Enzymatic DNA Synthesis (EDS) enables decentralized and same-day access to DNA oligos critical for the study and detection of SARS-CoV-2

Genomics

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The COVID-19 pandemic precipitated one of the most concentrated scientific efforts ever focused on the epidemiology, genomics, biochemistry and evolution of a single pathogen; and on the development of diagnostic tests, treatments and vaccines. One unforeseen consequence of this effort was a global bottleneck in synthetic DNA supply, which currently relies on highly centralized phosphoramidite-based production and third-party logistics.

We have developed a novel enzymatic DNA synthesis (EDS) technology, which utilizes a highly engineered TdT enzyme, reversibly terminated nucleotides and a solid support. This enables same-day, on-demand DNA production with a benchtop “printer” — in a standard laboratory environment, requiring no specialized technical skills.

We have used the SYNTAX™ EDS System to produce oligos for SARS-CoV-2 LAMP, NGS and FISH assays. In this study, we report on the performance of EDS primers in the ARTIC network’s hCoV-19 amplicon sequencing protocol (https://artic.network/ncov-2019). Libraries were prepared from two synthetic RNA control templates and five clinical samples with RT-qPCR Cq values ranging between 18.5 and 30.9. Comparable coverage (depth and uniformity) and 100% concordant SNP calling results were obtained with EDS primers and those obtained from commercial suppliers. Phylogenetic analysis of clinical isolates was performed in the context of >200 SARS-CoV-2 sequences submitted to public databases between December 2019 and June 2020.

Our study demonstrates that the EDS technology is mature enough to support genomics and life science applications, and holds the promise to revolutionize access to synthetic DNA — particularly in settings where in-house synthesis and fast iteration translates to tangible advantages.