Skoltech
Skolkovo Institute of Science and Technology

Jury Member Report – Doctor of Philosophy thesis.

Name of Candidate: Aleksandra Bezmenova

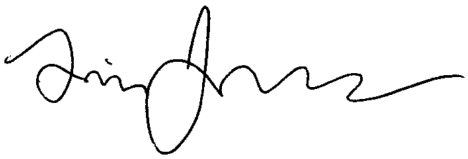
PhD Program: Life Sciences

Title of Thesis: Evolutionary processes in hypervariable fungus Schizophyllum commune

Supervisor: Professor Georgii Bazykin

Co-supervisor: Professor Alexey Kondrashov, University of Michigan, USA

Name of the Reviewer: Timothy Yong James

I confirm the absence of any conflict of interest  (Alternatively, Reviewer can formulate a possible conflict)	**Date: 20-11-2021**

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

This thesis explores the mutation and recombination rates of the mushroom Schizophyllum commune, a species remarkable for having the highest known amount of genetic variation within populations. The thesis is comprised of four data chapters, exploring mutation rates in haploids with various enforced bottleneck sizes, mutation rates in dikaryons (diploids) in both the wild and in the lab, and finally explores the impact of DNA sequence heterozygosity on the recombination rate. All data is based on the genotyping of offspring, typically using genome sequencing and assembly. Technically this thesis is quite sound, and the results are convincing and help support theory on the relationship between recombination and sequence divergence and provide a greater understanding of why this species is so species. For a fungus, mutation rates are probably normal, while compared to other organisms with some type of "economy mechanism". When scaled up, however, to generations, the level of mutation is quite high, though again not an extreme outlier.

I found the introduction and chapter 3 to be excellently crafted. Chapter 3 is already published in a leading journal and makes an important contribution to understanding the mutational process. Chapters 4 & 5 are extremely technically challenging with assembly of dikaryotic strains, though the candidate is able to extract meaningful estimates of the dikaryotic mutation rates. Both unintended mutation in culture and a surprising pattern of colonization of natural wood substrates represented challenges for these experiments. Perhaps Chapters 4 & 5 should be combined into a single publication. Chapter 6 is a nice experiment that provides a strong estimate of reduced recombination due to heterozygosity.

Recommendations/discussion points:

1. The candidate should review all chapters and correct typographic errors and improve the language as appropriate.
2. Please have a close look at the methods of analysis and make sure that they are crystal clear. I think this is something that we can discuss as a committee. For example particular methods of mapping will greatly influence the outcome. There were times when what was done was unclear to me: "non-reference variant frequency in reference sample <= 20%; pg 60).
3. On one level we know that Schizophyllum has a very high level of heterozygosity which means that recombination is inhibited at a very fine scale, yet at the population level, Schizophyllum shows very low levels of linkage disequilibrium. The relationship between overall recombination efficiency, map length (e.g., cM per genome), and efficiency of selection is something interesting for the committee to discuss.

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*