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Designation of Major Mycobacterial Interspersed Repetitive-Unit Types within *Mycobacterium tuberculosis* Beijing Genotype, an Important Point

We read with a great interest the article by Hanekom et al., about the *Mycobacterium tuberculosis* Beijing genotype in Cape Town (1). Colleagues from Stellenbosch University proposed an intriguing hypothesis in which the population structure of the clinically relevant lineage within *M. tuberculosis* had been shaped via adaptation to a local human population, whereas all of the founder strains had a common starting point, having been imported from East Asia at approximately the same time (1). This idea is exciting, although another explanation is that the disequilibrium of the local population structure, i.e., a predominance of the particular variants, may result from the founder effect due to initially very small imported human/*M. tuberculosis* populations (2, 3). These somewhat contrasting opinions deserve further testing; both scenarios may be true, while their interaction could have produced an even stronger effect.

We noticed, however, one minor but important omission, and we wish to have it corrected. Hanekom et al. (1) compared their mycobacterial interspersed repetitive-unit (MIRU) data from Cape Town with those published for East Asia and concluded that "nine of the Beijing MIRU types (the MT01, MT08, MT11, MT18, MT19, MT21, MT28, MT33, and MT54 types) were shared between these geographical settings (Table 1)." Furthermore, these types are discussed as founder types for the Cape Town population of the *M. tuberculosis* Beijing genotype (1). Unfortunately, it is not clear from the text or from Table 1 that in fact, all of these types, from MT01 to MT57, were described initially and named in the first global MIRU database of the *M. tuberculosis* Beijing genotype, compiled and developed in our laboratory in the St. Petersburg Pasteur Institute (3, 4). Its most recent update has just been published (2), and the database may be consulted on request. Our type definition and numbering (3, 4) provided a useful framework for further studies, as the cited article (1) demonstrated. Therefore, our correction to the otherwise valuable publication by Hanekom et al. (1) seems most appropriate.

REFERENCES

1. **Hanekom, M., G. D. van der Spuy, N. C. van Pittius, C. R. McEvoy, S. L. Ndabambi, T. C. Victor, E. G. Hoal, P. D. van Helden, and R. M. Warren.** 2007. Evidence that the spread of *Mycobacterium tuberculosis* strains with the Beijing genotype is human population dependent. J. Clin. Microbiol. **45:**2263–2266.
2. **Mokrousov, I.** 2007. Towards a quantitative perception of human-microbial co-evolution. Front. Biosci. **12:**4818–4825.
3. **Mokrousov, I., H. M. Ly, T. Otten, N. N. Lan, B. Vyshnevskyi, S. Hoffner, and O. Narvskaya.** 2005. Origin and primary dispersal of the *Mycobacterium tuberculosis* Beijing genotype: clues from human phylogeography. Genome Res. **15:**1357–1364.
4. **Mokrousov, I., O. Narvskaya, E. Limeschenko, A. Vyazovaya, T. Otten, and B. Vyshnevskiy.** 2004. Analysis of the allelic diversity of the mycobacterial interspersed repetitive units in *Mycobacterium tuberculosis* strains of the Beijing family: practical implications and evolutionary considerations. J. Clin. Microbiol. **42:**2438–2444.

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Authors' Reply

In two recent publications (1, 2), we reported using molecular epidemiological approaches to investigate the population structure of *M. tuberculosis* strains with the Beijing genotype in South Africa, and these data were compared to previously published data on the population structure of strains with the Beijing genotype in East Asia. We showed that strains within sublineage 7 were overrepresented in South Africa compared to those in East Asia (2). Accordingly, we hypothesized that either strains from sublineage 7 had evolved a higher level of fitness since their arrival in South Africa or that the host genetics of the South African population was different from that in East Asia and thereby was less likely to prevent disease progression with strains from this lineage (2). Mokrousov and Narvskaya have put forward an alternative explanation. It is suggested that the overrepresentation of sublineage 7 strains may have resulted from disequilibrium of the local population structure, i.e., the introduction of the sublineage 7 founder strain into a small human population. In this scenario, the sublineage 7 strain would have spread into the small population, amplifying the number of "founder" cases. The numerical advantage gained in this manner would imply that sublineage 7 strains would always be overrepresented in this population if founder strains from the other sublineages (1 to 6) were introduced only subsequently. This would imply that all strains with the Beijing genotype (irrespective of sublineage) would be equally fit. Although we acknowledge that this scenario could have occurred, we suggest that the statistical probability would be small, given that the sublineage 7 strains are underrepresented in East Asia, and therefore it would have been more likely that a strain from sublineages 1 to 6 was initially introduced into South Africa. Our suggestion is supported by the observation that founder strains from sublineages 1 to 6 were overrepresented in the South African study setting (2). Our hypothesis that sublineage 7 strains show a higher level of fitness in the South African population is supported by the observation that sublineage 7 strains show a higher propensity to transmit than strains from sublineages 1 to 6 (1). Molecular epidemiological studies also support the notion that the more recently evolved strains (termed typical Beijing strains) are adapted to spread and cause disease, given their frequency of occurrence, in comparison to distantly evolved strains (termed atypical Beijing strains) (3, 4).

Concerning the naming of the MT types, we acknowledge

the St. Petersburg Pasteur Institute's role in initially describing these MIRU types.

REFERENCES

1. **Hanekom, M., G. D. van der Spuy, E. Streicher, S. L. Ndabambi, C. R. McEvoy, M. Kidd, N. Beyers, T. C. Victor, P. D. van Helden, and R. M. Warren.** 2007. A recently evolved sublineage of the *Mycobacterium tuberculosis* Beijing strain family was associated with an increased ability to spread and cause disease. J. Clin. Microbiol. **45:**1483–1490.
2. **Hanekom, M., G. D. van der Spuy, N. C. van Pittius, C. R. McEvoy, S. L. Ndabambi, T. C. Victor, E. G. Hoal, P. D. van Helden, and R. M. Warren.** 2007. Evidence that the spread of *Mycobacterium tuberculosis* strains with the Beijing genotype is human population dependent. J. Clin. Microbiol. **45:**2263–2266.
3. **Mokrousov, I., O. Narvskaya, T. Otten, A. Vyazovaya, E. Limeschenko, L. Steklova, and B. Vyshnevskyi.** 2002. Phylogenetic reconstruction within *Mycobacterium tuberculosis* Beijing genotype in northwestern Russia. Res. Microbiol. **153:**629–637.
4. **Toungoussova, O. S., P. Sandven, A. O. Mariandyshev, N. I. Nizovtseva, G. Bjune, and D. A. Caugant.** 2002. Spread of drug-resistant *Mycobacterium tuberculosis* strains of the Beijing genotype in the Archangel Oblast, Russia. J. Clin. Microbiol. **40:**1930–1937.

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