Molecular mechanisms of drug resistance in *Mycobacterium tuberculosis*: Intrinsic and acquired resistance

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**Introduction**

Tuberculosis is a disease caused by the mycobacteria *Mycobacterium tuberculosis*. (1) Currently it can be cured thanks to the antibiotics. The problem is that the ability of this bacteria can mutate and acquire drug resistance and become MDR-TB or XDR-TB. Figure 1 presents the cases of TB and MDR-TB in Europe from 2005 until 2012.

**Objectives:**
- Define the mechanisms of intrinsic and acquired drug resistance in *M. tuberculosis*
- Describe the drug resistance mutations and their molecular changes.

**Intrinsic antibiotic resistance mechanism**

- Mycobacterial cell wall: The Figure 2 shows the structure of the cell wall. The peptidoglycan and the arabinogalactan layer, are covalently linked to a layer of mycolic acids that prevent the drug diffusion between the inside and the outside of the bacteria. (2)
- Porins: Research demonstrate that MspA porin in *M. smegmatis* makes the bacteria more sensitive towards the antibifilides. Figure 3 shows the molecular structure of the MspA porin. There is the possibility that the absence presence of *M. tuberculosis* McrB and OmpA porins may be linked at drug resistance. (3)
- Efflux pumps: The main function is to expel waste and toxic substances through the cell wall. There are 18 pumps coded in its genome giving it a low-level drug resistance. The main problem would be a mutation that causes an overexpression of this efflux pumps. (4)

**Spontaneous mutations are the only mechanism that can make M. tuberculosis a drug resistance bacteria.** In chart 1 we can observe the discovered mutations that *M. tuberculosis* can have to protect itself against antibiotics. 

**Chart 1. Antibiotics against *M. tuberculosis*, their targets and their main source. Source based on: (3)**

**Bibliography**


**Conclusions:**

As we could see in this review, besides the classic mutations there are other kinds of unknown of molecular changes. That’s why we have to keep improving the molecular tools in order to know better its drug resistance mechanism. After that we will be able to make more rational antibiotics or to reform the current treatments. It is also important to use the molecular tools to study how MDR-TB and XDR-TB strains work and to avoid their global expansion. However it’s important to keep investigating to discover new possible targets and to develop effective antibiotics which are effective despite their mutations.