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## ACCEPTED MANUSCRIPT

### Influenza virus replication raises the temperature of cells

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<sup>##</sup>To whom correspondence should be addressed Email: ayhonda85@gmail.com for biochemical and cell biology, arai@mech.nagoya-u.ac.jp for preparation of temperature sensor.

#### Highlights

- Influenza virus replication induced temperature rising of cell.
- Temperature sensor on cell was manufactured,
- ATP level in the influenza virus infected cell decreased after 3 hours of virus infection.
- Mitochondrial potential was decreased at higher level of viral multiplication.

#### Abstract

Influenza virus invades the cell by binding sialic acid on the cell membrane through haemagglutinin (HA), and then genome replication and transcription are carried out in the nucleus to produce progeny virus.

Multiplication of influenza virus requires metabolites, such as nucleotides and amino acids, as well as cellular machinery to synthesize its genome and proteins, thereby producing viral particles. Influenza virus infection forces the start of several metabolic systems in the cell, which consume or generate large amounts of energy. Thus, the viral multiplication processes involved in both genome replication and transcription are considered to require large numbers of nucleotides. The high-level consumption of nucleotides generates large amounts of energy, some of which is converted into heat, and this heat may increase the temperature of cells. To address this question, we prepared a tool based on rhodamine B fluorescence, which we used to measure the temperatures of influenza virus-infected and uninfected cells. The results indicated that influenza virus multiplication increased the temperature of cells by approximately  $4^{\circ}C - 5^{\circ}C$ , ATP levels in the cells decreased at 3 hours after infection, and mitochondrial membrane potential decreased with multiplication level. Thus, the increase in cellular temperature during influenza virus infection appears to be due to the massive consumption of ATP over a short period.

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