Zika virus (ZIKV) is a positive-stranded RNA virus of the family Flaviviridae, genus Flavivirus (1). ZIKV is spread among humans primarily through the bite of infected Aedes species mosquitoes (2), but it can also be transmitted from an infected mother to her child during pregnancy (3–7) or by sexual contact (8, 9) or blood transfusion (10). In nature, ZIKV is probably maintained in a sylvatic cycle involving wild primates and arboreal mosquitoes (11–16). Although ZIKV infection generally causes a mild and self-limiting illness in infected individuals (17, 18), it has recently been associated with a growing number of severe neurological disorders, including Guillain-Barré syndrome in adults and microcephaly in newborns (3–5, 19–21). Historically, ZIKV spread from equatorial Africa and Asia (22–33) to the Pacific Islands (34–40), and most recently, to Latin America (41–46); it is now a pandemic in progress (47–50).

Over the past half century, a significant number of ZIKV isolates have been obtained sporadically from three continents (Africa, Asia, and America); however, little is known about the genetic variation among these geographically and temporally distinct ZIKVs because of the limited number of fully sequenced ZIKV genomes (27, 51–61). Here, we have determined the complete genome sequences of three historically important, spatiotemporally distinct, and genetically divergent strains of ZIKV virus: MR-766 (African lineage, Uganda, 1947), P6-740 (Asian lineage, Malaysia, 1966), and PRVABC-59 (Asian lineage-derived American strain, Puerto Rico, 2015).

TABLE 1 Summary of the complete genome sequences of three spatiotemporally distinct genetically divergent ZIKVs with the accession numbers deposited at the GenBank sequence database

<table>
<thead>
<tr>
<th>Strain</th>
<th>Country of isolation</th>
<th>Collection date</th>
<th>Host</th>
<th>Complete genome size (nt)</th>
<th>5' NCR (nt)</th>
<th>ORF (nt)</th>
<th>3' NCR (nt)</th>
<th>Genetic lineage</th>
<th>GenBank accession no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MR-766</td>
<td>Uganda</td>
<td>April 1947</td>
<td>Monkey (Macaca mulatta)</td>
<td>10,807</td>
<td>106</td>
<td>10,272</td>
<td>429</td>
<td>African</td>
<td>KX377335</td>
</tr>
<tr>
<td>P6-740</td>
<td>Malaysia</td>
<td>July 1966</td>
<td>Mosquito (Aedes aegypti)</td>
<td>10,807</td>
<td>107</td>
<td>10,272</td>
<td>428</td>
<td>Asian</td>
<td>KX377336</td>
</tr>
<tr>
<td>PRVABC-59</td>
<td>Puerto Rico</td>
<td>December 2015</td>
<td>Human (Homo sapiens)</td>
<td>10,807</td>
<td>107</td>
<td>10,272</td>
<td>428</td>
<td>Asian</td>
<td>KX377337</td>
</tr>
</tbody>
</table>

* NCR, noncoding region.
* ORF, open reading frame.
* The genome of MR-766 has been fully sequenced in this study and by three other independent groups (accession numbers KU501215, KX087101, and KU955594), and their nucleotide sequences are not identical, most likely because of variations in the cultivation history of the virus.
* The genome of PRVABC-59 has been sequenced previously by two research groups (accession numbers KU501215 and KX087101), but both lack the 5' and 3'-terminal sequences.
by a 106- or 107-nt 5’ noncoding region (NCR) and a 428- or 429-nt 3’ NCR (Table 1). The ORF encodes a 3,423-amino acid (aa) polyprotein predicted to be cleaved into 10 proteins: 122-aa C, 168-aa prM, 504-aa E, 352-aa NS1, 226-aa NS2A, 130-aa NS2B, 617-aa NS3, 150-aa NS4A, 251-aa NS4B, and 903-aa NS5. The functionality of all three genomic sequences was validated by generating their full-length infectious cDNA clones (our unpublished data). A phylodynamic analysis using the nucleotide sequences of the 29 available ZIKV genomes (15 complete and 14 near-complete) revealed two major genetic lineages: African, including MR-766; and Asian, including both P6-740 and PRVABC-59, with PRVABC-59 derived from an ancestor of the Asian lineage, in agreement with recent reports (6, 7, 38, 43, 62, 65, 66). Our findings provide a foundation for comparative functional genomics studies of ZIKV biology.

Accession number(s). The accession numbers deposited at the GenBank sequence database are listed in Table 1.

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