

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Anna Moroz

PhD Program: Life Sciences

Title of Thesis: Preclinical testing of new modalities for PET visualization and treatment of RAS-driven cancers

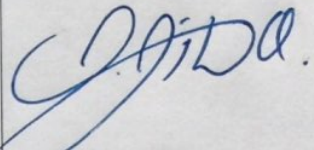
Supervisor: Prof. Konstantin Severinov

Chair of PhD defense Jury: Prof. Yuri Kotelevtsev

Email: y.kotelevtsev@skoltech.ru

Date of Thesis Defense: December 11, 2018

Name of the Reviewer: Ali Afshar-Oromieh, M.D., assistant professor of Nuclear Medicine, Department of Nuclear Medicine, Bern University Hospital, Switzerland

<p>I confirm the absence of any conflict of interest</p> <p>(Alternatively, Reviewer can formulate a possible conflict)</p>	<p>Signature:</p>  <p>Date: 01-12-2018</p>
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The purpose of this report is to obtain an independent review from the members of PhD defense Jury before the thesis defense. The members of PhD defense Jury are asked to submit signed copy of the report at least 30 days prior the thesis defense. The Reviewers are asked to bring a copy of the completed report to the thesis defense and to discuss the contents of each report with each other before the thesis defense.

If the reviewers have any queries about the thesis which they wish to raise in advance, please contact the Chair of the Jury.

Reviewer's Report

Reviewers report should contain the following items:

- Brief evaluation of the thesis quality and overall structure of the dissertation.
- The relevance of the topic of dissertation work to its actual content
- The relevance of the methods used in the dissertation
- The scientific significance of the results obtained and their compliance with the international level and current state of the art
- The relevance of the obtained results to applications (if applicable)
- The quality of publications

The summary of issues to be addressed before/during the thesis defense

Review of the PhD thesis of Ms. Anna A. Moroz by Dr. Ali Afshar-Oromieh

Title: "PRECLINICAL TESTING OF NEW MODALITIES FOR PET VISUALIZATION AND TREATMENT OF RAS-DRIVEN CANCERS"

General comments:

Ms. Anna Moroz presents in her doctoral thesis CDCP1 protein as a possible target for immunotherapy of RAS-driven cancers. In this context, anti-CDCP1 antibodies (4A06) were labeled with ^{89}Zr in order to enable Positron Emission Tomography (PET) and with ^{177}Lu , which enables endoradiotherapy. For the experiments cancer cell-derived xenograft animal models as well as patient derived biopsy materials of pancreatic cancer were used which significantly increases the value of the results. Ms. Moroz could successfully conduct PET-imaging with the ^{89}Zr -labelled antibody. In addition, and of very high relevance, she demonstrated in mice the effectiveness an endoradiotherapy with ^{177}Lu -labelled anti-CDCP1 antibodies: mice bearing subcutaneous HPAC tumours were treated with ^{177}Lu -4A06 and showed a significantly longer overall survival compared to the control group. These achievements can be regarded as significant as they enable a transfer of the results into the clinics.

In an additional experiment with ^{89}Zr -labeled transferrin, Ms. Moroz successfully describes a new molecular imaging approach that may improve detecting and monitoring procedures of clinically problematic cells arising from TSC and/or LAM.

Furthermore, experiments with ^{89}Zr -labeled Atezolizumab, a monoclonal IgG1 against PD-L1 measure tumour, revealed an importance of lower specific activity to measure tumour associated PD-L1. Ms. Moroz has already published a study about ^{89}Zr -atezolizumab ("A preclinical assessment of ^{89}Zr -atezolizumab identifies a requirement for carrier added formulations not observed with ^{89}Zr -C4") in "Bioconjugate Chemistry" which is a high impact journal in the field of biochemical research.

Overall, the dissertation is well written and scientifically sound. The introduction provides extensively important information about the background of the thesis. Although more details in the documentation of the experiments would be desirable, I believe that the experiments are reproducible for other groups and that the workflow can be understood. The results are clearly presented and the discussion sufficiently addresses the potentials and limitations of the results.

Overall, the dissertation submitted reflects significant achievements and fulfills the requirements for granting a PhD degree.

Provisional Recommendation

I recommend that the candidate should defend the thesis by means of a formal thesis defense

I recommend that the candidate should defend the thesis by means of a formal thesis defense only after appropriate changes would be introduced in candidate's thesis according to the recommendations of the present report

The thesis is not acceptable and I recommend that the candidate be exempt from the formal thesis defense