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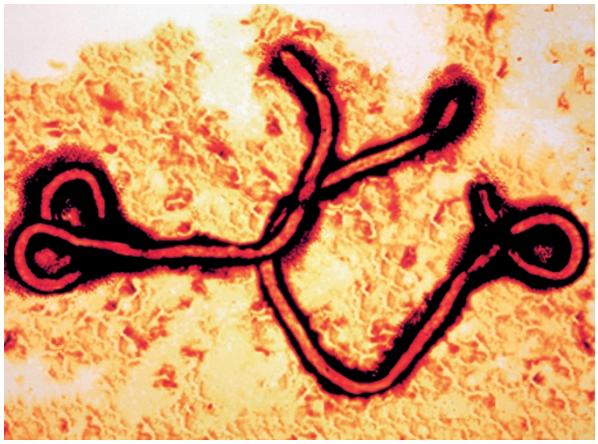
VIRAL EVOLUTION

Keeping a watchful eye on Ebola



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The ongoing outbreak of Ebola virus (EBOV) in West Africa is estimated to have caused more than 11,000 deaths and close to 30,000 infections, compared with 318 infections in the largest historical outbreak. The unprecedented scale and duration of the current epidemic has allowed the EBOV genome to mutate and give rise to new lineages. Whereas previous work established the origin of the outbreak as a single zoonotic transmission event in Guinea, probably in December 2013, and characterized several early transmission events, large-scale genome surveillance efforts are required to monitor the ongoing evolution and transmission dynamics of EBOV, and thus inform transmission prevention and vaccine development. Three new papers now report large-scale genome surveillance studies for two countries affected by the EBOV outbreak, Guinea and Sierra Leone.

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The three studies used Illumina sequencing to obtain genomic data from hundreds of patient samples. Each study also made use of published sequences — notably, those from the early phase of the outbreak in Guinea and Sierra Leone — which were combined with new data to analyse the phylogeny of viral lineages and to characterize mutation events in the EBOV genome. Carroll *et al.* and Simon-Loriere *et al.* sequenced 179 and 85 samples, respectively, that had been collected in Guinea between March 2014 and January 2015. In agreement with previous findings, these studies identified a founder lineage (‘A’ or ‘GUI-1’) that was confined to Guinea, and a second lineage (‘B’ or ‘GUI-2’), derived from the founder lineage, that was present across Guinea, Sierra Leone and Liberia and that has persisted into 2015. Simon-Loriere *et al.* also identified a third lineage (‘SLE-GUI-3’), which was a cross-border cluster of isolates from both Guinea and Sierra Leone.

In a previous report, the B lineage was linked to mourners attending the funeral of a Guinean victim of EBOV that took place in Sierra Leone, and Carroll *et al.* suggest that this event may have reignited the epidemic. As expected, this lineage was also identified in 232 new samples collected in Sierra Leone by Park *et al.*. However, over time it was replaced in Sierra Leone by a derivative lineage, ‘SL3’, which itself was replaced by a derivative lineage, ‘SL4’ (equivalent to the ‘SLE-GUI-3’ cluster identified by Simon-Loriere *et al.*).

A major objective of genome surveillance is to measure the rate of genome evolution during outbreaks and to identify mutations at candidate antigenic sites. Carroll *et al.* and Park *et al.* both calculated a rate of evolution for the EBOV genome during the current outbreak of $1.2–1.6 \times 10^{-3}$ substitutions per site per year, which is slightly higher than the long-term, between-outbreak rate of 0.8×10^{-3} substitutions per site per year. The difference might reflect an increased rate of evolution caused by the jump to a new host species from the natural reservoir of the virus, which is thought to be the fruit bat. However, the value calculated by Simon-Loriere *et al.* was 0.9×10^{-3}, which is closer to the rate in the reservoir.

All three studies noted prevalent nonsynonymous substitutions in the EBOV glycoprotein (GP), most notably in the mucin-like domain. As GP is the only exposed protein of the EBOV virion, Park *et al.* proposed that these substitutions might correspond to antigenic sites subjected to within-host diversifying selection to promote immune evasion. However, the sample size was too small to draw any statistically significant conclusions about selection. The authors hope that future experimental data will clarify the functional role, if any, of GP variants identified by genome surveillance.

Collectively, the three studies demonstrate the high capacity of EBOV to generate mutations in its genome over the course of an outbreak. This not only results in the establishment of new lineages but also in the circulation of nonsynonymous variants with possible important consequences for antigen recognition. Furthermore, by providing high-resolution data from which probable transmission routes can be inferred, these studies establish an important role for genome surveillance in public health efforts to combat EBOV outbreaks.

Naomi Attar, Associate Editor,
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ORIGINAL RESEARCH PAPERS Carroll, M. W. *et al.* Temporal and spatial analysis of the 2014–2015 Ebola virus outbreak in West Africa. *Nature* http://dx.doi.org/10.1038/nature14594 (2015) | Simon-Loriere, E. *et al.* Distinct lineages of Ebola virus in Guinea during the 2014 West African epidemic. *Nature* http://dx.doi.org/10.1038/nature14612 (2015) | Park, D. J. *et al.* Ebola virus epidemiology, transmission, and evolution during seven months in Sierra Leone. *Cell* **161**, 1516–1526 (2015)