

Reviewer's Report on PhD Thesis of Mgr. Eliézer Jäger
"Responsive and non-responsive soft matter nanomedicines for biomedical applications"

The research reported in the submitted PhD Thesis is an original contribution to scientific advances in the field of synthesis and application of novel biomedical polymers. In this thesis Mgr. Eliézer Jäger proposed and described synthesis of block copolymer micelles and biodegradable polymeric nanoparticles with incorporated drug.

The thesis is focused on (i) soft matters assemblies as nanomedicine platforms; (ii) combination chemotherapy through non-responsible soft matter assemblies as nanomedicine platform; (iii) pH-responsive soft matter assemblies for cancer chemotherapy and (iv) ROS-responsive soft matter assemblies for cancer chemotherapy. Responsible and non-responsible systems were fully characterized and their efficacy was determined *in vitro* and *in vivo*.

This PhD thesis is structured as a consistent set of six scientific articles. Mgr. Jäger is lead author of four of them. The thesis is providing comprehensive and detailed information on studied field of the development of novel approaches in treatment of cancer. Its main focus is on preparation of new types of drug delivery polymers based on block copolymer micelles and biodegradable polymeric nanoparticles aimed to improve efficacy of medical treatment in cancer and diagnostic methods.

Each chapter and the dissertation as a whole are clearly written, logically organised, and fully developed. The author communicates in a concise and coherent manner, results obtained in individual articles are well summarized and commented.

The work is well written, number of grammatical or spelling errors is relatively small. My comments and questions are minor and do not affect the overall very high rating of this thesis.

Formal typographical or grammatical errors:

- a) Abstract in Czech language: *in vivo in vitro*; should be in italic

- b) Contents:
- 2.51. no-responsible instead of non-responsible
 - 2.6.2 oxygen instead of oxigen
- c) List of abbreviations:
- –N-(2-hydroxypropyl methacrylamide) without bracket
 - Poly(L-lysine) instead of Poly-L-lysine; Poly(L-glutamic acid) instead of Poly(L-glutamic acid); also p. 19
 - p-Toluenesulfonic acid instead of P-Toluenesulfonic acid
 - Polyvinyl alcohol instead of Polyvinil alcohol
- d) Page 18: poly(vinylpyrrolidone) instead of poly(vinyl-pyrrolidone)
- e) Page 30: monomers instead of momoners
- f) two times inserted the same page 77

Questions:

- a) Block copolymers Poly(ethylene oxide monomethyl ether)-*b*-poly(ϵ -caprolactone) used for synthesis of pH-responsive diblock copolymers were prepared by ring-opening polymerization from the ϵ -caprolactone using modified PEG macroinitiator. The lengths of poly(ϵ -caprolactone) blocks were controlled by regulating of ϵ -caprolactone/macroinitiator ratio. Amount of freshly distilled ϵ -caprolactone is not defined neither in this thesis nor in the listed references. Please provide more details on polymerization reaction conditions.
- b) Could you provide reaction scheme of synthesis of monomer 1-pinacol-type boronic ester? The PhD thesis states that the synthesis is described in Appendix, reference 6. In that reference there is just provided information that the synthesis was performed according literature. Two reaction paths are introduced in the cited article and it is not clear which path of monomer synthesis was used.
- c) Polymer P1 was incubated in a 20% PBS/DMF solution containing various H₂O₂ concentrations. What was the reason of using DMF for polymer degradation study? Published data indicate that DMF serves as hydroxyl radicals scavenger [Elie Hayon, T. Ibata, N. N. Lichtin, M. Simic: Sites of Attack of Hydroxyl Radicals on Amides in Aqueous Solution, JACS 1970, 92(13), pp 3898–3903; DOI: 10.1021/ja00716a011]; in that case, the process of the P1 polymer degradation upon generating hydroxyl radicals could be influenced by the presence of DMF. Did the author carry out these

experiments also in another environment? What amount of P1 (eventually concentration of P1) was used for the experiment?

- d) Have you observed degradation just in presence of hydrogen peroxide or also for the other reactive oxygen species?

The research reported meets internationally recognized standards for doctoral research in its field. This conclusion can be documented by the fact that Mgr. Eliézer Jäger is author or co-author of 18 articles in the leading international peer-reviewed journals. He also demonstrated knowledge of the relevant literature, and the ability to exercise critical and analytical judgment of that literature. His research is satisfactory in its methodology and in its scholarly presentation and format.

Conclusion: I would like to state that Mgr. Eliézer Jäger met all legal requirements relating to Doctoral degree graduates. I recommend this thesis for his PhD defence and as a base for awarding of the candidate by the degree of Doctor of Philosophy.



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