

PhD Thesis Acceptance Report
Research Discipline Council of Biological Sciences
Jagiellonian University in Kraków

Candidate's name and surname: Marta Kamińska

PhD Thesis Title:The effect of carbamylation on the enzymatic activity and biological function of angiotensin I converting enzyme (ACE1).....

Thesis Supervisor:professor dr hab. Piotr MydelAssistant Supervisor / Second

Supervisor/ Co-supervisor (if applicable):.....

Reviewer:Professor Shauna Culshaw

THESIS EVALUATION

1. **Scientific merit of the thesis**

a. Originality of the research (25-200 words):

This thesis studies the effects of post translational modification, specifically carbamylation, in components of the Renin-angiotensin-aldosterone system. This is an exciting and novel area of research, in a system that is crucial to homeostasis and health.

b. Scientific merit of the chapters / articles (25-200 words):

The general introduction gives a very nice overview of the renin-angiotensin-aldosterone system and a nice synopsis of the topic of carbamylation. The methods are well described. The results chapters contain a series of experiments which elegantly show that ACE1 can undergo carbamylation, and crucially, that this modification results in a loss of activity. Subsequently, there are highly relevant studies showing that carbamylation alters the affinity of ACE1 to inhibitors – which are commonly used in clinical practice. Downstream effects of ACE1 carbamylation are documented on endothelial gene expression, and on monocyte adherence to these endothelial cells. There is a small pilot study of serum of patients with chronic kidney disease suggesting a difference in ACE1 activity compared with normal healthy control serum.

2. **Substantial merit of the thesis**

(ability to introduce the research topic and clarity of research hypotheses, the choice of research methods and statistical tools for data analysis, presentation and critical analysis of the research data, the ability to discuss research data and the theoretical background, clarity and quality of the conclusions) (25-200 words):

The hypothesis is clear and the thesis appropriately uses robust, well established techniques to address a highly relevant research question, which has significant potential clinical relevance. The choice of statistical methods for analysis of laboratory data such as these is open to interpretation and this is something that could be explored with the candidate in a viva. The presentation of data are excellent. There is a thorough critical analysis of the existing literature, and of the candidate's own work. The conclusions are appropriate.

3. **Layout and register**

(layout, register and the clarity of the language, the quality of the visual material etc.) (25-200 words):

The dissertation is generally very well written and the graphs are well presented, with good figure legends. The gel/blot images are notoriously difficult to manage and these are generally very clear.

4. **Critical notes**

There are some questions that could be explored in the defence. For example,

- why do you think there was a drop in endothelial ACE1 activity at 1 mM KCNO, while pure recombinant ACE1 loses activity in KCNO concentrations 10x higher?
- Is the housekeeping gene expression altered by exposure to KCNO?
- How did you control for non-specific antibody binding on the blots?
- In the small study of serum samples, were the CKD patients and healthy controls age matched? How would you develop this work in the context of CKD patients in the future?

There are several potential progressions of this work, and it would be interesting to explore the candidate's insight on how these could be prioritised. The clinical study is very small, and this is acknowledged by the candidate appropriately. Without doubt, every PhD project and PhD student, in the last 2 years has been significantly impacted by the global pandemic and the candidate is to be congratulated on completing this work during this time.

5. **Final grade** (justification 25-200 words):

Overall the thesis provides a novel and exciting contribution to understanding the importance of post translational modifications in the biology and physiology of an organisms. It provides strong evidence that the clinical significance of carbamylation merits further investigation, with far reaching consequences in pharmacology, personalised medicine, and as a measure of health.

I, hereby, declare that the reviewed PhD thesis by **Marta Kamińska** meets the criteria pursuant to art. 13.1 of Act of 14 March 2003 on Academic Degrees and Academic Title and Title in the Arts (O.J. no 65 item 595 as amended) and request that the Research Discipline Council of Biological Sciences of the Jagiellonian University in Kraków accepts **Marta Kamińska** for further stages of doctoral proceedings.

YES

I, hereby, request that the thesis is accepted with distinctions. Justification (25-200 words)

The thesis elegantly documents high quality, highly novel findings, which are the result of technically challenging experiments, carried out during global pandemic when all work was faced with additional complexities.

YES

.....18th January 2022..

date



Reviewer's signature

INFORMATION FOR THE REVIEWER:

1. Information on requirements concerning PhD thesis structure:
http://www.wb.uj.edu.pl/en_GB/stopnie-tytuly/doktoraty
2. A digital copy should be sent to:
nauki.biologiczne@uj.edu.pl

A duly signed original should be sent to:

**Rada Dyscypliny Nauki biologiczne
Dziekanat Wydziału Biologii
Uniwersytet Jagielloński w Krakowie
ul. Gronostajowa 7
30-387 Kraków**