Tuberculosis 95 (2015) S167–S176

Contents lists available at ScienceDirect

Tuberculosis

journal homepage: http://intl.elsevierhealth.com/journals/tube

Mycobacterium tuberculosis phylogeography in the context of human migration and pathogen's pathobiology: Insights from Beijing and Ural families

Igor Mokrousov*

St. Petersburg Pasteur Institute, St. Petersburg 197101, Russia

Keywords:
Mycobacterium tuberculosis
Beijing genotype
Ural genotype
Human migration
Phylogeography

S U M M A R Y

Here, I review the population structure and phylogeography of the two contrasting families of *Mycobacterium tuberculosis*, Beijing and Ural, in the context of strain pathobiology and human history and migration.

Proprietary database (12-loci MIRU-VNTR profiles of 3067 Beijing genotype isolates) was subjected to phylogenetic and statistical analysis. The highest rate (90%) and diversity (HGI 0.80–0.95) of the Beijing genotype in North China suggest it to be its area of origin. Under VNTR-based MDS analysis the inter-population genetic distances correlated with geography over uninterrupted landmasses. In contrast, large water distances together with long time generated remarkable outliers. Weak and less expected affinities of the distant *M. tuberculosis* populations may reflect hidden epidemiological links due to unknown migration. Association with drug-resistance or increased virulence/transmissibility along with particular human migration flows shape global dissemination of some Beijing clones.

The paucity of data on the Ural genotype prevents from high-resolution analysis that was mainly based on the available spoligotyping data. The North/East Pontic area marked with the highest prevalence of the Ural family may have been the area of its origin and primary dispersal in Eurasia. Ural strains are not marked by increased pathogenic capacities, increased transmissibility and association with drug resistance (but most recent reports describe an alarming increase of MDR Ural strains in some parts of eastern Europe and northwestern Russia).

Large-scale SNP or WGS population-based studies targeting strains from indigenous populations and, eventually, analysis of ancient DNA will better test these hypotheses. Host genetics factors likely play the most prominent role in differential dissemination of particular *M. tuberculosis* genotypes.

© 2015 Elsevier Ltd. All rights reserved.

"Happy families are all alike; every unhappy family is unhappy in its own way"

Leo Tolstoy, *Anna Karenina*

"A family is a unit composed not only of children but of men, women, an occasional animal, and the common cold"

Ogden Nash

1. Introduction

Tuberculosis (TB) is not only re-emerging disease of global concern but it is ancient disease that plagued humankind throughout its history and prehistory and was frequently mentioned by ancient scholars [1–3]. TB mortality peaked in Europe in the 17–18th centuries: 500/100,000, and started to decrease only in the end of the 19th century [4]. In Russia, due to delayed industrialization and urbanization, TB mortality was 400/100,000 in the early 20th century [5].

Mycobacterium tuberculosis sensu stricto is exclusively a human pathogen. The tubercle bacillus can persist in the form of a long-term asymptomatic infection and one third of the world population is estimated to have a latent TB infection. The latent or dormant TB was perhaps the main mode of *M. tuberculosis* co-existence with

* Laboratory of Molecular Microbiology, St. Petersburg Pasteur Institute, St. Petersburg 197101, Russia. Tel.: +7 812 2332149; fax: +7 812 2329217.
E-mail addresses: imokrousov@mail.ru, igormokrousov@yahoo.com.

http://dx.doi.org/10.1016/j.tube.2015.02.031
1472-9792/© 2015 Elsevier Ltd. All rights reserved.

its human host in a pre-industrialized time when transmission of the pathogen was historically vertical, i.e., mainly family/household-linked. I use the term 'vertical' not in the specific medical sense i.e., mother-to-child transmission but in the broader (in my opinion) socio-biological sense, referring to the family/household transmission.

During the long course of its evolution, species *Homo sapiens* has acquired the "second genome", a microbiome. From the phylogeographic point of view, human microbiome may be regarded as an alternative source of data for deciphering human migrations and origins. On the other hand, knowledge about human migration and demographics may explain, under certain limitations, origin and dispersal of human pathogens.

M. tuberculosis population structure is predominantly clonal which makes it reasonable to study separate genetic families as particular models of the species. Objective and interest of this review were to gain insights into global phylogeography of the two contrasting families, widely studied Beijing and less "popular" Ural, and to evaluate the role of human migration and other factors in shaping their population structures.

2. Phylogeography of the Beijing family and human migration

The Beijing family is arguably best known and most studied *M. tuberculosis* lineage to date. By CRISPR-based 43-spacer spoligotyping it is defined by characteristic profile of usually nine last signals and, in any case, signals 1 to 34 should be absent. A discovery of 'pseudo-Beijing' isolates with nine-signal spoligoprofile but due to deletion other than RD207 [6] requires to reconsider this definition and use other robust markers to negate such 'pseudo-Beijing' isolates.

Although a classical 12-MIRU-VNTR format is not sufficient for high-resolution typing of the Beijing strains, a large body of data on global diversity has been accumulated since early 2000s and was collected in the proprietary database which updates and analysis have been published since 2004 and the most recent one included 2400 profiles/isolates [7]. In the present review, my analysis is based on the current version of the database that includes profiles of 3067 Beijing isolates.

The phylogenetic network (Figure 1) shows relationships of the 50 major MIRU types of the Beijing genotype; a distribution of the 10 main types is shown on a map (Figure 2), based on published sources [7–30]. A highest prevalence (up to 90%) and diversity (HGI 0.80–0.95) of the Beijing genotype in North China indicate that it could be area of its origin.

Based on VNTR and RD181 deletion analysis of Chinese isolates, Wan et al. recently suggested that the presence in the South of China of strains representing early ancient Beijing lineage (RD181 intact) may indicate at the South of China origin of the Beijing family, probably in the Guangxi region [31]. However a closer look at their data reveals a misinterpretation. First, the rate of the early ancient lineage with intact RD181 in the southern province of Guangxi is indeed the highest (16.5%) but this rate is also similarly high (14.9%) in the province of Jilin located in the opposite, northeastern part of China. Second, in the VNTR-based MST, the strains from Guangxi are found in the secondary and unrelated nodes and no such strains is found in the founding core node of the network. In contrast, strains from Jilin take a large, one-third part of this central type in the VNTR-based network, and also are abundantly dispersed across the whole network. Taken together, these observations question South of China, and reconfirm North of China as place of origin of the Beijing genotype.

One may also note geographic specificity and gradients of some MIRU-types (Figure 2). For example, type M11 is prevalent throughout Eurasia, derived type M2 – across Russia and former Soviet Union, type M28 – in coastal areas in East Asia, South Africa and Australia.

Principal components analysis or its variant multidimensional scaling (MDS) is a helpful way to analyse complex genetic data although rarely used in *M. tuberculosis* research. The MIRU-based MDS-graph of certain Beijing populations (Figure 3) suggests that geography was the primary factor that defined genetic diversity of *M. tuberculosis*. However, this assertion is more complex and both time and space should be taken into consideration to explain the observed pattern. It appears that both large water distance (but not landmass) along with long time were required to produce the most prominent effect as exemplified by the case of South Africa since the Beijing genotype has been brought here since 17th century via slave trade of Dutch East India Company. One of these factors (time) is lacking in the case of Peru: importation of Beijing strains started only since the 19th century. Nonetheless in the MDS graph the Peru population is already drifting away from the Eurasian supercluster. Regarding the latter, it is interesting to note how Russian and Vietnam populations are overlapping with different parts of the large Chinese cluster. More dispersed position of Chinese populations reflects that China is area of origin of this genotype and its genetic and geographic diversity here is the highest due to the longest evolution. In case of Russia, these distant populations form a compact cluster because of combination of the demo- and geographic factors: (i) long time, but no water barrier (no strong founder effect); (ii) recent dissemination fuelled by mass population mixing during the 20th century.

In my opinion, these observations support a general robustness of this kind of analysis. In its turn, this indirectly supports a reliability of the less expected affinities between distant populations of *M. tuberculosis*, such as a relative proximity of South Africa and northern Vietnam (Figure 3), Ural and central Chinese populations (in a separate graph of Eurasia [not shown]) likely representing hidden or less known patterns of human migrations or unknown epidemiological links between distant regions.

Further, I will briefly discuss the Beijing diversity in some world areas less investigated in my previous publications [32,33].

2.1. Beijing genotype in Japan

The *M. tuberculosis* Beijing population in Japan is marked with a very high rate (up to 80%) of the ancient/ancestral sublineage (intact NTF region) [14]. One explanation of such a high rate of the ancient Beijing here is that the Beijing strains were brought to Japan in ancient times (when ancestral lineage was likely more prevalent). This resulted in the high rate of the ancient sublineage in Japan, via bottleneck. The data on TB history in Japan corroborate with this hypothesis. The palaeopathological paper of Suzuki and Inoue [34] provided a comprehensive information on the early history and likely sources of TB in Japan. In spite of intensive studies of the skeletal samples, no case of spinal tuberculosis has been found in Jomon period (Neolithic; ca. 10,000 BC to 300 BC) but was described in the subsequent Aneolithic Yayoi period 300 BC to AD 300. The Yayoi culture spread throughout Japan due to massive immigration from the continent at least four times outnumbering the Jomon population [35]. These immigrants from Korea and North China not only introduced various cultural characteristics but also brought new infectious diseases, including tuberculosis. The latter was usually fatal to the immunologically naïve Jomon population. Consequent host-pathogen co-evolution should have changed the population immunity resulting in a change of infection from an acute to a chronic form [34].

Download English Version:

https://daneshyari.com/en/article/2401488

Download Persian Version:

https://daneshyari.com/article/2401488

Daneshyari.com