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EVALUATION OF RESEARCH, DIDACTIC AND ORGANISATIONAL ACHIEVEMENTS OF **DR INŻ. UMESH KALATHIYA**

The review of the habilitation thesis has been conducted according to the recommendations of the Rada Doskonałości Naukowej (RDN).

1. BASIC INFORMATION ABOUT THE CANDIDATE, INCLUDING

a) The date of the doctoral degree and the name of the organizational unit in which the degree was conferred

Politechnika Gdansk on 6.11.2018

b) Information as to whether the candidate has previously applied for the conferment of the degree of doktor habilitowany, including, as far as it is evident from the case file, information on the course and termination of previous proceedings

Not to my knowledge

c) Scientific and professional work history (workplace, positions held)

International Centre for Cancer Vaccine Science (ICCVS), University of Gdańsk, Poland
Faculty of Chemistry, Gdańsk University of Technology, Poland

2. INFORMATION ON THE APPLICABLE LAWS AS OF THE DATE OF INITIATION OF THE HABILITATION PROCEDURE UNDER REVIEW, INCLUDING THE APPLICABLE EVALUATION CRITERIA

Art, 221 para 14 of the Act of 20 July 2018. - Law on Higher Education and Science (Journal of Laws of 2018., item 1668 as amended).

3. INFORMATION OF EVALUATED SCIENTIFIC ACHIEVEMENTS AS RECOMMENDED BY THE COUNCIL FOR SCIENTIFIC EXCELLENCE

a) The title of the research achievement

Molecular basis for innovative strategies of vaccine or drug development by exploring structural features of different functional proteins

b) Scientometric data, such as the cumulative Impact Factor, the cumulative Ministerial points, the number of citations, and the Hirsch Index

for details see autoreferat - I have independently checked the Hirsch Index (8), the number of citations (337), all listed publications and the respective author contribution statements, which are in agreement with the provided information. I did not conduct independent numeric analyses of cumulative ministerial points credits before and after the PhD of dr. Kalathiya.

c) Information on the number of scientific publications, monographs, chapters in monographs authored or co-authored by the candidate

for details see autoreferat – the correctness of the provided information has been checked independently.

d) information on the major journals in which the candidate has published his/her scholarly work

for details see autoreferat – the correctness of the provided information has been checked independently. I have to admit that the numerous publications in MDPI journals represent the only major weakness in the scientific curriculum of the candidate. The published scientific data seem sound and could/should have been published in journals with a better reputation.

e) Information on whether the candidate played a leading role within the production of co-authored scientific papers

for details see autoreferat – the correctness of the provided information has been checked. The author has most often published as co-corresponding author with his peers, but considering the detailed contributions this seems rather a consequence of hierarchical structures than a weakness of the candidate. In my opinion, the candidate has played a leading scientific role in all of the listed publications.

f) f. evaluation of the candidate's indicated research achievement, including whether it represents a significant contribution to the development of a specific scientific discipline

The work of dr Kalathiya work aims to reveal new scientific insights by combining computer simulations, structural biology, enzymology and molecular medicine. From the presented documents and published work, it seems clear that he has found a defined research path and vision by studying medically highly relevant drug targets and understand the effect of naturally occurring variations in human patients. His previous work on cancer-related proteins has also put him in a unique position to react quickly to the worldwide pandemic and contribute to our understanding of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its encoded proteins. He has also managed to secure external funding, supervise younger colleagues and establish international collaboration with numerous labs around the globe. These achievements further substantiate my overall very positive opinion about the scientific progress and his application to obtain a habilitation degree – from the provided documents, we seem to look at an ambitious, mature and independent scientist that defines interesting research questions and uses his technical skills to answer them most directly.

In general, I found the work of dr Kalathiya very interesting and stimulating. However, I do see quite some space for improvements in the future. The provided work and publications are very good, but they miss the opportunity to contribute truly outstanding studies to the community. At the current career stage, one could expect at least one work that is published as leading author in the top-tier international journals (e.g. 200-point category of $MEiN_{2021}$). It seems that dr Kalathiya sometimes stops at an early stage of the projects to fulfil the unfortunate destiny of many Polish scientists to publish many, but low impact, publications. Considering the high-quality of his work, I would encourage him to focus on few, but more impactful, publications in the future. I was impressed that in some of the most recent publications dr Kalathiya teams up with wet-lab scientists to challenge and validate his simulations experimentally – I would like to see more of these. Despite these minor shortcomings, his achievements and the quality of his work clearly qualify him to obtain a habitation degree.

Six research papers (and the one review) are presented as the main achievements for the habilitation and described in detail in the autoreferat. For all publications the applicants nicely elaborates the main aim of the study, describes the main results and highlights the impact of the obtained results. The descriptions are clear, concise and reflect the content of the original research articles.

1. Padariya, M., Fahraeus, R., Hupp, T., Kalathiya, U. (2021). Molecular determinants and specificity of mRNA with alternatively-spliced UPF1 isoforms, influenced by an insertion in the "regulatory loop". International Journal of Molecular Sciences, 22(23), 12744.

In this study the authors use all-atom molecular dynamics to test the binding specificity of UPF1 to different mRNA motifs. They also analyse two different isoforms of UPF1 and check the influence of an insertion (the main difference between the isoforms) on the catalytic activity of the enzyme. Last but not least, the authors simulate the effects of patient-derived mutations on the mRNA binding capacity of UPF1. This study appears to be a direct follow-up story from publication #3.

2. Padariya, M., Kote, S., Mayordomo, M., Dapic, I., Alfaro, J., Hupp, T., Fahraeus, R., Kalathiya, U. (2021). Structural determinants of peptide-dependent TAP1-TAP2 transit passage targeted by viral proteins and altered by cancer-associated mutations. Computational and Structural Biotechnology Journal, 19, 5072–5091.

In this study the authors provide a model for how viruses and cancer-associated mutations can affect MHC-I antigen presentation. In addition, they show how the IFN-c pathway alters MHC-I antigen presentation by affecting via the kinetics of peptide transport. They use a broad and complementary spectrum of experimental and theoretical approaches to consolidate their findings.

3. Kalathiya, U., Padariya, M., Pawlicka, K., Verma, C. S., Houston, D., Hupp, T. R., Alfaro, J. A. (2019). Insights into the effects of cancer associated mutations at the UPF2 and ATP-binding sites of NMD master regulator: UPF1. International Journal of Molecular Sciences, 20(22), 5644.

In this study the authors use structural modelling to predict the functional and structural consequences of 41 mutations in UPF2 that are linked to cancer. They identify a handful of variants that seem to show significant alterations in their simulations. They discriminate between distinct functionalities and predict the consequences of the mutations. For instance, they categorize mutations that might affect protein stability, ATP hydrolysis or the interaction with UPF1.

4. Kalathiya, U., Padariya, M., Baginski, M. (2019). Structural, functional, and stability change predictions in human telomerase upon specific point mutations. Scientific Reports, 9(1), 8707.

In this study the authors analyse human telomerase, which is overexpressed in cancer and mutated in other human diseases. The authors systematically simulate the effect of mutations on the available structures of human telomerase *in silico*. Moreover, they use molecular docking methods to predict the effects of these mutations on the affinity of certain ligands, which are used as telomerase inhibitors.

5. Kalathiya, U., Padariya, M., Mayordomo, M., Lisowska, M., Nicholson, J., Singh, A., Baginski, M., Fahraeus, R., Carragher, N., Ball, K., Haas, J., Daniels, A., Hupp, T. R., Alfaro, J. A. (2020). Highly conserved homotrimer cavity formed by the SARS-CoV-2 spike glycoprotein: A novel binding site. Journal of Clinical Medicine, 9(5), 1473.

In this study the authors explored conserved features in the spike protein of the SARS-CoV-2 to identify novel regions that could serve as drug target sites. Therefore, they predicted the structure of hundreds of spike protein variants from naturally existing viral genomes and studied their properties by molecular dynamics simulation. In particular, they study the trimer cavity and suggest a specific region as a target for virtual screening campaigns.

6. Kalathiya, U., Padariya, M., Fahraeus, R., Chakraborti, S., Hupp, T. R. (2021). Multivalent display of SARS-CoV-2 spike (RBD domain) of COVID-19 to nanomaterial, protein ferritin nanocages. Biomolecules, 11(2), 297.

In this study the authors assess the possibility to use ferritin nanocages as scaffolds to present the receptor-binding domain of the SARS-CoV-2 spike protein to the human immune system and develop a novel vaccination platform. The authors use previous structural models to design optimal constructs and simulate their possible conformations *in silico*.

- Kalathiya, U., Padariya, M., Faktor, J., Coyaud, E., Alfaro, J. A., Fahraeus, R., Hupp, T. R., Goodlett, D. R. (2021). Interfaces with structure dynamics of the workhorses from cells revealed through cross-linking mass spectrometry (CLMS). Biomolecules, 11(3), 382.

In this review article the authors highlight and discuss the principal role of chemistry in MS-based structural proteomics approaches, with a particular focus on the chemical cross-linking of protein–protein/DNA/RNA complexes.

g) information on the applicant's fulfillment of the criterion of demonstrating significant scientific or artistic activity

In my opinion, the presented scientific achievements and productivity clearly fulfil the criteria to award dr. Kalathiya with the habilitation title. In particular, I would like to highlight that dr. Kalathiya has delivered high-quality results in different polish institutions. This not only shows his mobility, but also a clearly indicates his suitability to continue his academic career track in the Polish research landscape.

h) information about the didactic, organizational, and popularization achievements of the candidate for the habilitation degree

Dr. Kalathiya has successfully supervised students and presented his work at a few conferences. I would highly encourage the candidate to attend more conferences, which is essential to be visible and establish a profile as an independent scientific leader. In summary, the achievements seem sufficient to fulfil the criteria to award dr. Kalathiya with the habilitation title.

4. General Conclusion

Umesh Kalathiya graduated from the Wrocław University of Science and Technology and conducted his PhD thesis at the Gdańsk University of Technology. Subsequently, dr Kalathiya moved to the newly founded International Centre for Cancer Vaccine Science (ICCVS) at the University of Gdansk. He has shown continuous and reasonable scientific productivity in the different institutions and at the different stages of his career. I do believe that he has reached a stage of the Polish academic career, where it becomes necessary to obtain a habilitation degree.

Thus, taking into account the scientific, organizational, and didactic achievements and the overall scientific output of dr. Kalathiya, the criteria for candidates for the degree of doctor of habilitation are met. I, therefore, request that candidate should be admitted to the next stages of the habilitation procedure.

Sincerely yours,

Dr hab. Sebastian Glatt

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Deputy Director Science MCB
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