

GENETIC VARIABILITY AND GEOGRAPHIC DISTRIBUTION OF MYCOBACTERIUM TUBERCULOSIS LINEAGE 2

S. Atavliyeva, D. Auganova, P. Tarlykov

National Center for Biotechnology, Republic of Kazakhstan, 000010, Astana, Qorgalzhyn highway 13/5
e-mail: atavliyeva@biocenter.kz

Mycobacterium tuberculosis (MTB) is a substantial threat to public health, infecting approximately 10 million individuals annually with tuberculosis. Among the genetic lineages of MTB, lineage 2 (L2), notably the Beijing family, plays a significant role in global tuberculosis epidemiology, accounting for nearly a quarter of all reported TB cases. Originating possibly in East Asia, this lineage spread globally, causing significant epidemics in Central Asia, Eastern Europe, and Eastern Africa.

Geographic variability in the distribution of MTB L2 strains reveals diverse prevalence patterns among sublineages across different regions. L2.1 (proto-Beijing) is primarily composed of isolates originating from China, Thailand, and Vietnam, with a smaller number from Japan, Malaysia, and Indonesia. The ancestral sublineage, named L2.2.A, is mostly spread in China, Japan, and Thailand, while the modern sublineage, L2.2.M, is widespread, spanning almost the entire world. Moreover, the L2.2.M1 clade demonstrates a wide geographic spread, encompassing various countries across Asia and Australia, while other subclades of the L2.2.M2, L2.2.M3, and L2.2.M4 clades show more localized distributions across different regions. The L2.2.M4 clade comprises nine subclades, L2.2.M4.1 and L2.2.M4.2 are primarily found in Thailand, while

L2.2.M4.3, L2.2.M4.6, and L2.2.M4.8 predominate in China. In South Africa, L2.2.M4.4 is the predominant subclade, whereas L2.2.M4.7 is associated with Nepalese isolates. In contrast, in regions such as Central Asia, Eastern Europe, and Russia, L2 strains, particularly the Modern Beijing sublineage, dominate. Notable examples include Europe/Russia W148 outbreak L2.2.M4.5 (B0W/148), Central Asia L2.2.M4.9 (CA), Central Asia outbreak L2.2.M4.9.1 (CAO), and Clade A L2.2.M4.9.2. Additionally, recent small clades like L2.2.M5 and L2.2.M6, originating from Vietnam, Thailand, and China, have emerged, with L2.2.M6 also detected in Kenya and South Africa. In Kazakhstan, we have identified such sublineages of L2 as CAO (n=69; 67.64%) L2.2.M4.9.1, CA (n=27; 26.47%) L2.2.M4.9, B0W/148 (n=5, 4.90%) L2.2.M4.5 and one isolate representative of a rare L2.2.M4 lineage (n =1; 0.98%). Strains of this lineage demonstrate the development of multidrug resistance (MDR) and extensive drug resistance (XDR), reflecting the emergence of resistance mechanisms against all available anti-tuberculosis drugs. In summary, *M. tuberculosis* lineage 2, especially the Beijing family, significantly impacts global tuberculosis epidemiology, with diverse prevalence patterns among sublineages across regions.