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Research Highlight

Low-cost low-maintenance paper-based sensor for the detection of Ebola virus

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Abstract: Recent outbreak of Ebola virus that causes hemorrhagic fever shows that the quick detection of this virus in a resource-poor environment is extremely important for controlling the epidemic. Existing methods based on enzyme-linked immunosorbent assay (ELISA), polymerase chain reaction (PCR) or isolation of the virus requires expensive equipment, skilled personnel and the highest biosafety level. We highlight here a recent demonstration of low-cost low-maintenance synthetic biology for detection of Ebola virus based on paper as a device substrate.

According to the Centers for Disease Control in Atlanta (USA), The 2014 Ebola outbreak has to date claimed about 4,960 lives. With over 13,000 cases, this epidemic is the largest in history. Ebola virus (EBOV) belongs to the family *Filoviridae* and causes hemorrhagic fever. The recent cases in Spain and the USA indicate that the virus can be easily introduced from the endemic areas to other countries. Because of the high risk of the life-threatening infection, research dealing with EBOV requires a biosafety level 4 (BSL-4) laboratories, which is only available in a few developed countries. Isolation and detection of EBOV in a BSL-4 environment is beyond the reach of developing countries where the disease is epidemic. Therefore, there is an urgent need for detection of the virus at remote and resource-poor locations. Currently, there are four main methods for the detection of EBOV: (i) isolation of EBOV, (ii) the detection of the viral antigen (Ag), (iii) the detection of Immunoglobulin M (IgM) basic antibody or Immunoglobulin G (IgG) basic antibody specific to EBOV, and (iv) detection of EBOV ribonucleic acid (RNA) through polymerase chain reaction (PCR) and [1].

Detection by isolation of EBOV is dangerous and requires BSL-4 laboratories, which are not available in developing countries. Detection using PCR depends on expensive equipment, skilled technician, availability of energy and water. IgG and IgM antibodies directed against EBOV viral antigens have been extracted from sera of animals and humans surviving EBOV infection. Antigen-capture enzyme-linked immunosorbent assay (ELISA) can be developed based on the antibodies isolated from sera. The presence of antibodies can also be detected by indirect immunofluorescence assay using virus antigens made from virus-infected cells [1]. Again, preparing authentic virus antigens requires BSL-4 laboratories.

Our last research highlight [2] mentioned the great potential of molecular-level manipulation of synthetic biology. Pardee *et al.* from the Wyss Institute for Biological Inspired Engineering of Harvard University recently shows how synthetic biology can

be used for building sensors to detect EBOV [3]. The sensing concept is built on a paper-based platform. Ribonucleic acid (RNA) was programmed to synthesize proteins that bind to the antigens of a particular strain of the EBV. The paper-based sensors can be freeze-dried for storage for up a year at room temperature. Simply adding water reactivates the freeze-dried paper-based sensor. A color change of the sensor within 30 minutes indicates the presence of the virus. This low-cost and low-maintenance sensor has a huge potential for remote low-resource locations where laboratories, refrigerators and electricity are not available.

[1] M. Saijo, M. Niikura, T. Ikegami, I. Kurane, T. Kurata, S. Morikawa, Laboratory diagnostic systems for Ebola and Marburg hemorrhagic fevers developed with recombinant proteins, *Clinical and Vaccine Immunology*, **2006**, 13 (4), 444-451.

[2] N.-T. Nguyen, Micro- and Nanosystems meet biology: artificial life on a chip, *Micro and Nanosystems*, **2014**, 6(1), 1-2.

[3] Keith Pardee, Alexander A. Green, Tom Ferrante, D. Ewen Cameron, Ajay Daley Keyser, Peng Yin, James J. Collins, Paper-Based Synthetic Gene Networks, **2014**, *Cell*, 159 (4), 940–954