Reviewer’s report

Title: Genetic variation of Mycobacterium tuberculosis circulating in Kharkiv Oblast, Ukraine

Version: 1 Date: 28 November 2010

Reviewer: Andrea Gori

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Dymova M.A. et al. describe the genetic variation of M. tuberculosis isolates in northeastern Ukraine. The authors have characterized the frequency of occurrence of mutations associated with the development of resistance to isoniazid and rifampicin and have characterized the principal phylogenetic families of M. tuberculosis occurring in Ukraine. The authors noted that a persistent increase of tuberculosis cases, mainly due to MDR-TB strains, has recently been reported in the Ukraine. They issued this manuscript to determine data on the genetic variation of Ukraine circulating isolates and on the spectrum and frequency of occurrence of mutations determining resistance to the principal anti-tuberculosis drugs isoniazid and rifampicin.

This is a clearly presented and well written paper discussing in deep the need to achieve a better understanding of the M. tuberculosis spread in East Europe. However there are some major concerns.

MAJOR COMPULSORY REVISIONS

The casuistry here presented is relatively small and dated (ninety-eight M. tuberculosis isolates collected from tuberculosis patients undergoing regular treatment for three months commencing January 2004). Moreover, a very high rate of defined chronic cases have been selected (37% patients who had never been treated were classified as new cases VS 63% patients that previously had active TB and considered clinically cured but had become smear-positive again) inducing a possible serious bias in the patient selection and analysis. The presented results could be impressive, although it could be difficult to contextualize them in the proper way if a careful and thorough description of the strains case study is not clearly presented and analyzed.

Due to the high rate of isoniazid and rifampicin resistance (49% of the isolates) could the authors provide any information regarding the impact of second drug resistance and the emergence of XDR-TB strains?

MINOR ESSENTIAL REVISIONS AND DISCRETIONARY REVISIONS

Abstract. Pag. 2. The second paragraph could be shortened and simplified. An abstract conclusion has to be added as last sentence

Introduction. Pag. 3; line 9. This sentence is misleading and can be deleted

Line 16-20. This sentence is too long and confuse and can preferably be deleted
Methods. A more detailed description of patient selection criteria need to be added.

Results. A very small amount of patients were analyzed by RFLP- IS6110 method, however a more clear and detailed description of the correlation between VNTR-typing and RFLP- IS6110 results is needed.

Discussion. Pag. 11; line 14. “Thus, it can be assumed that the predominance of resistant mycobacterium isolates in Kharkiv Oblast is most likely the result of transmission of resistant M. tuberculosis and not selection of resistant clones of mycobacteria due to ineffective anti-tuberculosis therapy. “ This sentence it is very difficult to be supported by the presented results, mainly considering both the high percentage of chronic cases and the high rate of clustered strains.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests' below