



**LIETUVOS SVEIKATOS MOKSLŲ UNIVERSITETAS
LITHUANIAN UNIVERSITY OF HEALTH SCIENCES**

Public enterprise, A. Mickevičiaus g. 9, 44307 Kaunas, tel. +370 37 327200, fax. (8 37) 220733, el. p. www.lsmuni.lt, rektoratas@lsmuni.lt
Data are collected and stored in the Register of Legal Entities, code 302536989

To whom it may concern

August 5, 2021, No. 2021-DVT2-01506

REVIEW OF THE DISSERTATION

Please find the enclosed review of the dissertation for the degree of Doctor of Philosophy (PhD) in the specialty 6D110100 - Medicine Arailym Assylkhanovna Abilbayeva on the theme "The Identification of diagnostically significant antigenic components of *M. tuberculosis* for use in early immunodiagnosis of tuberculosis" by Professor Skaidrius Miliauskas.

Rector ad Interim



Professor Vaiva Lesauskaitė

Lithuanian University of Health Sciences
Department of Pulmonology
Eiveniu 2, LT-50009, Kaunas, Lithuania

REVIEW of the dissertation for the degree of Doctor of Philosophy (PhD)
in the specialty 6D110100 - Medicine
Arailym Assylkhanovna Abilbayeva on the theme

**"The Identification of diagnostically significant antigenic components of
M.tuberculosis for use in early immunodiagnosis of tuberculosis"**

Scientific consultant:

Candidate of medical sciences

E.Zh. Bitanova

Foreign scientific consultant:

Doctor of medical sciences,

professor I.M. Khaertynova

I am really very glad to be invited to review of this dissertation and annotation. I would like to make and send some remarks.

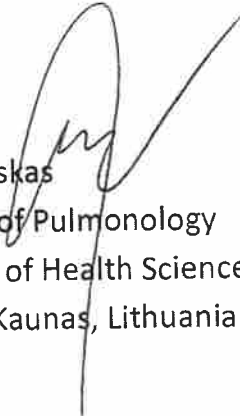
1. The research topic is very relevant and important. Tuberculosis is still one of the most prevalent human infections worldwide. Almost 1.7 billion people in the world's population have a latent tuberculosis infection (LTBI) and thus they are at risk of developing active tuberculosis disease during their lifetime (World Health Organization, 2019). The vaccination is widely used in high

burden countries but does not prevent from acquiring the disease. Although the diagnostic methods of active tuberculosis are well defined it is still unclear how to predict the risk and exact time of developing active disease for those who have latent tuberculosis infection. We need new diagnostic approaches. A.S.Abilbajeva made an investigation of *M. tuberculosis* antigens suggesting their new usage in the diagnosis of tuberculosis. Additionally different types of immune response on the efficiency of antigen-specific cytokine production and antibody production upon stimulation with *M. tuberculosis* antigens were investigated. The author suggests implementing wider usage of IL-2. IGRAs are widely used in this area but IL-2 is not. IGRAs can show latent tuberculosis but not an active disease and even can give false positive results. That shows there are unmet needs for such scientific works.

2. The outstanding work was performed. As the part of analysis of cytokines produced by *M. tuberculosis* after stimulation was made from the blood samples taken from 280 people (131 patients and 149 apparently healthy individuals). Modern diagnostic kits and methods were used. Adequate statistical methods were chosen. Almaty cohort of the same patients were included into the novel IGRA LIOFeron1TB/LTBI assay international testing. The conclusions and recommendations are well based on the obtained results.
3. The scientific novelty of work: the new set of *M. tuberculosis* antigens (Rv3875, Rv3874, Rv2654c and Rv0512) was assessed for the production of IL-2 and IFN- γ . Additionally diagnostic efficiency of these antigens was assessed based on the specific production of antibodies and IL-2 production. Also, the previously unused combination of mentioned antigens showed high diagnostic efficiency for tuberculosis. The optimal set of antigens was suggested as the next step for possible use in early diagnosis of active tuberculosis. From the practical point this is the most important thing. Currently clinicians simply wait for the symptoms or radiologic changes of tuberculosis then proceed further with diagnostic (bacteriological or molecular) steps. The new proposals by the author are clearly based.
4. Seven scientific papers were published. One was included in the international database Web of Science Core Collection (Clarivate Analytics, Impact factor - 3.2) and Scopus (International Journal of Infectious Diseases 91 (2020) 177–

181); four- in journals recommended by the Committee for Control in the Sphere of Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan; two- in materials of international conferences. The defender of thesis upholds the principles of academic honesty.

5. The author personally carried out immunological studies, interpretation of the results, and statistical analysis. Also, the author made primary processing of obtained materials etc.
6. The annotation of the dissertation is completely compatible with the dissertation.
7. There are several minor issues. The term "Latent tuberculosis infection" instead of "Latent tuberculosis" should be used. Maybe more core results and proposals (like practical usage of IL-2) should be included in the annotation.
8. Arailym Abilbayeva's dissertation work on the topic: "The identification of diagnostically significant antigenic components of M. tuberculosis for use in early immunodiagnosis of tuberculosis", presented for the degree of Doctor of Philosophy (PhD) in the specialty 6D 110100 "Medicine" is a complete independent project. The obtained results are of theoretical and practical importance. The dissertation work meets the requirements for dissertations for the degree of Doctor of Philosophy (PhD) and can be recommended for defense.



Prof. Skaidrius Miliauskas
Head of Department of Pulmonology
Lithuanian University of Health Sciences
Eiveniu 2, LT-50009, Kaunas, Lithuania