

O0933 Exploring the phenotypic and genetic basis of drug-resistant *Mycobacterium tuberculosis* strains in Lisbon, Portugal

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Background: The emergence of multi and extensively drug resistant tuberculosis (MDR-/XDR-TB) demands accurate and reproducible drug susceptibility testing (DST) and increased knowledge about the genetic basis of *Mycobacterium tuberculosis* (Mtb) drug resistance and epidemiology. To determine the most prevalent genotypes associated with drug resistance, we undertook a prospective population level molecular epidemiological study of incident tuberculosis in Lisbon.

Materials/methods: The study population consisted of all MDR-TB strains (n=30) received at the Laboratório de Micobactérias (IHMT/UNL) (years 2009-2017). DST was performed on MGIT 960 platform. Mutation analysis was made with line probe assays and/or DNA sequencing. Strains were typed by spoligotyping and 24-*loci* MIRU-VNTR. As comparators, we included non-MDR-TB isolates (n=807) received during the same period.

Results: MDR-TB strains belong mostly (n=26/30) to the LAM genotype (LAM 1 – SIT20, cluster Lisboa3 or LAM 4 – SIT1106, cluster Q1), and others (4/30) belong to the Beijing (n=2), H1 (n=1), and H3 (n=1) genotypes. All these strains have mutations associated with drug resistance showing a clear correlation between the resistance genotype and the resistance levels. Lisboa3 strains can be distinguished by the following mutations: *inhA* S94A, *rpsL* K43R, *embB* P397T, *embA* C-11A, *tlyA* GT 755/756, *eis* G-10A, and *gyrA* S91P. Q1 strains are characterised by *inhA* I194, *embB* M306V/M423T, *pncA* V125G, *gidB* A80P, *rrs* A1401G, and *gyrA* D94A. The non-MDR-TB Mtb strains presented a high diversity of genotypes, and MDR-TB isolates were exclusively in Lisboa3 or Q1 clusters.

Conclusions: The results demonstrated high diversity of genotypes among the Mtb strains circulating in Lisbon, except when MDR- or XDR-TB. MDR-/XDR-TB cases in Lisbon continue to be caused by a closely related family of strains, Lisboa 3 and Q1. A possible explanation is the preferential co-evolution of these clusters within this population, associated with their strain genetic background that favours drug resistance. The non-LAM MDR-TB strains were imported into the Lisbon area. Continuous surveillance is necessary to determine if they represent sporadic imported cases without further transmission along with the ongoing close surveillance of the MDR-/XDR-TB epidemiology.

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