A Thermal Digital Microfluidic Device and Its Application to Disease Diagnostics

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Prompt point-of-care (POC) diagnostic tests based on amplification of pathogen DNAs are critical to effective treatment and control of infectious diseases. Loop-Mediated Isothermal Amplification (LAMP) is a potential powerful method for POC disease diagnostics as it is easy handling and cost effective with a short result turn-around time [1]. Especially, the DNA amplification can be observed with naked eyes by adding a DNA binding dye, Sybr Green I, into the final product solution. However, opening of the cap of the amplification tube may cause DNA contamination in the ambient environment inducing false-positive diagnosis later. To solve this problem, an enclosed system with internal sample manipulation is highly demanded. Digital microfluidics is a recently merged technique to manipulate (dispense, transport, mix and separate) microliter to nano-liter droplets containing biological/chemical samples on a two-dimensional electrodes array, which can reduce sample volume, provided fast heat transfer, has high reaction rate and possesses integration capacity.

In the present study, we developed a simple, inexpensive, field-deployable, fast and contamination-free thermal digital microfluidic device for LAMP on-chip. Trypanosoma Brucei, which is transmitted by tsetse fly and cause sleeping sickness in humans and animals was used as a model system. In this novel thermal DMF device, a heat sink and a temperature sensor were integrated into the Digital Microfluidic (DMF) chip. The DMF device was a sealed system with a bottom plate pattered with electrodes array and a top plate made of ITO glass with drilled holes. The two plates were coupled together by a framed spacer. There were six isothermal reaction electrodes for positive sample and negative control reaction on the chip. The device was preloaded with hexadecane oil for smooth droplet transportation and preventing of sample evaporation. The samples were loaded into the device through the holes and transported to the reaction electrodes for LAMP. After reaction, SYBR-Green I was loaded into the device and mixed with post-reaction samples for bare eye observation. By this way, the contamination was avoided because the samples were totally separated from the open air during the whole process.

The sensitivity of the on-chip detection of the assay was 10 ng/μl, same as the off-chip detection sensitivity, with less chemical reagents, simpler and more flexible device. It has shown great potential for a wide variety of life science analyses, especially for disease diagnosis in endemic regions of infection diseases. The flexibility of droplet manipulation on DMF chip and the precise temperature regulation of the droplet on DMF chip will make it a perfect POC device for prompt disease diagnostics in the field.

REFERENCES:

1. “Loop-mediated isothermal amplification technology: Towards point of care diagnostics,” Z. K. Njiru, PLOS Neglected Tropical Diseases, 6, 1(2012).