# A Genomic Landscape of Haplotype Diversity and Signatures of Phylogeographic Distribution in Zaire Ebolavirus during the 2014 EVD Epidemic

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#### Abstract

The Ebola virus (EBOV) disease epidemic from 2013 to 2015 is the largest in history, affecting multiple countries in West Africa. Genome sequencing of EBOV has revealed extensive genetic variation and mutation rate. The evolution and the variations among genotypes of EBOV observed remain low, which suggests that the viral haplotypes may be common in this transmission. To address this hypothesis, we investigated the genomic portrait of haplotype diversity in EBOV from 1976 to the 2014 outbreaks. We obtained 176 haplotypes in 305 gene-coding sequences of EBOV and found that the Hap8 in multiple viral haplotypes is the major epidemic lineage in the 2014 Sierra Leone outbreak. The phylogeographic analysis of EBOV transmission in Sierra Leone during 2014 outbreaks indicated that the genetic flow in EBOV was no more likely to occur within or without populations and the correlation between genetic and geographical distance is not significant. Our study first detected the diversity of viral haplotypes with systematic calculation of phylogeographic distribution in EBOV. This observation highlighted how Ebola virus is substantially different in virulence or transmissibility in comparison to the virus lineages associated with 2014 outbreaks in Sierra Leone, which provides a clue to understand the 2014 EBOV spreading.

Keywords: Ebolavirus, Genome sequencing, Evolutionary, Haplotype diversity, Phylogeographic distribution

### 1. Introduction

The recent Zaire Ebolavirus (EBOV) epidemic (2013–2015) was the largest in history, affecting multiple countries in West Africa.

The Zaire Ebolavirus (EBOV) is an unprecedented epidemic in West Africa during 2013 to 2015. Started from December 2013 in Guinea [1], the current EBOV outbreak spread into Liberia in March, into Sierra Leone in May, into Nigeria in late July, into Senegal in late August, and into Democratic Republic of Congo in early September [2]. Ebola virus disease (EVD) has become a global concern in 2014.

Genome sequencing of EBOV samples isolated from affected individuals during this outbreak revealed extensive viral genetic variation and mutations.

As the Ebola epidemic sweeps through West Africa, the genetic data of EBOV will answer some questions regarding the evolution dynamic of EBOV. Recently, *Tong et al.* published 175 genomes of EBOV [3], collected in Sierra Leone from September to November 2014 and *Hoene et al.* reported 4 viral genomes obtained in Mali from October to November 2014 [4]. Gire *et al.* published 99 genomes from 78 patients infected in or around Kenema, Sierra Leone during May and June of 2014 [5]. Additionally, Baize *et al.* released three EBOV genomes, collected in Guinea during March 2014 [1]. Those previous studies indicated that the EBOV is evolving slowly and is not undergoing rapid evolution in humans during the current outbreak [3, 4]. However, the detailed information of the lineage of virus, the viral mutational pattern, and the dispersal route among districts are still largely unknown, which should show the signatures of transmission and is of strategic importance to find the acquiring mutations evading diagnostic tests or vaccines [6–8].

Recent studies have investigated the genomic 'portrait' of haplotype diversity in EBOV outbreaks from 1976 onwards, and the recent major outbreak presented a unique opportunity to understand genetic variation and evolution with regards to EBOV.

Currently, the patterns of EBOV genomes variation within and between hosts have shown that human-to-human transmission can involve two or more viral haplotypes. It is possible to use geographic, temporal, and epidemiological metadata work together with the transmission clustering inferred from viral genetic data. Thus, we use the coding sequences of EBOV genomes from 1976 to 2014 to investigate haplotypes of EBOV and apply phylogeographic analysis on them [1, 3–5].

The aim of this chapter is to describe the methodology for the investigation of the genomic landscape of haplotype diversity and signatures of phylogeographic distribution in Ebola virus.

This study aims to identify the major haplotype of EBOV and the snapshot of transmission with viral genetic distance during this outbreak, which may shed light on the underlying mechanisms of EBOV spreading with a clear landscape of the 2014 outbreak.

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