Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Biosensors and Bioelectronics 181 (2021) 113134

Contents lists available at ScienceDirect

Biosensors and Bioelectronics

journal homepage: http://www.elsevier.com/locate/bios

Short communication

Multiplex quantitative detection of SARS-CoV-2 specific IgG and IgM antibodies based on DNA-assisted nanopore sensing

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ARTICLE INFO

Keywords:
COVID-19
SARS-CoV-2
Antibody
In vitro diagnostics
Nanopore

ABSTRACT

The coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread into a global pandemic. Early and accurate diagnosis and quarantine remain the most effective mitigation strategy. Although reverse transcriptase polymerase chain reaction (RT-qPCR) is the gold standard for COVID-19 diagnosis, recent studies suggest that nucleic acids were undetectable in a significant number of cases with clinical features of COVID-19. Serologic assays that detect human antibodies to SARS-CoV-2 serve as a complementary method to diagnose these cases, as well as to identify asymptomatic cases and qualified convalescent serum donors. However, commercially available enzyme-linked immunosorbent assays (ELISA) are laborious and non-quantitative, while point-of-care assays suffer from low detection accuracy. To provide a serologic assay with high performance and portability for potential point-of-care applications, we developed DNA-assisted nanopore sensing for quantification of SARS-CoV-2 related antibodies in human serum. Different DNA structures were used as detection reporters for multiplex quantification of immunoglobulin M (IgM) and immunoglobulin G (IgG) antibodies against the nucleocapsid protein of SARS-CoV-2 in serum specimens from patients with conformed or suspected infection. Comparing to a clinically used point-of-care assay and an ELISA assay, our technology can reliably quantify SARS-CoV-2 antibodies with higher accuracy, large dynamic range, and potential for assay automation.

1. Introduction

In December 2019, China reported a new coronavirus that causes an acute respiratory disease named as coronavirus disease 19 (COVID-19) (Zhou et al., 2020). The virus was named SARS-CoV-2 as it was identified to be a betacoronavirus related to severe acute respiratory syndrome coronavirus (SARS-CoV) (Gorbalenya et al., 2020). As of January 2021, the COVID-19 pandemic has caused nearly two million death among 91 million confirmed cases worldwide. Before the large-scale deployment of vaccination, early detection and quarantine of asymptomatic or mild-symptomatic cases, as well as critical care for severely ill patients are key steps for mitigating the pandemic.

To date, amplification of the viral RNA from clinical specimens (*i.e.* nasal swabs, pharyngeal swabs, etc.) by RT-qPCR is still the gold-standard for COVID-19 diagnosis (Corman et al., 2020; Huang et al., 2020; Udugama et al., 2020). However, due to complexities in sample collection and processing, false results are commonly seen in clinical practice (Ai et al., 2020; Alvin et al., 2020; Fang et al., 2020; Xiao et al., 2020). Comparing to RT-qPCR and imaging tests, immunoassay based COVID-19 antigen/antibody tests are often faster, inexpensive, and user-friendly to medical staffs with minimal to no laboratory training (Xiang et al., 2020). In addition, serology analysis also supports a number of highly relevant applications: (1) detection of asymptomatic cases to reduce transmission (Bai et al., 2020); (2) identification of

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https://doi.org/10.1016/j.bios.2021.113134
Received 20 October 2020; Received in revised form 24 February 2021; Accepted 27 February 2021
Available online 3 March 2021
0956-5663/