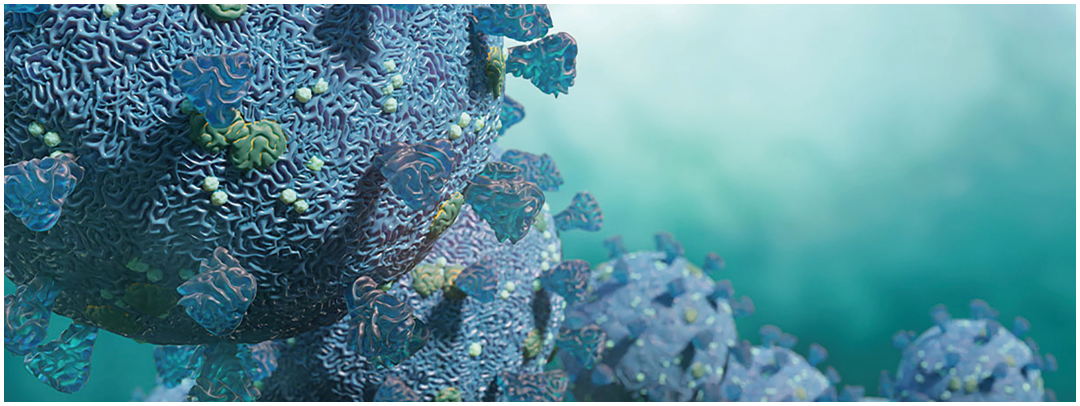
Genexus System news **Issue 4:** January 2021

Beyond oncology clinical research and back



A solution for epidemiological surveillance and new mutations/strains detection

RNA viruses like SARS-CoV-2 share the biological feature of high genetic variability, making it challenging to predict patterns of evolution. Next-generation sequencing (NGS) enables variant-level data, offering valuable information like mutations and serotypes, to help find answer to questions like "where did the virus originate?", "is it the new strain?" or "what is the mutation rate?" Ion AmpliSeq™ SARS-CoV-2 Research Panel has an intelligent design, with a majority of the viral genome covered by two amplicons.

The SARS-CoV-2 Research Panel provides exceptional protection against naturally occurring variation and ensures robust performance even as the virus rapidly mutates, making it usable in a wide variety of epidemiological research applications including the B.1.1.7 SARS-CoV-2 variant surveillance. It comes as a rapid and highly automated NGS workflow that enables labs to go from nucleic acid to report in a single day with 5 minutes of hands-on time.

Ion Torrent™ Genexus™ Integrated Sequencer

1 touchpoint; 5 min of hands-on time
Total turnaround time: 1 day

Company I's NGS systems

>10 touchpoints; ~7 hr of hands-on time
Total turnaround time: 3–4 days

Figure 1. Comparison of the targeted NGS workflows for SARS-CoV-2 on the Genexus Integrated Sequencer and Company I's NGS system. The Genexus Integrated Sequencer enables labs to go from nucleic acid to report in a single day with minimal user intervention.

"Quote of the month

Only the NGS data could allow us to identify the particular strain so fast, enabling us to draw important conclusions … within two days of receipt of the samples. This information gave leaders at our institution greater confidence in our ability to provide a safe environment for our patients and our team members."

–Timothy J. Triche, MD, PhD, Co-Director, Center for Personalized Medicine at CHLA

To read more about this topic, please see page 3.

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The Ion AmpliSeq SARS-CoV-2 Research Panel and the Genexus Integrated Sequencer were used to sequence the SARS-CoV-2 genome from positive samples with a range of viral loads, demonstrating high coverage uniformity and percent reads on target across different viral titers. (Figure 2)

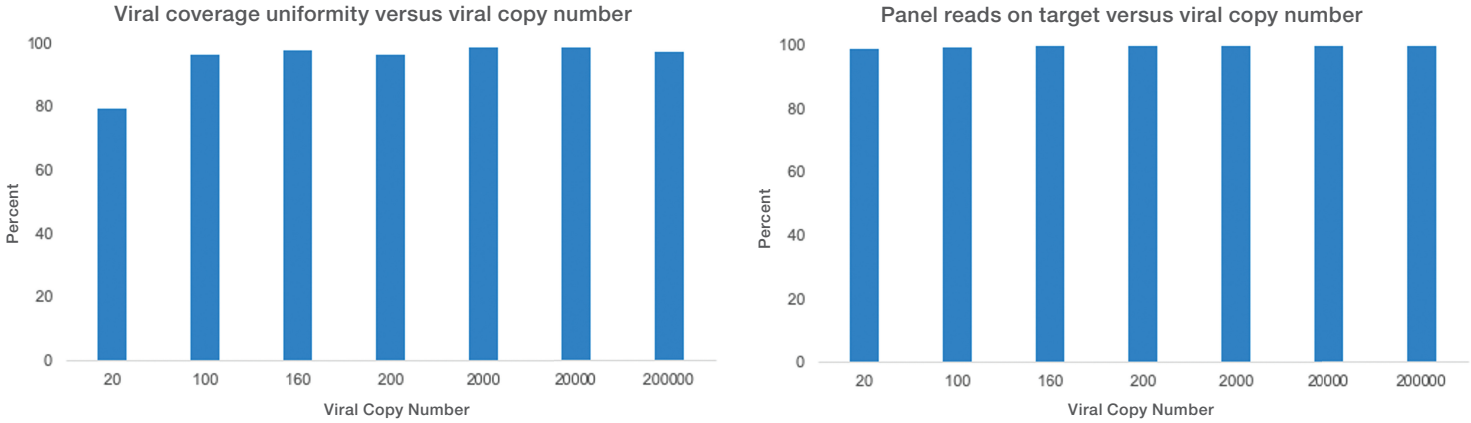


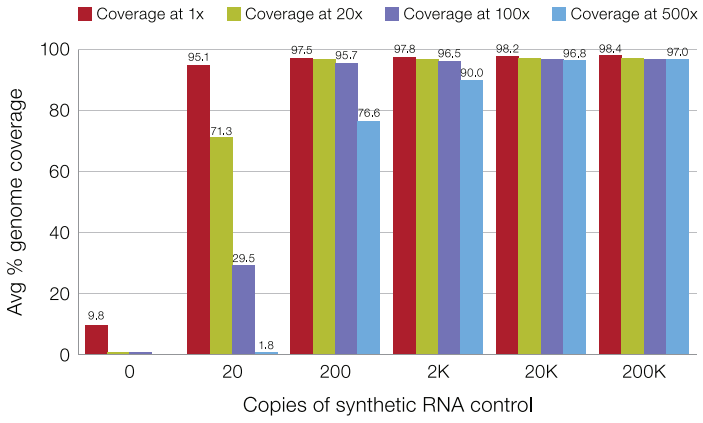
Figure 2. Coverage uniformity and percent base reads on-target for Ion AmpliSeq SARS-CoV-2 Research Panel on the Genexus Integrated Sequencer across a range of viral titers with inactivated virus. N=2 for each condition with aTCC VR1986HR in background of 5 ng human RNA.

Ampliseq SARS-CoV-2 Research Panel on Genexus Integrated Sequencer workflow performance evaluation—Study overview

To demonstrate the simplified workflow and performance of the Ion AmpliSeq SARS-CoV-2 Research Panel on the Genexus Integrated Sequencer, a synthetic SARS-CoV-2 RNA control (Twist Bioscience, Cat. No. 102019) was used. This control uses GenBank™ database ID MT007544.1 (Wuhan strain) as a reference and includes 3 SNVs and one 10 bp deletion relative to GenBank ID MN908947.3 (Australian strain). The synthetic RNA control was synthesized as 6 nonoverlapping ~5 kb fragments that cover 99.9% of the SARS-CoV-2 genome. The synthetic RNA control was received at a concentration of 1 x 10^6 copies/µL. Serial dilutions were made and then spiked into 5 ng of Invitrogen™ Human Lung Total RNA (Cat. No. AM7968) to obtain final viral copy numbers ranging from 20 to 200,000 copies in a final volume of 25 µL per sample.

Results

All samples across both runs returned reads mapping to the 5 human expression controls of the Ion AmpliSeq SARS-CoV-2 Research Panel (continues on next page).



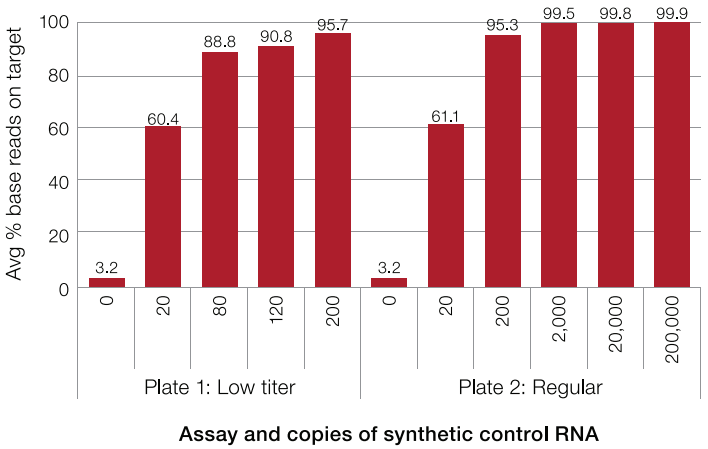


Figure 3. Average percent genomic coverage at varying depths per copies of input RNA for the SARS-CoV-2 Research Assay. At inputs as low as 200 copies per sample, the Genexus Integrated Sequencer generated 95.7% genomic coverage at 100x for the SARS-CoV-2 genome.

Figure 4. Average percent base reads on target across both runs. "Percent base reads on target" refers to reads mapped to the SARS-CoV-2 reference after removing human expression controls. Averages were taken from all replicates for each synthetic RNA control input and assay used.

To learn more or download the application note, visit **thermofisher.com/coronavirus-genexus**

Variant calling results provided by the SnpEff plugin successfully identified all three SNVs and a 10 bp deletion for all samples with 120 copies of synthetic control RNA

Conclusion

The Genexus Integrated Sequencer, combined with the Ion AmpliSeq SARS-CoV-2 Research Panel, provides a highly automated nucleic acid–to-report NGS workflow in a single day, enabling labs to survey the complete SARS-CoV-2 genome at a speed never possible before. With unmatched ease of use and less operational hands-on time compared to other technologies, this new solution makes the power of NGS accessible to labs that want to easily and quickly adopt the technology for epidemiological studies.

Beyond emergency testing: staying ahead of SARS-CoV-2 with NGS to help disrupt the current trajectory

The pivotal case of Children's Hospital Los Angeles (CHLA) to help mitigate a crisis

Key highlights

- The continuing spread of SARS-CoV-2 shows that emergency testing alone is not enough to manage the crisis
- Accessible NGS can help optimize mitigation policies for both country-level and localized interventions
- Using Ion Torrent™ targeted NGS technology, CHLA analyzed viral isolates in under 48 hours to mitigate potential spread and ensured the pediatric intensive care unit (PICU) remained open

Introduction

Effective tracking and monitoring of SARS-CoV-2 is critical to help address the current global crisis. But with the continuing spread of SARS-CoV-2 in the United States [1] and numbers rising in Europe at a higher rate than during the peak in March 2020 [2], increasing emergency testing is simply not enough. While the mutation rate of this virus is ~30–50% slower than influenza virus [3], the ability of SARS-CoV-2 to rapidly spread means that new strains can still appear, which in turn means that attempts to contain the spread are made more difficult.

Multiple studies report that the complex biology of SARS-CoV-2 makes mitigation of the crisis even more challenging. Epidemiological modeling shows that most transmission occurs either during the presymptomatic or asymptomatic infection stage [4]. During the presymptomatic stage, which potentially lasts up to 14 days [5], carriers may shed more virus particles and thus be more contagious [6]. Interestingly, 40–45% of SARS-CoV-2–infected individuals are asymptomatic [7,8], with children suggested as a notable group of carriers [9].

These concerning aspects add to the difficulty of mitigating SARS-CoV-2 compared with similar coronaviruses [10]. Each strain needs to be correctly identified for proper viral surveillance, to potentially guide preventative measures, and to help inform development of future treatments. Researchers have identified a multitude of SARS-CoV-2 strains [11] by using NGS. Experienced professionals now recognize the need for epidemiological insights regarding SARS-CoV-2 and favor the rapid turnaround time and highly automated workflows of Ion Torrent NGS. These critical factors help communities track and contain the virus, and keep essential facilities open.

Conclusions

With wide availability of an effective vaccine still many months away at best [12] and the safety of such a vaccine unclear [13], it is critical we continue to innovate and invest to advance our ability to address SARS-CoV-2 and potential future viruses. Thermo Fisher Scientific has a history of responding promptly and efficiently to public health emergencies. Customers like Dr. Triche use our NGS solutions to aid their investigations and keep the communities they serve safe. With our latest innovation—the Ion Torrent™ Genexus™ System—we continue to lead the way and enable health agencies to determine their next steps in controlling the SARS-CoV-2 crisis, and help get the global economy moving again responsibly.

To learn more or download the application note, visit **thermofisher.com/coronavirus-genexus**

Rapid, automated workflow to identify relevant genetic variants in hereditary cancer research samples

Ion AmpliSeq™ On-Demand Panels enables simple and practical customization of panels using a catalog of over 5,000 pretested genes that are most relevant in research on inherited diseases, including hereditary cancer, autoimmune diseases, cardiovascular disorders and many more. With the Ion Torrent™ Genexus™ System and Ion AmpliSeq On-Demand Panels, labs can analyze genetic variants of interest in a highly automated workflow that allows them to go from specimen to variant report in as little as a single day.*

In collaboration with two genetic service providers, we analyzed uncharacterized cell line samples and clinical research samples using Ion AmpliSeq On-Demand panels and the Genexus Integrated Sequencer. Single-nucleotide variants from two different hereditary cancers were identified; data were verified with the results generated from the same samples using the Ion GeneStudio S5 System and the Genexus Integrated Sequencer, showing highly concordant (>95%) data.

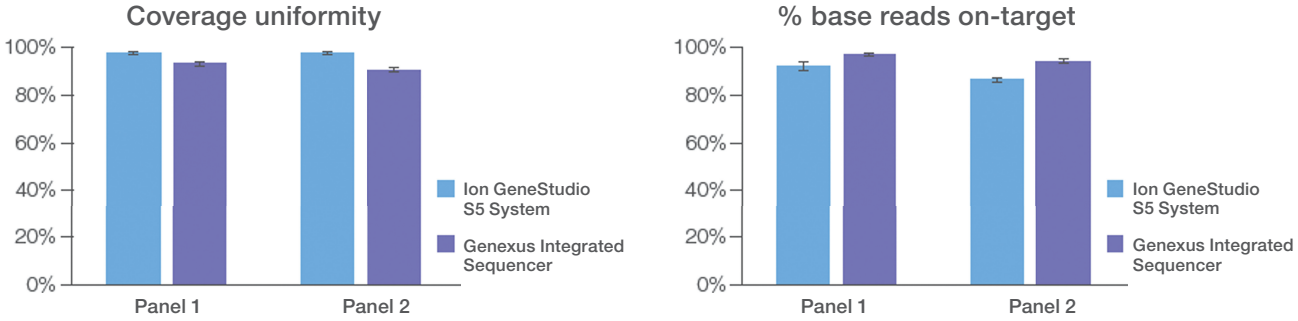


Figure 1. Coverage uniformity and percent base reads on-target for panel 1 and panel 2 on the Ion GeneStudio S5 System (n = 8) and Genexus Integrated Sequencer (n = 7).

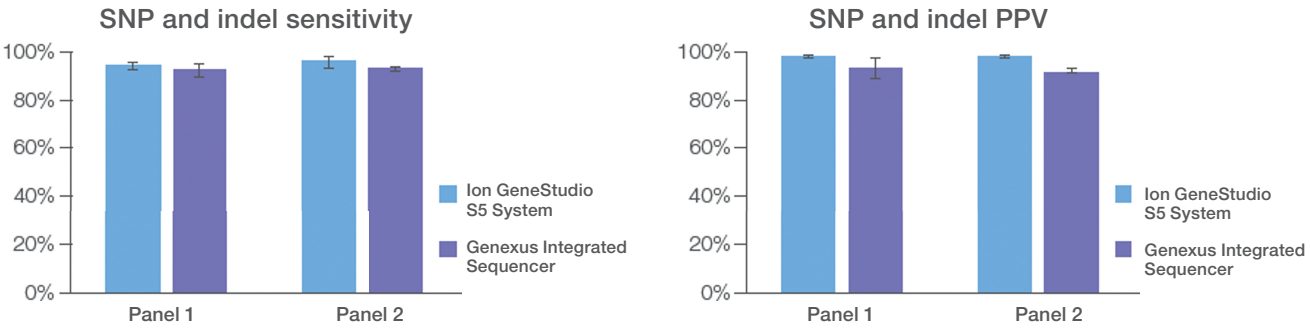


Figure 3. Sensitivity and PPV for SNPs and indels, for panel 1 and panel 2 on the Ion GeneStudio S5 System (n = 6) and Genexus Integrated Sequencer (n = 5). For SNPs and indels combined, sensitivity of >91% and PPV of >92% were observed for both the Ion GeneStudio S5 System and Genexus Integrated Sequencer.

Sample	n	Gene variant	Referance	Mutation	Concordance
Sample 1	3	*MSH6*	C	C>G	Yes
Sample 2	3	*BRCA1*	G	G>C	Yes
Sample 3	3	*ATM*	GA	DelGA	Yes
Sample 4	3	*BRCA1*	-	InsG	Yes
Sample 5	3	*BRCA1*	C	C>T	Yes

Table 1. Concordant results from hereditary cancer research samples analyzed using the Ion AmpliSeq On-Demand Panel. Clinical research samples (n = 5) obtained from a genetic service provider were analyzed in a blind study on both the Ion GeneStudio S5 System and the Genexus Integrated Sequencer using an Ion AmpliSeq On-Demand Panel for hereditary cancer research. Sample variant information for concordance assessment was obtained by the genetic service provider using the Ion GeneStudio S5 System.

*Specimen-to-report workflow will be available after the Genexus Purification System and integrated reporting capabilities are added in 2021.

To learn more or download the application note, visit **thermofisher.com/inherited-genexus**

More News

Hear from more Genexus System and Oncomine Solutions users as they presented at recent virtual events

Craig Mackinnon, MD, PhD

Director, Genomic and Bioinformatics - Professor, Department of Pathology, University of Alabama at Birmingham, US, has evaluated both Oncomine Precision Assay and Oncomine Myeloid Assay GX and also presented impressive business case showing how implementing Genexus in their lab will facilitate significant resources savings. You can see his presentation at the Oncomine World on demand.

Javier Hernandez-Losa, PhD

Director of Molecular Biology Laboratory, Department of Pathology, Vall d´Hebron Hospital, Spain, has presented his first experience with Oncomine Precision assay and even included short video capturing the Genexus system operating in their laboratory. You can see his presentation and the video at the Oncomine World on demand.

Michael Hummel, PhD

Head of Molecular Pathology Department, Charite, Professor at Universitätsmedizin Berlin has presented astounding results of Oncomine Precision Assay evaluation in his and other 3 European laboratories during our satellite symposium at virtual ESP/IAP congress. You can view on demand here.

Yi Ding, MD, PhD

System and Core Laboratory Director of Molecular Diagnostics at Geisinger Medical Laboratories in US, has presented at our workshop at virtual AMP 2020 results of their evaluation of Oncomine Myeloid Assay GX including great performance for important variant detection such as FTL3, fusions. You can watch her presentation on demand here.

Don’t wait to get specimen-to-report NGS automation*

Discover flexible financing options for the Genexus System

Ion Torrent Genexus System automates specimen-to-report workfl ow in a single day with just two user touchpoints*, making in-house next-generation sequencing (NGS) accessible like never before.

Now you don’t have to wait for CAPEX approval to access the Genexus System. We are committed to supporting your work by off ering a wide range of fi nancial and leasing programs for even easier adoption of in-house NGS.

Options include the subsidized pricing to support global collaborative SARS-CoV-2 and oncology clinical research, the Subscription Services program, and trade-in off ers.

Ask about our flexible financing options for the Genexus System today at **thermofisher.com/genexusfinancing**

*Specimen-to-report workfl ow will be available after the Ion Torrent™ Genexus™ Purifi cation System and integrated reporting capabilities are added in 2021