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TOYOHASHI
UNIVERSITY OF TECHNOLOGY

PRESS RELEASE

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Release Title: Development of rapid and simultaneous diagnosis of COVID-19/influenza diseases by manipulating microfluidic flow with a microfluidic chip

Overview

A research team consisting of Daigo Natsuhara, a first year Ph.D. student and Professor Takayuki Shibata etc. at the Department of Mechanical Engineering, Toyohashi University of Technology, and Professor Hirotaka Kanuka, etc. of the Jikei University School of Medicine has developed a microfluidic chip which is capable of simultaneous diagnosis of COVID-19 and influenza diseases, by applying the microfluidic chip technologies. The team has built a theoretical model that manipulates microfluidic flow with an extremely simple microchannel design and has established an optimal design theory for microfluidic chips. Further, by using the diagnostic device they developed, they performed genetic amplification experiments on four types of infectious diseases, including COVID-19, and demonstrated that multiplexed rapid and simultaneous diagnosis was possible within 30 minutes. The device can be utilized for genetic diagnoses in a range of fields (e.g. agriculture, farming, and fisheries industries, food industry, and health and medical care), not only human infectious diseases.

Details

As shown during the global COVID-19 pandemic, viral diseases cause immense public concern and have a massive impact on economic activity. In this research, as a technology supporting our safe and secure life, the team developed a diagnostic technology that enables anyone, anywhere, any time to detect viral diseases in a rapid, simple, and low-cost way.

The LAMP (Loop-Mediated Isothermal Amplification) method[*1] is a genetic test technology. This simple test method does not require an expensive accurate temperature control equipment, etc., in contrast to the widespread PCR test, and can be conducted on site because it allows genetic amplification at a constant temperature for a constant length of time (60 to 65℃, 30 minutes to an hour or so). However, to diagnose multiple types of viruses, the conventional LAMP method entails considerable effort to perform as many preparations of samples and reagents and genetic amplification reactions as the number of analytes, requiring expert knowledge and skills.

Therefore, the research team of Toyohashi University of Technology and the Jikei University School of Medicine developed a polydimethylsiloxane (PDMS)-based multiplexed genetic diagnostic device (size:

45mm x 25mm, reaction chamber: 3μL x 5 pieces) (refer to the photo in the figure) by applying the microfluidic chip technology. It autonomously, equally, and accurately dispenses samples and reagent into an array of reaction chambers simply by introducing the liquid, a mixture of an extremely small amount of sample extracted from the analytes and a reagent, into the diagnostic device. By heating the device in warm water (at 60 to 65℃, for 30 minutes to an hour or so), it is capable of simultaneous diagnosis of multiple types of viruses with only one operation (one work process per sample).

The genetic diagnosis result shown in the figure indicates that four types of infectious diseases including the COVID-19 (seasonal influenza A, SARS, and influenza H1N1 pdm09) have been successfully detected with this diagnosis device. Only the reaction chamber that reacted when a sample containing the gene of each virus was introduced turned sky blue (denoting a positive reaction) after 30 minutes, which means that visual detection is possible.

In addition, to support on-site diagnoses, the team has developed a smartphone app, which automatically diagnoses the reaction as positive or negative based on photographs taken with a smartphone camera, jointly with OptTech LLC. (Toyohashi, Aichi; founded by a graduate from the university). As shown in the figure, the diagnosis device is capable of easy automatic test result diagnosis (positive or negative), by placing the device after LAMP reaction in a simple LED illumination device and taking photographs with a smartphone. As a result, it is expected that anyone will be able to easily perform the test, anywhere and anytime.

Note: The LAMP method is a loop-mediated isothermal amplification method developed by Eiken Chemical Co., Ltd. (https://www.eiken.co.jp/). Four to six types of primers are set for six to eight areas of a targeted gene to amplify the gene at a constant temperature (60 to 65℃) through strand displacement reaction.

Future Outlook

In the future, aiming to commercialize the diagnosis device, the research team will develop devices capable of multiplexed rapid diagnosis of variants of the COVID-19 and human infectious diseases for a safe life during and after the COVID-19 pandemic. To provide technologies that contribute to food safety and security, it will aim to realize multiple simultaneous diagnosis of food allergic substances (seven specific raw materials: wheat, soba, peanut, egg, milk, shrimp, and crab) and food poisonous fungi (e.g. salmonella and O-157).

Reference

Daigo Natsuhara, Ryogo Saito, Hiroka Aonuma, Tatsuya Sakurai, Shunya Okamoto, Moeto nagai, Hirotaka Kanuka, and Takayuki Shibata, (2021) A method of sequential liquid dispensing for the multiplexed genetic diagnosis of viral infections in a microfluidic device. *Lab on a Chip*, 21(24), 4779-4790, 10.1039/d1lc00829c

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Further information

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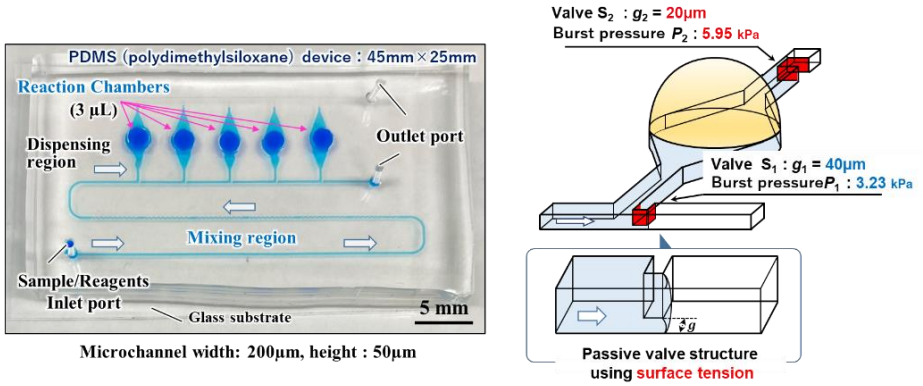
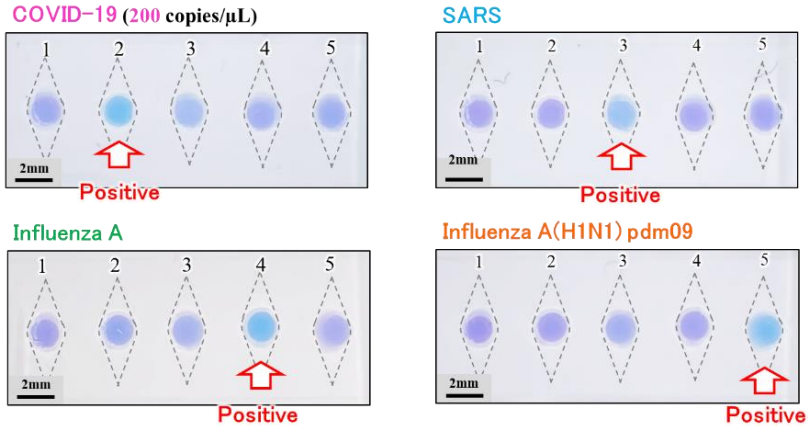
Figure1:



Caption: Photo of the multiplexed genetic diagnostic device and detailed design of the reaction microchamber

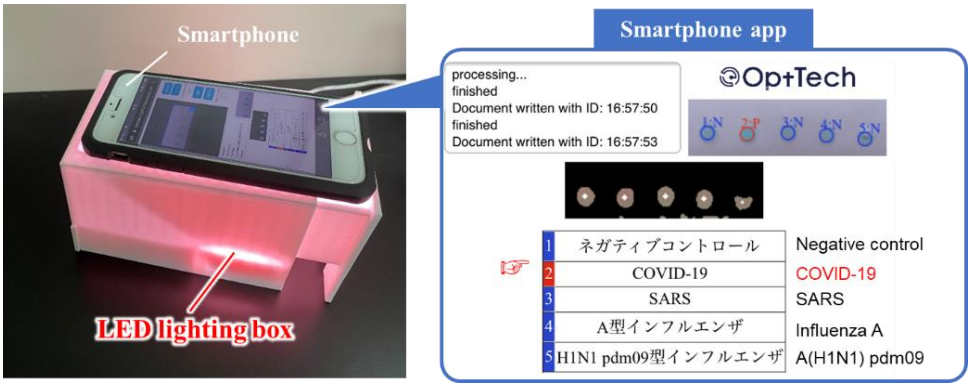
Figure2:



Caption: Results of multiplexed rapid diagnosis of infectious diseases

(The reaction chamber corresponding to the targeted virus changed color from purple to sky blue, which was diagnosed as positive)

Figure3:



Caption: Simple LED illumination equipment and diagnosis screen on the smartphone app.

(The second reaction chamber was diagnosed as positive for the COVID-19 disease)

Keywords: Microfluidics, Genetic technology, COVID 19, Virus testing, Medical technology, Mechanical engineering, Health care industry