Disease Watch

EBOLA UPDATE

Outbreak news. The number of Ebola virus (EBOV; formerly known as Zaire ebolavirus) infections continues to increase in West Africa, making this the largest ever reported Ebola epidemic. The outbreak is presumed to have started in Guinea, and more than 3,000 cases and 1,500 deaths have been confirmed in Guinea, Liberia, Nigeria and Sierra Leone. A separate outbreak has been reported in the Democratic Republic of Congo (DRC). The virus is spread by direct contact with infected bodily fluids and, although EBOV infection is usually associated with an 80–90% fatality rate, the survival rate during this epidemic is around 47%. **WHO**

Emergence of the virus. In a preliminary report, Baize *et al.* used whole-genome sequencing and phylogenetic analysis to show that EBOV isolates from Guinea form a new clade but are closely related to EBOV strains from previous outbreaks in the DRC and Gabon. The analysis suggests that the outbreak resulted from a single transmission from the natural animal reservoir and the index case was a 2 year old child who died in December 2013. In addition, Gire, Goba *et al.* generated 99 EBOV genome sequences from 78 confirmed cases in Sierra Leone and compared them with previous EBOV isolates. Their analysis confirms that the outbreak originated from a single transmission from the natural reservoir and suggests that EBOV was imported to Sierra Leone by 12 people who attended a funeral in Guinea.

Experimental drugs. There are currently no licensed vaccines or drugs for the treatment of EBOV, which has prompted debate about whether experimental drugs could and should be used. A WHO committee recently announced that unapproved treatments can be used, as long as patient consent is obtained. Qiu *et al.* showed that the experimental drug ZMapp — a combination of three monoclonal antibodies that target EBOV envelope proteins — can cure non-human primates that are infected with the Kikwit variant of EBOV, even when treatment was started in animals with advanced disease. Some patients have been treated with ZMapp, but with mixed success. **WHO**

Viral pathogenesis. A hallmark of EBOV infection is the inhibition of type I interferon (IFN) signalling by binding of the viral protein 24 (eVP24) to karyopherin-α (KPNA) nuclear transporters. Xu *et al.* describe the crystal structure of the human KPNA5 carboxy terminus in complex with eVP24, which reveals that eVP24 binds to a non-classical nuclear localization signal (NLS) binding site on KPNA5 that overlaps with the binding site of phosphorylated STAT1 (pSTAT1). Binding of eVP24 to KPNA5 did not perturb the binding of other proteins that use the classical NLS binding site, which suggests that eVP24 specifically inhibits IFN signalling by preventing the binding of pSTAT1 without blocking the transport of other cargo that might be required for viral replication.

ORIGINAL RESEARCH PAPERS Baize, S. *et al.* Emergence of Zaire Ebola virus disease in Guinea — preliminary report. *N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1404505 (2014) | Gire, S. K., Goba, A. *et al.* Genomic surveillance elucidates Ebola virus origin and transmission during the 2014 outbreak. *Science* http://dx.doi.org/10.1126/science.1259657 (2014) | Qiu, X. *et al.* Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp. *Nature* http://dx.doi.org/10.1038/nature13777 (2014) | Xu, W. *et al.* Ebola virus VP24 targets a unique NLS binding site on karyopherin alpha 5 to selectively compete with nuclear import of phosphorylated STAT1. *Cell Host Microbe* **16,** 187–200 (2014)