Author's response to reviews

Title: Functional examination of MLH1, MSH2, and MSH6 intronic mutations identified in Danish colorectal cancer patients

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To the Editor
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Title: Functional examination of MLH1, MSH2, and MSH6 intronic mutations identified in Danish colorectal cancer patients.

Dear Editor

Thank you for your letter with the reviewer’s comments. We appreciate the constructive criticism and have revised the manuscript according to the comments from the reviewer’s. Please find below a point-by-point reply.

Regarding ethical approval, the local ethical committee has now formerly stated that no ethical approval is necessary as the study is part of routine clinical diagnostics (H-4-2013-FSP-082). The protocol number is now included in the material and methods section, patients and clinical data section, line 3.

Point-by-point reply:

Reviewer 1 (Oliver Sieber)

1) Abstract: We agree with the reviewer that the conclusion in the abstract could be better framed in terms of the implications for patient management. The conclusion in the abstract has now been changed (line 2-5).
2) Results: Unfortunately IHC staining of MLH1, MSH2 and MSH6 (and MSI) was not performed routinely on the Lynch syndrome patients included in this study. Therefore no IHC data are available. This is now stated in the results section page 1, line 14.

3) Results: RNA was not available form the patients included in this study to validate the findings from mini-gene assays. This is stated in the results section, page 2, line 6.

Reviewer 2 (Monika Morak)

1) The allelic frequencies of the intronic sequence changes are now mentioned in Table 2. Only the MSH6 c.3439-16C>T variant is reported in the exome sequencing project (ESP) database.

2) Unfortunately IHC staining of MLH1, MSH2 and MSH6 (and MSI) was not performed routinely on the Lynch syndrome patients included in this study. Therefore no IHC data are available. This is now stated in the results section page 1, line 14.

3) The family history from the Amsterdam positive families without pathogenic mutation (one family – H229) is now discussed in the discussion section (page 4, line 3-12).

On balance we feel that the changes have improved the manuscript and we hope that you will find the manuscript acceptable for publication in BMC Medical Genetics.

Yours sincerely

Thomas v. O. Hansen, Ph.D.