion Torrent™ Genexus™ System? Phillip Jermann of the Institute of Medical Genetics and Pathology, University Hospital Basel, Switzerland, commented, "The Ion

Torrent™ Genexus™ System enables laboratories that want to implement next-generation sequencing into their laboratory workflow and do not yet have the background and the knowledge around NGS to do that easily. That is because the system is basically a fully automated end-to-end workflow that requires very little human input. Therefore, it is very difficult to make any errors and, at the same time, it is very easy to learn how to use it, making it quickly implementable."

And what about experienced laboratories?

Jermann says, "Experienced laboratories like ours can also benefit from the from Ion Torrent™ Genexus™ System because it allows us to automate many steps that are otherwise error-prone when done manually, even by skilled users. So, again, it's the automation that benefits us

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most. And of course, that goes along with another big advantage of the system – the short turnaround time. This will enable us to generate results much faster than we currently can. No need to pile up cases and then hurry to analyze them all at once. We can better distribute the workload in the laboratory."

An important aspect of today's NGS-based molecular profiling is the percentage of failed tests. Does the Ion Torrent™ Genexus™ System reduce that percentage? Jermann says, "The Ion Torrent™ Genexus™ System is based on technology that has evolved over the last 10 years. I was an early adopter, so I have followed its entire development. The method, to the best of my knowledge, has been cited in more than 6,000 scientific papers. Recently, a seminal retrospective study from the University of Heidelberg in Germany that used the Ion Torrent technology demonstrated a nearly 97 percent sequencing success rate across >3,000 non-small cell lung cancer samples, and a rejection rate, mostly due to quantity not sufficient errors, of only around 3 percent (1). The Ion Torrent™ Genexus™ System represents a further

evolution of that robust methodology, so it is conceivable to expect it will deliver excellent results."

The Ion Torrent™ Genexus™ System is a Research Use Only platform. However, Luca Quagliata stated, "Thermo Fisher intends to seek regulatory marketing authorization of the system so that it can potentially be made available in every clinical setting. Additionally, we plan to develop and seek approval for a broad portfolio of diagnostic assays in oncology. The Ion Torrent™ Genexus™ is made to shift the cancer testing paradigm. That is what we have worked for – and we will keep on working for it."

For research use only. Not for use in diagnostic procedures.

**Specimen-to-report workflow will be available after the Genexus™ Purification System and integrated reporting capabilities are added in 2020.*

Reference

1. AL Vockmar et al., "Combined targeted DNA and RNA sequencing of advanced NSCLC in routine molecular diagnostics: Analysis of the first 3,000 Heidelberg cases", *Int J Cancer*, 145, 649 (2019). PMID: 30653256.