Origin and outbreak of HIV-1 CRF55_01B among MSM in Shenzhen, China

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Background

In China, early co-circulation of two HIV-1 subtypes B and C among injection drug users (IDUs) had led to the generation of CRF07_BC and CRF08_BC. After origin, CRF07_BC and CRF08_BC rapidly spread to other regions of China via drug trafficking routes and cause outbreak among IDUs. CRF55_01B was the third CRF identified in China, among 3 men who have sex with men (MSM) from two southern cities. When and where CRF55_01B originated and whether it causes an outbreak among high-risk groups like CRF07_BC and CRF08_BC deserve investigation.

Shenzhen, a developed city in southern China, has attracted many young internal migrants from all over the country, including 70,000 MSM. HIV prevalence among MSM in Shenzhen has increased from 0.9% in 2002 to 6.7% in 2008, and 10.3% in 2011.

Methods

From 2006 to 2013, we collected 4931 HIV-1 seropositive blood samples from MSM and heterosexuals in Shenzhen and 40% of MSM were recently infected with HIV-1. From them, a total of 1072 pol sequences were obtained for HIV subtyping. The maximum clade credibility (MCC) tree was built. The evolutionary rate, the time to the most recent common ancestor, and the demographic history of CRF55_01B were inferred using BEAST v1.7.5.

Results

A total of 100 CRF55_01B were identified, accounting for 9.3% of all subtyped sequences. Majority of CRF55_01B (85.0%) were circulating among MSM, significant higher than those in heterosexuals (p=0.025).

Of particular importance, the earliest sample carrying CRF55_01B was traced back to 2007, indicating that CRF55_01B had a relative long history among MSM in Shenzhen. The maximum clade credibility (MCC) tree of CRF55_01B shows that CRF55_01B from Shenzhen MSM are located at the root of the tree, and strains from heterosexuals and MSM in other regions (Changsha, Dongguan, Shanghai and Beijing) are dispersed within the strains from Shenzhen MSM. These indicate that CRF55_01B have spread to other regions of China via floating MSM. Bayesian-coalescent analyses show that CRF55_01B originated among Shenzhen MSM in 2001 (1996-2004).

The Bayesian skyline plot (BSP) analyses show that HIV-1 CRF55_01B experienced an initial phase of fast exponential growth during 2006-2009 and then remained stable. The exponential growth coalescent model indicates that the CRF55_01B expanded during 2006-2009 with a mean growth rate of 0.66 year⁻¹ (95%HPD: 0.33-1.03).

Conclusions

Our results suggest that Shenzhen is the epicenter for CRF55_01B transmission.

We predict that CRF55_01B will become a new HIV-1 recombinant most commonly transmitted among MSM after the prevalence of CRF07_BC and CRF08_BC among IDUs in China. Recently, sporadic detection of CRF55_01B in Dongguan, Hunan, Shanghai and Beijing might be a prelude of CRF55_01B outbreak among MSM in these city/provinces and even other regions of China in the near future.

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Figure 1. Proportion of annual reports of HIV cases by transmission routes in Shenzhen (2004-2013).

(a) Proportion of annual reports of HIV cases by transmission routes in China (1985-2006).

(b) Proportion of annual reports of HIV cases by transmission routes in Shenzhen (2004-2013).

Figure 2. Prevalence of CRF55_01B among MSM and heterosexuals in Shenzhen during 2007-2012. No detection of CRF55_01B among heterosexuals in 2010-2011 might be due to too small sample size.

Figure 3. The Bayesian skyline plot (BSP) estimated the past population dynamics of CRF55_01B among MSM and heterosexuals in Shenzhen. The thick solid line in the plot represents the median estimate and the shaded region represents the 95% highest posterior density (HPD) credible region.

Figure 4. MCC tree of CRF55_01B. The MCC tree was constructed based on a data set of 31 CRF55_01B pol sequences (GenBank accession numbers: JX190085-JX190115 and JX190124-JX190154) using Bayesian MCC analysis implemented in BEAST v1.7.5. The analysis was performed using an uncorrelated lognormal relaxed clock model and a relaxed coalescent+Yule substitution model under an exponential coalescent+Yule. The MCC analysis was run for 100 million generations, with sampling every 10,000 generations. The red, blue, and pink branches indicate the strains from Dongguan, Changsha, and Shanghai, respectively. The green branches indicate the strains circulating in heterosexuals.

Figure 5. Bayesian analysis of HIV-1 CRF07_BC and HCV coinfections in Anhui. PLoS One. 2011; 6:e23347.

Figure 6. The Bayesian skyline plot (BSP) estimated the past population dynamics of CRF55_01B among MSM and heterosexuals in Shenzhen. The thick solid line in the plot represents the median estimate and the shaded region represents the 95% highest posterior density (HPD) credible region.

Figure 7. The Bayesian analysis of HIV-1 CRF07_BC and HCV coinfections in Anhui. PLoS One. 2011; 6:e23347.

Figure 8. The Bayesian analysis of HIV-1 CRF07_BC and HCV coinfections in Anhui. PLoS One. 2011; 6:e23347.

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