

On Feb 14, 2021, an Ebola virus disease (EVD) outbreak was declared in Guinea. As of Mar 7, 18 EVD cases have been identified, including 9 deaths. These are the first reported cases of EVD since the 2013-2016 outbreak that resulted in over 28,000 cases and ~11,000 deaths mainly in Guinea, Liberia, and Sierra Leone.

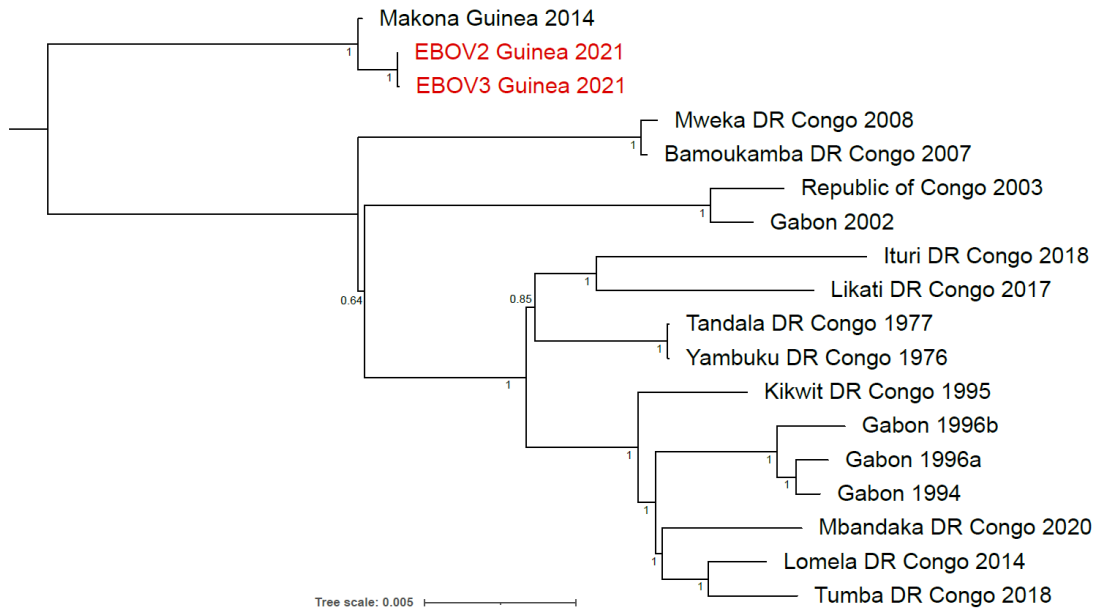
Three samples were sent by the Ministry of Health Guinea to the regional WHO reference laboratory at the Institut Pasteur de Dakar, Senegal for sequencing. Samples were processed with a hybrid-capture based approach using a probe panel that included Ebola virus (EBOV) specific targets [1]. One coding complete genome (99.6%) and one draft genome (98.7%) were obtained.

The new EBOV genomes were initially aligned to single representatives from previous EVD outbreaks, and a phylogenetic tree was inferred (Figure 1). The two genomes grouped with the 2014 Makona variant, which caused the 2013-2016 West Africa EVD outbreak.

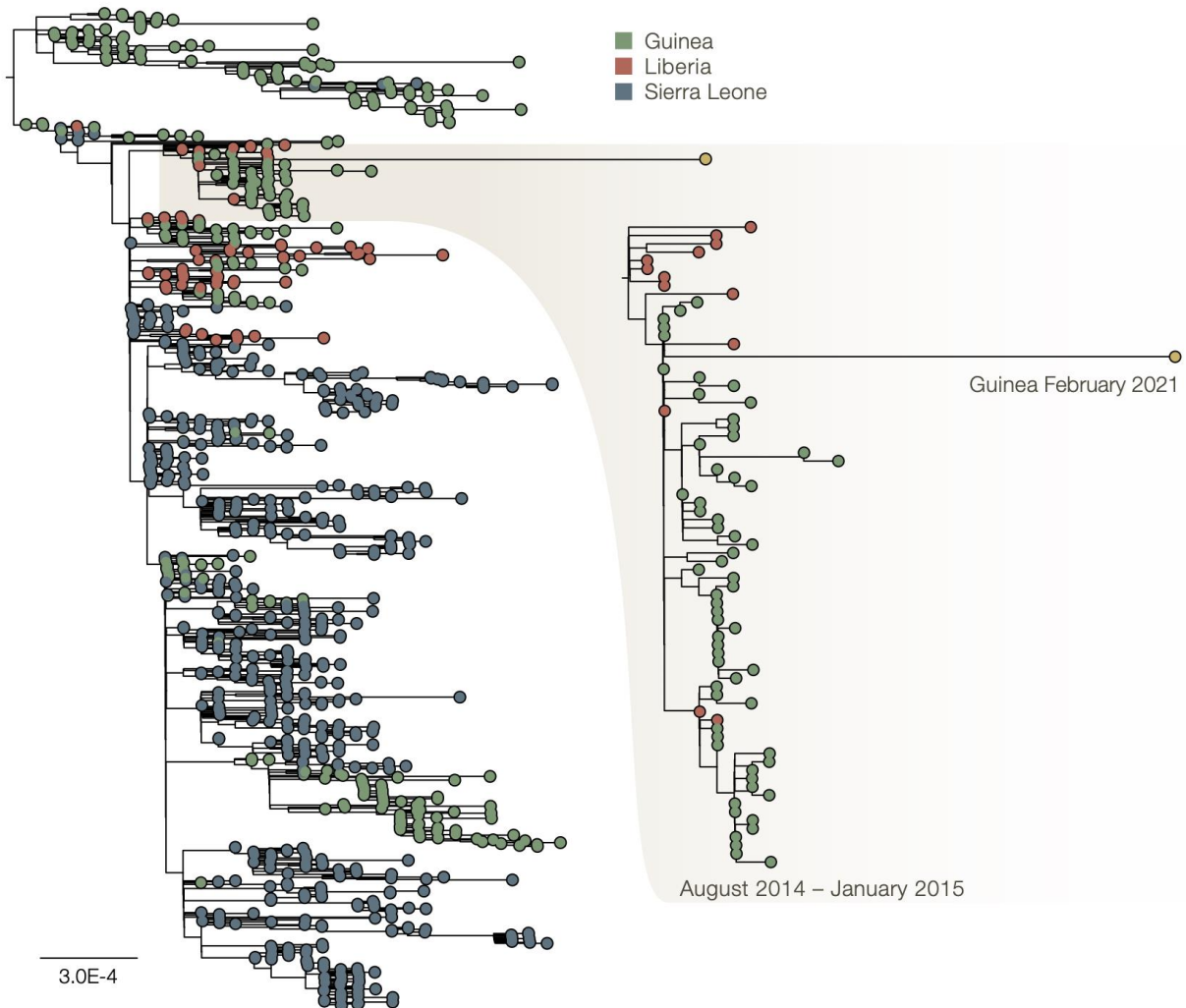
We then aligned the two 2021 Guinea EBOV genomes with a representative 1063 genomes from the 2013-2016 West Africa outbreak (Figure 2). The 2021 Guinean genomes share 10 substitutions that accumulated during the West Africa EVD outbreak (compared to KJ660346), including an A82V mutation in the glycoprotein, which arose when the virus spread to Sierra Leone and is considered a marker for human adaptation [2,3]. These shared mutations make it unlikely that the new cases are a result of a new spillover from the animal reservoir, but instead are directly linked to human cases in the 2013-2016 West Africa EVD outbreak.

The new genomes are most closely related to five identical Ebola virus Makona variant genomes sampled in August 2014 from the same region, but are diverged by 12 (Ebov-0002) and 13 (Ebov-0003) substitutions (compared to KR534588). This number of substitutions is far less than what would be expected during sustained human-to-human transmission.

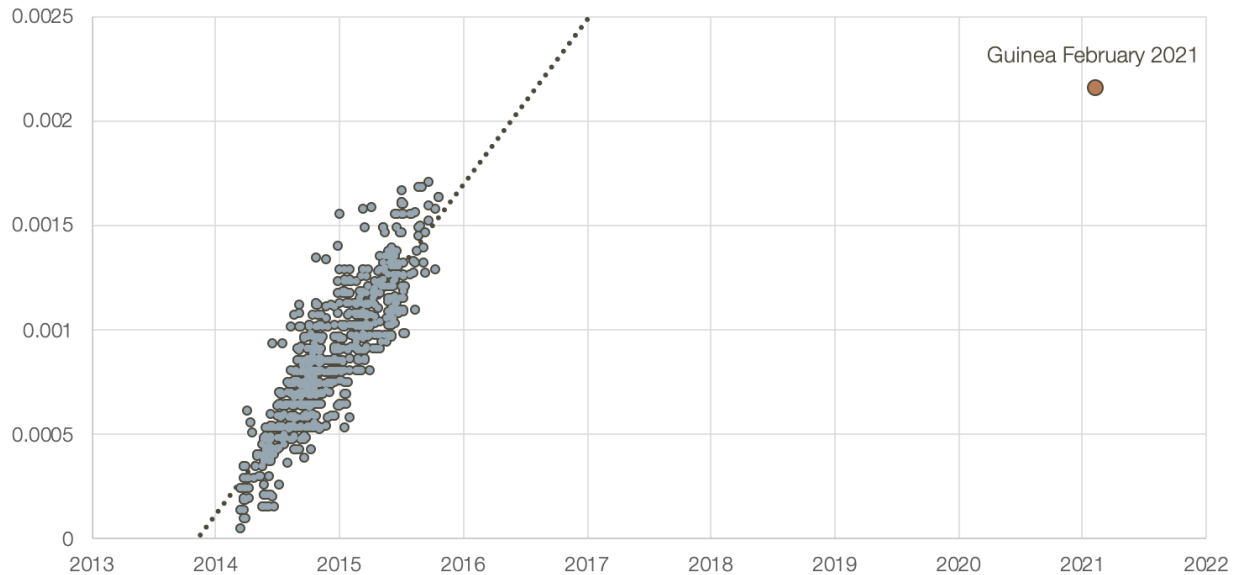
The estimated evolutionary rate of 0.0012 substitutions per site per year [4] translates to 22-23 substitutions per year and we would expect over 110 substitutions in the 5 years separating the outbreaks if it had been evolving at that rate. Root-to-tip analysis (Figure 3) also infers a lower-than-expected sequence divergence compared to genomes from the 2013-2016 West Africa EVD outbreak (95% prediction interval). A slowed evolutionary rate is a hallmark of persistent infections [5-8]. Therefore, the index case of the 2021 Guinea cluster was likely infected from a persistent source, such as via sexual transmission from an EVD survivor. These results are still preliminary, and more sequencing and analyses are underway.



**Figure 1** | Phylogenetic tree of representative genome sequences from sixteen previous ebola virus outbreaks and from the 2021 outbreak in Guinea (red). Maximum likelihood tree constructed using RAxML under the GTR+gamma substitution model.



**Figure 2** | Phylogenetic tree of a sample of 1000 genome sequences from Guinea (green), Sierra Leone (blue) and Liberia (red) from the 2014-2016 epidemic. The yellow circle represents a genome from the 2021 outbreak in Guinea. An inset shows the phylogenetic position of the 2021 genome in a group predominantly from Guinea sampled between August 2014 and January 2015. Maximum likelihood tree constructed using IQTREE2 under the HKY+gamma substitution model.



**Figure 3** | Temporal divergence plot of genetic divergence from the root of the phylogenetic tree against time of sampling for genomes in the 2014-2016 epidemic (blue circles) and a genome from the 2021 Guinea outbreak (yellow circle).

#### Data availability

Genome sequences for the two samples are available [here](#)

#### Partners and collaborators

This work is part of ongoing research collaborations between several partners:

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#### Statement on continuing work and analyses prior to publication

These genomes are being shared pre-publication. Please note though that this data is still based on work in progress and should be considered preliminary. Our analyses of this data is ongoing and a publication communicating our findings on these and other published genomes is in preparation. If you intend to use these sequences prior to our publication, please communicate with Dr. Sakoba Keita and Dr. Amadou Sall for coordination.

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