Docket #: S19-021

RUSPseq- Multiplex Gene Sequencing from Ultra-Low Amounts of DNA with Rapid COVID Applications

Dr. Curt Scharfe and colleagues have developed RUSPseq, a method for next generation molecular testing originally conceived to diagnose metabolic disorders in newborns. **This method has now been adapted for simple, fast, and inexpensive whole genome sequencing of SARS-CoV-2. The researchers have shown that the entire SARS-COV-2 genome can be captured in a streamlined PCR-based assay with a total run time of about 24 hours. More below.**

RUSPseq was first developed to improve screening for inborn metabolic disorders as it reduces the number of false positives and enables early detection and management of life-changing genetic diseases. Newborn screening is performed to detect metabolic disorders that could cause debilitating disease in children but may have better clinical outcomes with early detection and treatment. Methods have been developed to detect more than 40 metabolic disorders on the Recommended Universal Screening Panel (RUSP) from newborn dried blood spots (DBS). These methods, while beneficial, suffer from high false positive rates and thus a second round of more specific testing is often required to rule out false positives. This can cause significant emotional and financial burden. RUSPseq enables comprehensive analysis of 72 genes for inborn metabolic disorders from a single 3.2mm punch from a newborn DBS.

Stage of research

Without further optimization, >95% of the genome of SARS-CoV-2 has been covered with >20x coverage for 87.5% of ~200 clinical samples that were processed with a Ct of 28.

RUSPseq was rigorously validated using DBS samples from newborns that screened positive for methylmalonic acidemia (MMA).

Applications

- Fast and simple whole genome sequencing of SARS-CoV-2/identification of COVID-19 variants
- Newborn genetic screening for inborn metabolic disorders

Advantages

- **Counter-pandemic - high sensitivity, speed, sequence coverage, scaling and cost effective ($18-$30) compared to commercial assays**
- Requires only a very small amount of DNA- 1ng of genomic DNA
- First highly multiplexed gene sequencing assay to work from DBS specimens
- Can analyze 72 genes from single 3.2 mm DBS punch
- Highly sensitive, specific and rapid
- Cost effective- 20 or more samples can be pooled and run simultaneously
- Potential to replace existing molecular assays
- Can be adapted for high throughput screening

Publications

- Gang Peng, Peidong Shen, Neeru Gandotra, Anthony Le, Eula Fung, Laura Jelliffe-Pawlowski, Ronald W. Davis, Gregory M. Enns, Hongyu Zhao, Tina M. Cowan & Curt Scharfe. Combining newborn metabolic and DNA analysis for second-tier testing of methylmalonic acidemia. Genetics in Medicine. 2018 Sept 13;(21):896–903

Patents

- Published Application: WO2020056004
- Published Application: 20220098640

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