Spatiotemporal Dynamics of Dissemination of Non-Pandemic HIV-1 Subtype B Clades in the Caribbean Region

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Abstract

The Human immunodeficiency virus type-1 (HIV-1) epidemic in the Caribbean region is mostly driven by subtype B; but information about the pattern of viral spread in this geographic region is scarce and different studies point to quite divergent models of viral dissemination. In this study, we reconstructed the spatiotemporal and population dynamics of the HIV-1 subtype B epidemic in the Caribbean. A total of 1,806 HIV-1 subtype B pol sequences collected from 17 different Caribbean islands between 1996 and 2011 were analyzed together with sequences from the United States (n = 525) and France (n = 340) included as control. Maximum Likelihood phylogenetic analyses revealed that HIV-1 subtype B infections in the Caribbean are driven by dissemination of the pandemic clade (BPANDEMIC) responsible for most subtype B infections across the world, and older non-pandemic lineages (BCAR) characteristics of the Caribbean region. The non-pandemic BCAR clades circulating in Hispaniola, Jamaica and Trinidad and Tobago appear to have experienced an initial phase of exponential growth, with mean estimated growth rates of 0.35–0.45 year⁻¹, followed by a more recent stabilization since the middle 1990s. These results demonstrate that non-pandemic subtype B lineages have been widely disseminated through the Caribbean since the late 1960s and account for an important fraction of current HIV-1 infections in the region.

Introduction

Globally, an estimated 34 million people were infected with the human immunodeficiency virus-type 1 (HIV-1), the aetiologic agent of acquired immunodeficiency syndrome (AIDS), at the end of 2012 [1]. The Caribbean is one of the most severely affected regions in the world after Sub-Saharan Africa. About 250,000 people (1.0% of the adult population) were living with HIV-1 in the Caribbean in 2012, 78% of whom were reported in Hispaniola, the island shared by the Dominican Republic and Haiti [1]. HIV prevalence greatly varies among countries ranging from <0.1% in Cuba to over 2% in the Bahamas and Haiti [1]. The first AIDS cases were recognized in Haiti in 1978–1979 [2] and in other Caribbean countries in 1982–1984 [3,4,5]. The main mode of HIV transmission in the region is heterosexual sex [6].

The subtype B dominates the HIV-1 epidemic in most Caribbean islands [7,8,9,10,11,12,13,14], with exception of Cuba where several non-B genetic forms are collectively more prevalent [15,16,17,18,19,20]. Genetic evidence suggests that the HIV-1 subtype B was introduced from Central Africa into America through Haiti around the middle 1960s, coinciding with the return of many Haitian professionals who worked in the Democratic Republic of Congo [21]. According to that study, one subtype B strain was disseminated from Haiti to the United States (US) around 1969 and from the US to the rest of the world, establishing a “BPANDEMIC” clade. Other subtype B lineages, here called “BCAR” clades, remain mostly restricted to Haiti and neighboring Caribbean islands. The study of Gilbert et al. (2007), however, analyzed a very low number of HIV-1 subtype B Caribbean sequences (Haiti = 11 and Trinidad and Tobago = 11) and the relative prevalence of the BPANDEMIC and BCAR clades across different Caribbean islands remains largely unknown.

A more recent study that analyzed 836 HIV-1 subtype B pol gene sequences from 13 different Caribbean countries, suggests a
Table 1. HIV-1 subtype pol sequences.

<table>
<thead>
<tr>
<th>Region</th>
<th>Country</th>
<th>N (PR/RT)</th>
<th>N (RT)</th>
<th>Sampling time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean Greater Antilles</td>
<td>Cuba</td>
<td>319</td>
<td>-</td>
<td>1999–2011</td>
</tr>
<tr>
<td></td>
<td>Dominican Republic</td>
<td>168</td>
<td>-</td>
<td>2002–2011</td>
</tr>
<tr>
<td></td>
<td>Jamaica</td>
<td>146</td>
<td>-</td>
<td>2001–2010</td>
</tr>
<tr>
<td></td>
<td>Haiti</td>
<td>16</td>
<td>15</td>
<td>2004–2005</td>
</tr>
<tr>
<td></td>
<td>Guadeloupe</td>
<td>-</td>
<td>243</td>
<td>1999–2004</td>
</tr>
<tr>
<td></td>
<td>US/Virgin Islands</td>
<td>-</td>
<td>54</td>
<td>2003–2004</td>
</tr>
<tr>
<td></td>
<td>Trinidad and Tobago</td>
<td>52</td>
<td>-</td>
<td>2000–2003</td>
</tr>
<tr>
<td></td>
<td>Others*</td>
<td>25</td>
<td>14</td>
<td>1996–2000</td>
</tr>
<tr>
<td>Caribbean Bahamas</td>
<td>Bahamas</td>
<td>11</td>
<td>-</td>
<td>2004</td>
</tr>
<tr>
<td>North America</td>
<td>US</td>
<td>525</td>
<td>-</td>
<td>1982–2010</td>
</tr>
</tbody>
</table>

* Antigua and Barbuda (n = 7), Barbados (n = 14), Dominica (n = 3), Grenada (n = 4), Montserrat (n = 1), Saint Lucia (n = 4) and Saint Vincent and the Grenadines (n = 6). doi:10.1371/journal.pone.0106045.t001

The objective of this study was to estimate the current prevalence of the BPANDEMIC, BCAR, and BCAH clades in the Caribbean islands and to reconstruct the spatiotemporal dynamics of dissemination of the HIV-1 subtype B in the region. For this, we used a comprehensive dataset of HIV-1 subtype B pol sequences (n = 1,806) isolated from 17 different Caribbean islands between 1996 and 2011. These Caribbean sequences were combined with subtype B sequences from the US (n = 525) and France (n = 340) and subjected to Maximum Likelihood and Bayesian phylogenetic analyses.

Materials and Methods

HIV-1 subtype B pol sequence dataset

We retrieved all HIV-1 subtype B pol sequences with known sampling date from the Caribbean, US and France that covered the entire protease and partial reverse transcriptase (PR/RT) regions (nt 2253–3260 relative to the HXB2 clone) that were available at the Los Alamos HIV Database (http://www.hiv.lanl.gov) by June 2013. Additional HIV-1 subtype B pol sequences available in the same database, but only covering part of the RT (nt 2673–3203 relative to the HXB2 clone) were also downloaded from Barbados, Guadeloupe, Haiti, Martinique, Puerto Rico, and US Virgin Islands. Only one sequence per subject was selected and those sequences containing frameshift mutations were removed from the alignment. The analyses to run in a reasonable time, some sequences from the US, the most overrepresented country in our dataset with about 10,000 sequences, were removed. In order to generate a “non-redundant” subset representative of the HIV-1 subtype B diversity in the US, highly similar (identity ≥95%) sequences from this country were clustered with the CD-HIT program [26] using an online web server [27] and only one sequence per cluster was selected. This resulted in a final data set of 2,671 subtype B pol sequences isolated from the Caribbean (n = 1,806), US (n = 525), and France (n = 340) between 1982 and 2011 (Table 1). The number and geographic representation of subtype B Caribbean sequences available from other genomic regions was very limited, thus we decided to focus on the pol gene only. The subtype assignment of all sequences included was confirmed using the REGA HIV subtyping tool v.2 [28] and by performing Maximum Likelihood (ML) phylogenetic analyses (see below) with HIV-1 group M subtype reference sequences. Sequences were aligned and all sites associated with major antiretroviral drug resistance in PR (30, 32, 46, 47, 48, 50, 54, 76, 82, 84, 88 and 90) and RT (41, 65, 67, 69, 70, 74, 100, 101, 103, 106, 115, 130, 151, 181, 184, 188, 190, 210, 215, 219 and 230) detected in at least two sequences were excluded. All alignments are available from the authors upon request.

Phylogenetic analysis

Maximum Likelihood (ML) phylogenetic trees were inferred under the GTR+I+F nucleotide substitution model selected using the jModeltest program [29]. The ML trees were reconstructed with the PhyML program [30] using an online web server [31]. Heuristic tree search was performed using the SPR branch-swapping algorithm and the reliability of the obtained topology was estimated with the approximate likelihood-ratio test (aLRT) [32] based on the Shimodaira-Hasegawa-like procedure. The ML trees were visualized using the FigTree v1.4.0 program [33].
Figure 1. ML phylogenetic tree. A) HIV-1 subtype B pol PR/RT sequences (~1,000 nt) circulating in the Caribbean (n = 743), US (n = 525), and France (n = 340); B) HIV-1 subtype B pol RT (~600 nt) sequences from Barbados (n = 14), Guadeloupe (n = 243), Haiti (n = 15), Martinique (n = 452), Puerto Rico (n = 285), US Virgin Islands (n = 54) and representative sequences of the BPANDEMIC (US = 165, France = 135) and the B_{CAR} (Caribbean = 200) clades. Branches are colored according to the geographic origin of each sequence as indicated at the legend (bottom right). Arcs indicate the
Values are indicated at key nodes: *(0.81–0.90), **(0.91–1.0). Trees were rooted using HIV-1 subtype D reference sequences. The branch lengths are well supported (a LRT = 0.85, aLRT = 0.77, aLRT = 0.85) monophyletic subgroup (the BPANDEMIC clade) nested within basal non-pandemic lineages (the B CAR clade) selected from the previous analysis. The new ML analysis confirmed the complete segregation of the BPANDEMIC and B CAR reference sequences and the co-circulation of both pandemic and non-pandemic lineages in all Caribbean islands (Fig. 1B); although their relative prevalence greatly vary across countries (Table S1). These results support the existence of three major HIV-1 molecular epidemiologic scenarios in the Caribbean region (Fig. 2). The first one, represented by Haiti, Dominican Republic, Trinidad and Tobago and some other Lesser Antilles, is characterized by the predominance (>70%) of non-pandemic B CAR clades. The second one, represented by Jamaica, Guadeloupe, Martinique, US Virgin Islands and probably the Bahamas, is characterized by roughly similar frequency of both BPANDEMIC and B CAR clades. The third one is represented by Cuba and Puerto Rico where the vast majority (>97%) of subtype B sequences belong to the BPANDEMIC clade.

Spatiotemporal dispersal pattern of the HIV-1 B CAR clades in the Caribbean

The origin and spatiotemporal dynamics of non-pandemic subtype B Caribbean lineages was then reconstructed using a Bayesian phylogeographic analysis. The B CAR pol (PR/RT) sequences from the Dominican Republic, Haiti, Jamaica, and the Lesser Antilles were classified into nine discrete locations: Hispaniola (n = 136), Jamaica (n = 73), Trinidad and Tobago (n = 52), Antigua and Barbuda (n = 4), Dominica (n = 2), Grenada (n = 3), Montserrat (n = 1), Saint Lucia (n = 4) and Saint Vincent and the Grenadines (n = 6), and combined with subtype D sequences from the Democratic Republic of Congo (DRC). The estimated evolutionary rate of the HIV-1 B/D pol dataset was 1.74 × 10−3 (95% HPD: 1.70 × 10−3–1.80 × 10−3) substitutions/site per year and the corresponding coefficient of rate variation was 0.27 (95% HPD: 0.22–0.32), thus supporting the selection of a relaxed molecular clock model.

Consistent with the previous ML analysis, the overall topology of the Bayesian MCC tree showed that most sequences from Jamaica and Trinidad and Tobago branched in two country-specific subclades that were nested within the basal sequences from Hispaniola (Fig. 3). The mean estimated TMRCA for the major HIV-1 lineages were as follows: subtypes B/D = 1952, subtype D = 1965, subtype B = 1964, B CAR, TT = 1969, and B CAR, JM = 1971; very similar to that previously described by Gilbert et al (2007).
The most probable root location of the HIV-1 subtype B ancestor was placed in Hispaniola (posterior state probability \[PSP\] = 0.92) (Figs. 3 and 4A). Because most of the HIV-1 BCAR sequences included in our dataset were from Hispaniola (48.7%), we generated five “balanced” subsets containing up to 25 sequences from each location (Table S2). Hispaniola was pointed out as the most probable root location of the B clade in all “balanced” subsets, although the support was lower than that obtained for the complete dataset (\[PSP\] = 0.44–0.81) (Figs. 4B to 4F).

Reconstruction of viral migrations across time from the complete dataset revealed a rapid dissemination of BCAR clades across the Caribbean region (Figs. 5A–5D). After the introduction of HIV-1 subtype B into Hispaniola around the middle 1960s, non-pandemic BCAR lineages were independently disseminated to Trinidad and Tobago and Jamaica around the late 1960s and the early 1970s, respectively. Those early introductions seeded secondary outbreaks in Trinidad and Tobago and Jamaica that resulted in the origin of the BCAR-TT and BCAR-JM clades. Several independent transmissions of non-pandemic BCAR clades from Hispaniola to Jamaica (\(n = 7\)), Trinidad and Tobago (\(n = 1\)) and the other Lesser Antilles (\(n = 8\)) were detected from the late 1970s onwards. In the same time period, our data indicates that the BCAR-TT clade was also independently disseminated from Trinidad and Tobago to other Lesser Antilles (\(n = 6\)), Jamaica (\(n = 2\)) and Hispaniola (\(n = 1\)). In contrast, we found no evidence of dissemination of the BCAR-JM clade out of Jamaica.

The Bayes factor tests for significant nonzero rates, supports epidemiological linkage between DRC and Hispaniola; between Hispaniola and Jamaica/Trinidad and Tobago/Antigua and Barbuda/Dominica/St. Lucia/St. Vincent and the Grenadines;

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\begin{table}[h]
\centering
\caption{Bayesian time-scale estimates for the origin of HIV-1 subtypes B and D.}
\begin{tabular}{|l|l|l|}
\hline
Clade & Current \(T_{MRCA}\) estimates & Previous \(T_{MRCA}\) estimates* \\
\hline
\hline
\end{tabular}
\end{table}

\[\text{doi:10.1371/journal.pone.0106045.t002}\]
and between Trinidad and Tobago and Jamaica/Grenada/Montserrat/St. Vincent and the Grenadines (Fig. 5E and Table S3). The Markov jump counts analysis indicates that the most viral transitions between epidemiologically linked locations were from Hispaniola to Jamaica and the Lesser Antilles (except Trinidad and Tobago), and from Trinidad and Tobago to the other Lesser Antilles (Fig. 5F and Table S4). Lower numbers of viral migrations were detected between Jamaica/Trinidad and Tobago and between Hispaniola/Trinidad and Tobago. The highest net viral migration flux (efflux minus influx) was for Hispaniola (11.45), followed by Trinidad and Tobago (7.30), Jamaica (2.45), and other Lesser Antilles (2.14).

Demographic history of the HIV-1 B\textsubscript{CAR} clades in the Caribbean

We reconstructed the population dynamic pattern of the HIV-1 B\textsubscript{CAR} clades from Hispaniola (n = 136), the B\textsubscript{CAR-TT} clade from Trinidad and Tobago (n = 49) and the B\textsubscript{CAR-JM} clade from Jamaica (n = 50). Substitution rate and T\textsubscript{MRCA} estimates obtained in the previous Bayesian analysis were used as prior intervals for demographic reconstructions. The Bayesian skyline plot (BSP) coalescent analysis suggests that all Caribbean clades experienced an initial phase of fast exponential growth followed by a more recent decline in growth rate since the middle 1990s, consistent with a model of logistic growth (Fig. 6). The log ML for the logistic, exponential, and expansion growth models were then calculated using both PS and SS methods. The model of logistic
population growth was strongly supported over the other for all HIV-1 Caribbean clades (log BF = 3) (Table 3). According to the logistic growth coalescent model, the Caribbean clades exhibited mean initial growth rates that range from 0.36 year\(^{-1}\) to 0.46 year\(^{-1}\), with great overlap of the 95% HPD intervals (Fig. 6).

**Discussion**

This study demonstrates that the HIV-1 subtype B epidemic in the Caribbean is driven by dissemination of the pandemic clade (B\(_{\text{PANDEMIC}}\)), responsible for most subtype B infections across the world, as well as non-pandemic lineages (B\(_{\text{CAR}}\)). The relative prevalence of the different subtype B clades greatly varies among countries, giving rise to three major epidemiologic scenarios: 1) islands where B\(_{\text{CAR}}\) lineages are predominant (Haiti, Dominican Republic and some Lesser Antilles); 2) islands where epidemic is mainly driven by the B\(_{\text{PANDEMIC}}\) clade (Cuba and Puerto Rico); and 3) islands where both B\(_{\text{PANDEMIC}}\) and B\(_{\text{CAR}}\) clades circulate at roughly similar proportions (Jamaica, Guadeloupe, Martinique, US Virgin Islands and the Bahamas).

The differential spreading of B\(_{\text{PANDEMIC}}\) and B\(_{\text{CAR}}\) clades across Caribbean islands probably resulted from the combination of chance effects and socio-ecological factors. The HIV-1 epidemic in most Caribbean countries is mainly driven by heterosexual sex [6], with exception of Cuba and Puerto Rico where the epidemic is driven primarily by populations of men having sex with men (MSM) [20,50] and injection drug users (IDUs) [6,51], respectively. As a commonwealth of the United States, an extensive migration/travel of Puerto Rican IDUs between Puerto Rico and New York has been reported [52,53]. It is also interesting to note that the origin of the major HIV-1 subtype B Cuban clades, estimated around the early 1990s [24], coincides with an abrupt increase in the number of tourists from North America and Europe that visited Cuba [54]. These singular socio-ecological factors may have fueled the chance introduction of the B\(_{\text{PANDEMIC}}\) clade in the Cuban MSM and Puerto Rican IDUs, which explains the preferential dissemination of this subtype B variant in those islands.

Our study indicates that HIV-1 subtype B likely entered in the Americas through the island of Hispaniola around the middle...
1960s, in agreement with the model proposed by Gilbert et al (2007). HIV sequences from Haiti and the Dominican Republic were phylogenetically intermixed among each other, consistent with the geographic proximity and intense human mobility between those countries [55], making it difficult to determine which country of Hispaniola was the entrance point for this subtype. Notably, the HIV prevalence in the Dominican Republic is particularly high (5%) among the Haitian-origin communities of the bateyes [56]; suggesting that the Dominican Republic epidemic has been partially driven by links to Haiti. This epidemiological context combined with historical data that also links Haiti to the DRC in the 1960s [21], supports the notion that subtype B was
Table 3. Best fit demographic model for different HIV-1 subtype BCAR clades.

<table>
<thead>
<tr>
<th>Model Clade</th>
<th>Models compared</th>
<th>Log BF (SS)</th>
<th>Log BF (PS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCAR-TT</td>
<td>Freq/Expo</td>
<td>-15092.0</td>
<td>537</td>
</tr>
<tr>
<td>BCAR-JM</td>
<td>Freq/Expo</td>
<td>-15143.8</td>
<td>543</td>
</tr>
<tr>
<td>BCAR-TT</td>
<td>Freq/Expa</td>
<td>-15145.7</td>
<td>126</td>
</tr>
<tr>
<td>BCAR-JM</td>
<td>Freq/Expa</td>
<td>-15146.0</td>
<td>263</td>
</tr>
<tr>
<td>BCAR-TT</td>
<td>Freq/Log</td>
<td>-6873.6</td>
<td>-6896.4</td>
</tr>
<tr>
<td>BCAR-JM</td>
<td>Freq/Log</td>
<td>-6893.9</td>
<td>-6896.6</td>
</tr>
<tr>
<td>BCAR-TT</td>
<td>Freq/Log</td>
<td>-6034.7</td>
<td>-6034.9</td>
</tr>
<tr>
<td>BCAR-JM</td>
<td>Freq/Log</td>
<td>-6044.0</td>
<td>-6044.1</td>
</tr>
</tbody>
</table>

Log marginal likelihood (ML) estimates of the logistic (Log), exponential (Expo) and expansion (Expa) growth demographic models obtained using the path sampling (PS) and stepping-stone sampling (SS) methods. The Log Bayes factor (BF) is the difference of the Log ML between alternative (H1) and null (H0) models (H1/H0). Log BF > 3 indicate that model H1 is more strongly supported by the data than model H0.

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The results presented here also clearly contrast with the hypothesis that BCAR clades early disseminated from Haiti and were most likely first introduced into the Caribbean and then disseminated to the Dominican Republic at multiple times.

Non-pandemic BCAR strains probably started to spread from Haiti and/or Dominican Republic to Trinidad and Tobago and Jamaica between the late 1960s and the early 1970s, seeding secondary outbreaks that gave rise to local non-pandemic BCAR clades here called BCAR-TT and BCAR-JM. The BCAR-TT clade was previously described by Gilbert et al. (2007) and comprises 94% of subtype B sequences from Trinidad and Tobago here included, supporting that this clade probably resulted from dissemination of a single founder non-pandemic strain [7,21,57]. The BCAR-JM clade comprises 34% of subtype B sequences from Jamaica, indicating a polyphyletic origin of the Jamaican epidemic. Indeed, the second largest Jamaican-specific clade that comprises 19% of subtype B sequences from this country was nested among BPANDEMIC strains. The BCAR strains may have also seeded secondary HIV epidemics in other Lesser Antilles islands, although more sequences should be analyzed to confirm this observation.
BPANDEMIC clade [22]. In our opinion, clusters I and II matched with the B\textsubscript{CAR} and BPANDEMIC clades here described, respectively. The clear distinction between pandemic and non-pandemic subtype B lineages was probably hampered in the previous study because the absence of reference subtype B sequences from US/Europe and the use of an unrooted phylogenetic tree.

The study of Holguin and Pagan (2013) proposes that the earliest subtype B Caribbean epidemics arose in the islands of Puerto Rico and Antigua around 1980 and that epidemics in Haiti, Dominican Republic and Jamaica only arose around the middle 1980s (95% HPD: 1980–1990). Our study and the study of Gilbert \textit{et al} (2007), however, indicate that the subtype B epidemics in Hispaniola, Jamaica and Trinidad and Tobago probably arose before 1975. Of note, the mean evolutionary rate estimated for the HIV-1 \textit{pol} gene in the previous study (3.6 \times 10^{-3} subs/site/year) [22] was two times higher than the corresponding mean rate estimated here (1.7 \times 10^{-3} subs/site/year). That rate was also higher than that usually estimated for the \textit{pol} gene of HIV-1 subtype B (1.0–3.0 \times 10^{-3} subs/site/year) [24,38,39,40,60,61], and other HIV-1 group M clades (1.0–2.5 \times 10^{-3} subs/site/year) [24,61,62,63,64,65,66,67,68,69,70,71,72,73]. That extremely fast calibration clock rate for the HIV-1 \textit{pol} gene may have pushed TMRCAs estimates of Caribbean epidemics toward misleading young ages.

The study of Holguin and Pagan (2013) also suggests that subtype B was mainly disseminated through the Caribbean following two routes: clade I would have jumped from Antigua to other Lesser Antilles, the Bahamas, Haiti and Jamaica; and clade II would have spread from Puerto Rico to Cuba, Jamaica, Haiti and Dominican Republic. Our study suggests a very different scenario in which the B\textsubscript{CAR} clades (clade I) were disseminated from both Hispaniola and Trinidad and Tobago to the other Caribbean islands. We have not determined the most important hubs of dissemination of the BPANDEMIC clade (clade II); but it is highly improbable to trace the origin of all BPANDEMIC Caribbean sequences to Puerto Rico. The real scenario is probably more complex and other countries that maintain intensive migration/travel with the Caribbean like the US, England, Netherlands, France and Spain may have also acted as important hubs of dissemination of the BPANDEMIC clade into the region.

Our demographic reconstruction suggests that B\textsubscript{CAR} clades circulating in Hispaniola, Jamaica and Trinidad and Tobago experienced an initial phase of exponential growth followed by a more recent stabilization since the middle 1990s. This reconstructed demographic pattern fully agrees with the epidemiological profile of the Caribbean region, where the number of people living with HIV has remained relatively stable since the late 1990s [1,6], and resemble the patterns previously described for subtype B epidemics in other American countries including Brazil [74] the US [75] and Panama [25]. Interestingly, the mean growth rates estimated for the B\textsubscript{CAR} clades from Hispaniola, Jamaica and Trinidad and Tobago (0.35–0.45 year\textsuperscript{-1}) were similar to those estimated for BPANDEMIC clades mainly circulating among heterosexual populations from Panama (0.20–0.40 year\textsuperscript{-1}) [23]; but lower than those estimated for BPANDEMIC clades mainly transmitted among MSM populations from Cuba, Italy, Hong Kong and the United Kingdom (0.5–1.6 year\textsuperscript{-1}) [24,38,39,40].

**Figure 6. Demographic history of the HIV-1 B\textsubscript{CAR} (A, B), B\textsubscript{CAR-JM} (C, D), and B\textsubscript{CAR-TT} (E, F) clades circulating in Hispaniola, Jamaica and Trinidad and Tobago, respectively.** Effective number of infections (y-axis; log10 scale) through time (x-axis; calendar years) estimated using Bayesian skyline (A, C, E) and logistic (B, D, F) growth coalescent model. Median estimates of the effective number of infections (solid line) and 95% HPD intervals of the estimates (dashed lines) are shown in each graphic. The median growth rate (with the corresponding 95% credibility interval in parenthesis) of each clade estimated under logistic growth model is indicated in the upper left corner.

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This suggests that ecological factors, rather than viral lineage characteristics, are the major determinants of the HIV-1 subtype B epidemic growth rate across different countries.

In summary, this study demonstrates that non-pandemic HIV-1 subtype B viral strains have been widely disseminated through the Caribbean since the late 1980s and account for an important fraction (≥50%) of current HIV-1 infections in Haiti, Dominican Republic, Jamaica, the Bahamas and the Lesser Antilles. This study also indicates that Haiti, Dominican Republic and Trinidad and Tobago were probably the major hubs of dissemination of B_{CAR} in the region. Although this is the most comprehensive study of HIV-1 spread in the Caribbean performed to date, future studies would be improved by the use of more geographically balanced datasets as well as longer (ideally full-length) viral genomic sequences.

Supporting Information

Table S1 Distribution of HIV-1 subtype pol sequences from different countries within the B_{PAE} and the B_{CAR} clades.

(PDF)

Table S2 Number of sequence per location included in the complete and in the country “balanced” HIV-1 B_{CAR} datasets.

(PDF)

References


Phylogenetics of HIV-1 Subtype B in the Caribbean

Table S3 Bayes factor (BF) rates of epidemiological links between locations for dispersal of non-pandemic B_{CAR} lineages in the Caribbean region.

(PDF)

Table S4 Mean estimated number of viral migrations between locations for dispersal of non-pandemic B_{CAR} lineages in the Caribbean region.

(PDF)

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Author Contributions

Conceived and designed the experiments: GB. Performed the experiments: MC YM GB. Analyzed the data: MC GB. Contributed reagents/materials/analysis tools: MC GB. Contributed to the writing of the manuscript: GB MC YM.
Phylodynamics of HIV-1 Subtype B in the Caribbean


