Title: Genotyping of *Mycobacterium tuberculosis* strains isolated of recurrent cases of disease in southern Brazil

**Authors:** Diniz, J.L.C.G., Ramis, I.B., Abileira, F.S., Brum, C.B., Ramos, D.F., Silva, A.B.S., Bierhals, D.V, vonGroll, A, Silva, P.E.A.

**Institution:** Universidade Federal do Rio Grande – FURG - Núcleo de Pesquisa em Microbiologia Médica -Rio Grande, Rio Grande do Sul, Brasil

## Abstract:

Tuberculosis (TB) remains a major public health problem in developing countries, remaining as the second leading cause of death by infectious disease worldwide. The TB control involves the management of several factors, among them, a correct diagnosis, a successful treatment and still an adequate handling of the patients with active disease in order to avoid the disease transmission. In Brazil, although it is relevant for improvement of disease control programs, the studies evaluating the dynamics of TB recurrence are still scarce. In this sense, this study aimed to characterize the genotypic profile of the Mycobacterium tuberculosis isolated from cases of TB recurrent from patients of Rio Grande, Rio Grande do Sul, Brazil, between 2011-2014. In this period, were isolated 74 strains from 35 patients with recurrent episodes of TB, among which, most were male (74.3%), co-infected with HIV (57.1%) and with aged between 32 to 39 years (37.5%). About the period of duration free of TB between the episodes of the disease, there was a higher frequency in the periods of six to 12 months (40.0%) and 13 to 24 months (37.5%), which may be related with the cases of endogenous reactivation that generally are more frequent in the first two years after completion of treatment, fact this proven in this study. The genetic diversity of strains was determined by analysis of MIRU-VNTR 15 loci, being possible identify recurrent cases isolated of 28 patients due to endogenous reactivation and of seven patients due to exogenous reinfection. In addition, in the clonal expansion analysis was possible to observe that isolates from 13 patients presented single genotypes and it was verified the formation of a cluster comprising isolated from five patients with reactivation episodes and from one patient with reinfection episode. The results obtained characterize cases of transmission by exogenous reinfection even in a short period of time, confirming that these cases may come from areas with high disease incidence. This reinforces the importance of molecular epidemiology studies allowing understand the dynamics of TB, and thus determine important measures that enable the disease control.

Key words: Tuberculosis, MIRU-VNTR, endogenous reactivation, exogenous reinfection

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