

Overall, Evgenia's thesis provides a strong foundation for a review. The thesis is based on two studies that explore the coevolution between the host's B cell adaptive immunity and the intra-host evolution of SARS-CoV-2.

In Chapter 3, the candidate utilizes longitudinal B cell immune repertoires obtained from healthy individuals. The dataset is generated using target sequencing of full BCR length with UMI correction, enabling accurate detection of somatic hypermutations in B cell clonal lineages. The candidate employs common approaches of evolutionary genomics to investigate the history of B cell clonal lineages, including phylogenetic reconstruction, analysis of mutation frequency spectrum, and dNdS ratio. This study reveals two distinct modes of evolution in B cell immune repertoires: the persistence of B cell memory and the involvement of antibody-secreting B cells in ongoing immune responses.

In Chapter 4, the candidate focuses on tracking the evolution of SARS-CoV-2 within an immunocompromised host. The candidate predicts the impact of viral population mutations on the binding of viral epitopes to the host's HLA class I alleles. The results indicate that nearly a third of the mutations could be escape variants evading cytotoxic T cells. These findings are corroborated by the candidate's co-authors, as the host's T cell response diminishes when stimulated with mutated viral epitopes compared to their ancestral states. Additionally, the candidate evaluates the implications of this SARS-CoV-2 variant, developed within a single host, on the general human population.

While Chapter 2, the literature review, is well-written and adequately referenced, it would be beneficial to expand the section discussing B cell clonal evolution analysis, particularly in the context of lymphomas.

Evgenia's research has been published in several high-impact journals, meeting the requirements of Skoltech University. However, there are a few minor comments:

1. The results from the two chapters of the manuscript could be more interconnected, enhancing the overall coherence of the thesis.
2. It would be logical to include the B cell repertoire analysis in the second chapter as well.
3. The manuscript contains minor grammatical and proofreading errors that should be corrected.

With these revisions and improvements, Evgenia's thesis will become an even stronger piece of scientific work.

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

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