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Supervisor report of the dissertation thesis “Generation and Characterization of Glutamate Carboxypeptidase II (GCPII)-Deficient Mice”

Mgr. Barbora Vorlová, MSc worked out her dissertation thesis “Generation and Characterization of Glutamate Carboxypeptidase II (GCPII)-Deficient Mice” at the Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences in Jan Konvalinka’s group.

The dissertation thesis consists of three parts. The first is an introduction and literature review, where Barbora describes state of knowledge of her dissertation topic. It starts by the history of the GCPII discovery, general description of the GCPII from the gene to the protein level, expression in healthy and pathologic tissues with connection to functions in that conditions. Review of the gene disruption techniques is followed by specific literature investigation of the GCPII knock out mice already produced by different groups. The introduction is completed by description of GCPII paralogues and review of GCPII in disease states that shows importance of GCPII in current medicine.

The second part describes material and methods used in this work, which mirrors wide range of techniques that Barbora applied: from genetics, molecular biology and cell biology to biochemistry and protein engineering.

The third part contains the thesis results and discussion in which Barbora asks scientific questions, shows results in a very comprehensive way and concludes new findings, which will help to the research community in further research on GCPII function. In my opinion, the major achievements of Barbora Vorlová work were generation of knock out mouse by novel TALEN technology, and novel observation of an interesting phenotype – seminal vesicle enlargement on adult animals. In the process of investigation of the phenotype, Barbora did not give it up after no obvious phenotype was found on young mice and continued to examine older animals.

Her findings on the GCPII phenotype have been recently accepted and published by a respected journal in the field. On top of that, Barbora also performed detailed analysis of the comparison of mouse and human recombinant GCPII that was published and well accepted by the scientific community. The third publication on the interesting differences in the metabolomics of GCPII null mice in comparison with the wild type is now in preparation. We are also submitting an invited review on GCPII biology to a respected international journal.

Barbora is hard working student, who does not only cherry pick the most interesting work but also takes regular work like the mouse colony breeding and maintenance. Barbora is always helpful to other colleagues in our lab and as a lecturer on First Faculty of Medicine she is very good in passing her knowledge to new generation of students. Apart of the scientific life, her good mood keeps friendly atmosphere and makes the lab life more pleasant.

According to my opinion this PhD. thesis fulfils all the requirements and criteria for doctoral thesis expected for a PhD student at the Charles University and I recommend this thesis for the approval.

RNDr. Pavel Šácha, PhD.

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