COVID-19 Surveillance Through Next Generation Sequencing

During the past year, the world has felt the deep impact of the SARS-CoV-2 virus. While the pandemic is not yet over, the areas of need to help combat the disease have shifted. Identification of variant strains of SARS-CoV-2 in the UK, Brazil, South Africa, and India have brought global awareness that virus mutation must be closely monitored. While vaccines are now available, there is uncertainty about whether they will be as effective against these new viral strains. Efforts to monitor and evaluate changes to the SARS-CoV-2 virus are more important than ever. An automated DNA sequencing workflow managed by Biosero workcells enabled by Green Button Go® Scheduler is streamlining high-throughput surveillance efforts conducted by the leading provider of sequencers.

Next Generation Sequencing Test Kit for COVID-19

The majority of the existing front-line PCR test kits for SARS-CoV-2 are based upon a known sequence of the virus to determine whether an individual has COVID-19. Illumina's COVIDSeq test, on the other hand, sequences the entire viral genome. Unlike PCR tests, this sequencing-based approach can detect mutations of SARS-CoV-2 virus and provide data that is critical for genomic surveillance.

The added depth of the Illumina COVIDSeq test can now provide scientists in biopharma, biotech, healthcare systems, and government agencies with important information to help them:

- Identify viral mutations that could affect vaccine potency
- Track routes of the virus transmission globally
- Prevent the spread of new strains
- Provide insight into whether treatment adjustments are needed to combat the emergence of new strains
- Identify potential targets that can be used to produce COVID-19 therapeutics

Isolation of SARS-CoV-2 Viral RNA

This **Nucleic Acid Extraction Workcell** manages the extraction and purification of viral genomic content from patient samples needed for the Illumina COVIDSeq Test.

Viral material is bound to magnetic beads and subsequently isolated using the Thermo Fisher Scientific KingFisher Presto. Magnetic rods on the Presto instrument bind the magnetic beads containing the SARS-CoV-2 nucleic acid, followed by buffers and cleaning steps. After the viral material is purified, it is then eluted or released into a microtiter plate that will proceed to the next preparation step.

As there are eight KingFisher Presto purification systems and numerous wash and purification reagent dispenses required in the process, the coordination of these events is critical to the successful purification of the viral material.

The Biosero Green Button Go Scheduler sequence-based driver is able to coordinate the order of events leading to the purification of viral material within any reagent stability restrictions. Automating the extraction process provides robust sample preparation, minimizes handling errors, and improves efficiency by freeing up workers to focus on other tasks.

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BIOSERO

Nucleic Acid Extraction Workcell

RNA to cDNA Conversion + Amplifications

Once the viral genetic material purification is completed by the extraction system, samples can be immediately transferred into a **Pre-PCR Workcell** where the RNA of the SARS-CoV-2 virus is annealed and then converted to a more stable cDNA form. Through partnership with SPT Labtech, the cDNA material is partitioned and the necessary reagents dispensed (master mixes for each directional strand template) to accomplish this conversion using the Mosquito liquid handler and Dragonfly liquid dispenser. Once in cDNA form, the sample material can then be amplified by thermal cyclers.

Green Button Go Scheduler orchestrates the compression of sample input plates and sample tracking while automating the workflow and handling reagent stability restrictions. Samples are processed in the most efficient timeframe while preserving the consistency of each process, thereby ensuring the highest robustness and integrity.

Amplicon Tagmentation

After cDNA is amplified in a PCR step, the samples are introduced to the next Biosero automation workcell. This **Post-PCR workcell** will recombine the amplified material and tag the PCR amplicons with adaptor indices that will allow subsequent detection from sequencing.

Green Button Go Scheduler tracks and audit sample processing throughout the entire workflow. Importantly, it traces index adapter primer additions to each well, as the added index adapter will be needed to properly analyze the sample after sequencing and report results. As with the other workcells, sample robustness and consistent processing maintain integrity and data quality.

In a step after the Post-PCR workcell, the tagmented amplicons are amplified in a PCR program. This PCR reaction step also attaches multiple index adapters and sequences that will generate clusters for use in sequencing and analysis.

Green Button Go Orchestrator captures the events throughout the workcells operations. The accessioning of these details from all the processes can then be utilized to produce a thorough audit trail that traces all reagents used in the entire workflow.