Reviewer's report on the dissertation thesis entitled „ Structural studies of an abasic site DNA damage repair and DNA interstrand cross-link formation "

PhD candidate: Barbora Landová, MSc

Scientific supervisor: Mgr. et Mgr. Evžen Bouřa, Ph.D.

The aim of this PhD thesis is the structural and functional characterization of the MutM DNA glycosylase from *Neisseria meningitidis* that is involved in the repair of abasic sites of genomic DNA. The thesis is written in English in a "long" format with a total of 99 pages, including two reprints of manuscripts published in peer-reviewed journals where the candidate is the first author (FEBS letters) and joint first author (DNA repair). In addition to the appended manuscripts, the thesis follows a conventional structure consisting of Introduction, Aims, Materials and Methods, Results, Discussion, and Conclusions along with a list of 108 references.

Being outside the field of DNA damage and repair, I appreciated the concise introduction to the topic. At the same time, however, the candidate may want to pay more attention to several details in her future written assignments, including style, spelling, and references. I would also appreciate a brief description/commentary on her contribution to individual experiments. Despite this criticism, the thesis and related publications clearly document that Barbora has mastered a number of experimental techniques during her PhD training, including heterologous protein expression and purification, X-ray crystallography, and kinetic and binding assays, which will provide a solid foundation for her future scientific career.

I would like the candidate to elaborate on the following issues/questions:

1. Your binding data (Fig. 7.2) suggest that MutM does not discriminate between undamaged dsDNAs and dsDNAs containing Ap sites (or mimetics thereof). In the real-world scenario, where there is one Ap site per hundred thousand "correct" base-pairs in a genome, how is efficient Ap repair ensured? In other words, is there any mechanism in place (e.g., auxiliary factors) that helps MutM to efficiently locate Ap sites in a genome?

2. Concerning your crystallographic data (Table 7.1), could you please comment on the cut-off criteria used to set resolution limits? Could you please elaborate in more detail on common current trends (if there are any) regarding what data collection parameters (or combination thereof) might be the most useful in setting resolution limits to obtain the best possible electron density maps?

In conclusion, the PhD thesis by Ms. Barbora Landová fulfills all criteria required for the successful defense of her work. Therefore, it is my pleasure to recommend the candidate to be awarded a PhD degree.

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