Approaching Anti-Viral Therapeutics via Sequence Analysis of Nucleoprotein and Glycoprotein Precursor Genes of Lassa Virus

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The rapid evolution of viral species complicates the management of chronic infections and the control of other emerging microbiological, infectious agents. The accumulation of these polymorphisms contributes to the high genetic diversity of the Lassa viral genome. Resultantly, Lassa viral populations are able to rapidly adapt to dynamic environmental changes and adeptly evolve resistance to contemporary anti-viral therapeutics. With the vastly branched network of polymorphic Lassa strains, developing variegated anti-viral treatments is critical to both public and military health safety. This investigation provides concrete genetic evidence for a commonly presumed hypothesis regarding viral genetic divergence, which claims that with decreasing geographic proximity, individual viral strains are given opportunities to amass polymorphisms. Conducted at the U.S. Naval Research Laboratory, we performed pan-arenavirus multiplex polymerase chain reaction of 217 samples collected from various regions of West Africa. Samples were screened using novel microarray technology, the High-Density Resequencing Microarray assay (RPM-TEI v.1.0) to identify and differentiate Lassa strains. Because RPM-TEI uses an in situ-hybridization method that follows a novel combinatorial algorithm, it provides greater accuracy to this experiment. In particular, we focused our attention to the nucleoprotein (NP) and glycoprotein precursor protein (GP) genes of the Lassa genome, which are important for viral replication and encapsulation. Following RPM-TEI screening and high-throughput sequencing, nucleotide-based sequence analysis showed an 18.9% genetic divergence among NP sequences and 21.2% divergence among GP sequences. Phylogenetic tree analysis showed clustering and increased diversity.