# MOLECULAR ANALYSIS OF DRUG RESISTANCE DETERMINING MUTATIONS IN X-DR *MYCOBACTERIUM TUBERCULOSIS* ISOLATES IN LATVIA

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Incidence of tuberculosis (TB) in Latvia makes 1238 TB cases in 2005. Among them 95 persons suffered from primary multi drug resistant TB (MDR-TB) and 63 represented retreatment MDR-TB cases. Treatment of such patients requires serious changes in chemotherapy where drug of choice are fluorquinolones (FQ). However, among primary MDR-TB cases 5% meet the criteria as extensive drug resistant TB (XDR TB) and up to 22% among retreatment MDR-TB cases. Therefore detailed studies on these drug resistant isolates are of great significance especially in FQ cases where degree of drug resistance and mutations are discrepant sometimes

The goal of present study is molecular analysis of MDR-TB and XDR-TB isolates to evaluate drug resistance determining mutations especially to quinolones, where such data about Latvian isolates are absent. In order to follow possible infection transmission we used molecular genotyping.

The samples represented collection of 2003-7 year isolates. Bacteriological analysis of drug resistance was determined by absolute concentration method and BACTEC system. Mutations were detected by sequencing of polymerase chain reaction amplified appropriate gene fragments. Genotyping by *PvuII* restriction analysis and spoligotyping.

Regarding to rifampicin, isoniazid, streptomycin, pyrazinamide and ethambutol found drug resistance determining mutations mainly were the same as it was found in previous years – *rpoB* (S531L;D516V), *katG* (S315T), *Rrs*(A315C;C516T) and *rpsL* (K43R), *pncA* (T76P;Y103H), *embB* (M396V/I) respectively. Flourquinolone resistance determining mutation was found in *Gyr A* gene in its product protein 90 and 94 positions (A90V and D94G) equally .

Most of XDR isolates belonged to different Beijing genotype subgroups , however similarity among HIV positive patients were observed indicating on transmission in this group.

Necessity to elaborate PCR based molecular diagnostic kits for determination of complex drug resistance is obvious and attempts to work in this direction have been started.