

An integrated microfluidic platform for rapid detection and subtyping of influenza viruses from clinical samples

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Abstract This study reports on the development of an integrated microfluidic system that performs sample pre-treatment, nucleic acid amplification, and optical detection for molecular diagnosis of influenza viruses. The entire analysis protocol including virus lysis, extraction of ribonucleic acid, reverse transcription, polymerase chain reaction, and optical detection was successfully performed using the microfluidic system, which automatically performed the rapid diagnosis and subtyping of the influenza viruses. Signals obtained from an optical detection module could accurately differentiate influenza A/H1 (infA/H1), influenza A/H3 (infA/H3), influenza B (infB), and positive and negative control samples. More importantly, the entire process could be integrated and performed automatically

with less human intervention. The experimental results demonstrated that this developed microfluidic system can successfully distinguish between infA/H1, infA/H3, and infB within 60 min. Furthermore, oral swabs from 92 patients were successfully tested using the developed microfluidic system. Thus, it may be a promising tool for rapid detection of novel and seasonal influenza strains in the near future.

Keywords Microfluidics · Molecular diagnosis · Subtyping · Influenza virus · Magnetic bead · Clinical specimen

Abbreviations

| | |
|--------------------|----------------------------------|
| bp | Base pairs |
| CNC | Computer-numerical-control |
| cDNA | Complementary DNA |
| ddH ₂ O | Double-distilled water |
| dUTP | Deoxyuridine triphosphate |
| EMVs | Electromagnetic valves |
| HA | Hemagglutinin |
| HAU | Hemagglutinin unit |
| infA/H1 | Influenza A/H1 |
| infA/H3 | Influenza A/H3 |
| infB | Influenza B |
| LOD | Limit of detection |
| MEMS | Micro-electro-mechanical systems |
| NA | Neuraminidase |
| NP | Nucleoprotein |
| PCR | Polymerase chain reaction |
| PDMS | Polydimethylsiloxane |
| PMMA | Polymethylmethacrylate |
| RNA | Ribonucleic acid |
| RNase | Ribonuclease |
| RT | Reverse transcription |

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