The devastating 2014 Ebola virus (EBOV) disease outbreak in West Africa has sparked the development and regulatory approval of antiviral countermeasures, including an emergency-use vaccine and therapeutic monoclonal antibodies. While these countermeasures are highly beneficial to block EBOV infection and interfere with disease progression at early stages, they are less suitable for the treatment of late-stage EBOV disease (EVD), which is less studied. This includes gastrointestinal symptoms, and diarrhea, in particular. Affected EVD patients lose copious amounts of fluids in a matter of days, rapidly deteriorating into hypovolemic shock and death. Similar intestinal manifestations were also reported for MARV disease, another filovirus. At present, no available animal models, including non-human primates, can recapitulate the gastrointestinal symptoms of EVD patients. To fill this gap, we proposed to establish a human intestinal infection model to study the effects of filovirus infection on intestinal epithelial integrity.

CONCLUSIONS

- Successful robust EBOV and MARV infections of iPSC-derived HIOs, affecting mostly epithelial CDX2+ enterocytes was achieved.
- The infected cells showed signs of cell damage, and transcriptomics analysis indicated the modulation of cell junction pathways and a set of ion transporters known to play a role in the induction of diarrhea.
- Taken together, these data suggest EBOV and MARV compromise barrier integrity of the intestinal epithelium and cause abnormal ion flux as the basis for gastrointestinal dysfunction and diarrhea.

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