

Łódź, March 28th, 2025

**Evaluation of the dissertation for the doctoral degree in the field of exact and natural sciences in the discipline of biological sciences for Hummaira Sadaf, MSc, entitled:**

**The molecular mechanism of PD-L1 overexpression in classical Hodgkin lymphoma (cHL)**

performed at

the Department of Experimental Immunotherapy of Maria Skłodowska-Curie National Research Institute of Oncology, Warsaw

**under the supervision of dr hab. n. med. Elżbieta Sarnowska, prof. NIO,  
and co-supervision of Ryszard Konopiński, PhD**

Clinical Hodgkin lymphoma is a type of malignancy that originates from normal B cells. PD-L1 surface overexpression is a hallmark of the malignancy. PD-L1, as a immune checkpoint, is utilized in cancer immunotherapy for several types of malignancies. Therefore, Hummaira Sadaf, MSc, decided to better understand the molecular mechanisms of PD-L1 action and its regulation in classical Hodgkin lymphoma. Author focused on the understanding the mechanism of CD274 gene encoding PD-L1 overexpression on promoter regulation level and the function of PD-L1 protein in HRS cells.

#### **Assessment of the structure and substantive content of the dissertation**

The dissertation presented for the review has a classical layout and is a very carefully prepared typescript of 88 pages. In the *Introduction*, Hummaira Sadaf, MSc, makes a brief characterization of classical Hodgkin lymphoma (cHL), including epidemiology, clinical presentation, diagnosis, and treatment based on the immunotherapy. Author defines the PD-1-PD-L1 axis, SWI/SNF-type remodelling complex. Finally, Hummaira Sadaf, MSc, describes a significance of SWI/SNF complex in cancer. Thus, this chapter prepares a good ground for understanding the numerous substantive aspects contained in the work and publications. The scope and objectives of the study are formulated correctly.

In the following chapter *Materials and methods*, the Author presents the research methods used in the work. It should be emphasized that the Author used a large number of advanced research methods, which fully allowed for the achievement of the set goals of the work. The results were analysed using properly selected statistical methods.

In the *Results* chapter, the Hummaira Sadaf, MSc, presents results obtained in the course of the implementation of the planned research objectives. Author investigated the PD-L1 translocation into cell nuclei and identified potential nuclear partners in L-1236 cell line. Hummaira Sadaf, MSc, found that PD-L1 may interact with splicing machinery, thus regulating the RNA posttranscriptional alternative processing. Than it was found that subunits of SWI/SNF, PRC2 complex, PD-L1 are located at the same position on the promoter region of CD274 gene. Additionally, Author showed that EZH2 is not an essential component to be targeted for therapeutic reasons.

The *Discussion* of the obtained results is conducted concisely and critically, using current literature. The discussion was conducted in a broad scope in each of the original publications in a multi-threaded, yet very transparent manner, which shows the Author's large knowledge and the ability to properly select arguments and literature data. It also indicates the Author's understanding of the complex issues of the undertaken research problem. The ability to analyse and interpret the obtained results indicates the dynamic scientific development of Hummaira Sadaf, MSc, which occurred during the implementation of the research, as well as her extensive experience, which will certainly pay off in the near future.

It should be emphasized that Hummaira Sadaf, MSc, used a large number of sophisticated research methods to achieve goals. She obtained a great amount of results. Knowledge of a wide range of methods proves the versatility and methodological skills of Hummaira Sadaf, MSc, and her excellent readiness for the implementation of the research tasks. The ability to analyse and interpret the results obtained using these methods indicates the dynamic scientific development of Author that took place during the implementation of the research and the extensive experience that will probably pay off in the near future.

## **Summary**

The doctoral dissertation presented for review is a reliable, valuable, original and independent scientific study of aspects concerning the molecular mechanism of PD-L1 overexpression in

classical Hodgkin lymphoma. Hummaira Sadaf, MSc, undertook an ambitious task - she properly planned the work, substantiated the substantive basis of the conducted research, properly formulated and implemented research objectives, and drew a number of interesting conclusions from obtained results. The dissertation is a good example of a conceptual approach to a selected scientific problem. The work makes an contribution to the existing knowledge in the researched field.

Therefore, I believe that the doctoral dissertation meets the conditions specified in art. 187 of the Act on the Law on Higher Education and Science (Dz.U. z 2021, poz. 478)

I hereby submit to the Scientific Council of Maria Skłodowska-Curie National Research Institute of Oncology a request for admission of Hummaira Sadaf, MSc, for further stages of the doctoral thesis.

Taking into account the very high value of the dissertation, the use of novel research methods, and the performance of an in-depth, critical analysis of the outlined topic, as well as the unique dimension of the research obtained, I request the Council to recognize the doctoral dissertation of Hummaira Sadaf, MSc, as outstanding and accept it with distinction.

Maciej Chałubiński, MD, PhD, Professor of the Medical University of Lodz