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An Ebola virus-encoded microRNA-like fragment serves as a biomarker for early diagnosis

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In a new study, Chen-Yu Zhang's group at Nanjing University collaborate with Ze-liang Chen's group at academy of Military Medical Sciences report that an Ebola virus-encoded microRNA-like fragment serves as a biomarker for early diagnosis. It is published in *Cell Research*.

Ebola virus disease (EVD) is a severe infectious disease caused by Ebola virus species. EBOV caused an epidemic in West Africa in 2013-2015, and have resulted in at least 24,000 suspected cases and 10,000 confirmed deaths. Early diagnosis of EVD is not only essential for implementation of effective interventions but also critical for prevention of the spread of infection. However, it is particularly difficult to diagnose EVD at an early stage. Ebola causes symptoms seen in many other infections, including malaria, typhoid, and influenza, and some patients even developed illness without specific signs and symptoms. Current methods to diagnose suspected Ebola virus infection include reverse transcription polymerase chain reaction, antigen-capture enzyme-linked immunosorbent assay, and immunoglobulin M and immunoglobulin G ELISA.

In previous studies, the same group along with others had demonstrated that microRNAs (miRNAs) produced by eukaryotic cells and viruses are present in human blood in highly stable, cell-free forms and these so called circulating miRNAs can serve as non-invasive biomarkers for the

early diagnosis of various diseases, including viral diseases. Since there are insufficient feasible methods established to diagnose EVD at early stage, Zhang's trying to make breakthroughs by speculating EVDV-specific small non-coding RNAs that could be detected in human blood.

A gratifying finding was reported that the group extrapolated a putative sequence of miRNA-like fragment encoded by EVDV using the principle of miRNA production in eukaryotes. In cellular environment, the existing and maturation of the putative miRNA-like fragment in the presence of a cloned pre-miR sequence were then verified. With the collaboration of Academy of Military Medical Sciences, they further identified the Ebola virus-encoded miRNA-like fragment in serum of EVD patients by qRT-PCR, Northern blotting and TA-cloning/sequencing. Strikingly, subsequent results showed that this miRNA-like fragment existed in acute phase but disappeared in recovery phase of EVD survivors. With great clinical significance, this miRNA-like fragment was detectable in EVD patients before development of viremia with detectable Ebola genomic RNA, suggesting that it is an earlier biomarker than genomic RNA and could advance diagnosable window for EVD.

Early diagnosis is critical for Ebola epidemic control:

1) Early diagnosis increases the chance of survival of EVD patients. It is estimated that about 60% of Ebola infections remain undiagnosed in the community; while 60-90% of untreated patients with Ebola die, supportive medical care could reduce this rate to below 30%. Even among the patients who managed to arrive at the hospital for treatment, most died within 2 days after admission, as it was too late for those patients to receive proper treatment for such a severe disease.

2) Early diagnosis helps curtail the spread and intentional release of EBOV. Each Ebola patient is estimated to transmit the virus to around

1.8 additional people without effective isolation, leading to the exponential growth of infections. Early diagnosis and isolation can reduce the transmission to well under one additional person per infected case, thereby minimizing the possibility of virus transmission to others. In developed countries, the well-established medical system can rapidly identify and isolate potential patients; however, in West Africa effective management was not taken in time, resulting in the present massive Ebola outbreak. Thus, in the region with fragile and underfunded health systems, early diagnosis is particularly important for containing the epidemic. Accordingly, the currently identified miRNA-like fragment may function as an early biomarker of EVD to advance the diagnosable window and reduce the difficulties in the isolation and treatment of patients who develop suspicious symptoms. More importantly, because the miRNA-like fragment of EBOV is highly conserved, it may predict and prevent Ebola outbreaks in the future if Ebola arises again.

Provided by Nanjing University

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