

A genome-wide insight into the molecular events accompanying the emergence and the expansion of a multidrug-resistant *mycobacterium tuberculosis* outbreak strain

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To get a genome-wide insight into the molecular events accompanying the emergence and the expansion, in Tunisia since 2001, of a severe multidrug-resistant tuberculosis (MDR-TB) outbreak, we sequenced and compared the genomes of two MDR outbreak strains and one phylogenetically closely related drug susceptible strain. With regard to the genome of the *M. tuberculosis* reference strain H37Rv, the 3 clinical strains shared 786 single nucleotide polymorphisms (SNPs) and 85 insertions/deletions (indels), a finding in favor of their close phylogenetic relationships. However, the drug-sensitive strain showed a consistent number of specific SNPs and indels and thus could not represent the immediate progenitor of the two MDR outbreak strains. Furthermore, and despite the fact that the two MDR outbreak strains display identical MIRU-VNTR24 patterns and differed only by one IS6110 copy, they could be differentiated by 49 SNPs and as much as 97 indels, a finding that may indicate a high level genomic instability during the outbreak expansion. Strikingly, some deletion events in functionally important genes shared by all the MDR outbreak strains were found to be restricted to the outbreak strain. These deletions could thus represent a critical step in the acquisition of the epidemic phenotype of the Tunisian MDR outbreak strain.

In conclusion, comparative genomics disclosed the relative instability of the genome of an MDR *M. tuberculosis* outbreak strain and unraveled new clues that may lead to better understanding of its epidemic phenotype.

Biography

Helmi Mardassi after obtaining his doctorate in Veterinary Medicine (1988) at the Tunisian National School of Veterinary Medicine, moved to the University of Montreal (Canada) where he completed a master degree in Microbiology and Animal Pathology. In 1996, he obtained his Ph.D. degree in Molecular Virology at the Institut Armand-Frappier (University of Quebec, Canada), and next joined the Biotechnology Research Institute of Montreal for a post-doctoral training. Actually he is leading a research unit focusing on molecular epidemiology, evolution and genetics of *Mycobacterium tuberculosis*. He has published more than 26 papers in reputed journals.

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