Author's response to reviews

Title: Simplifying the detection of MUTYH mutations by high resolution melting analysis

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Version: 3 Date: 22 July 2010

Author's response to reviews: see over
Dear editor,

In response to reviewers’ comments:

Dear reviewer Maartje Nielsen:

**Reviewer’s comment:**

- Results and discussion section:

  Associations of monoallelic and G338H carriers with differences in the phenotype are analysed. It should be mentioned here that this analysis is done in an already selected group and there are no data of a healthy control group. For example all subjects had metachronous or synchronous polyyps. Therefore it is not possible in general to state whether monoallelic carriers (and G338H carriers) associate with polyyps (metachronous and/or synchronous) or not.

  I suggest author’s state at the end of their sentence ‘in this selected group’. For example:

  In relation to the 19 carriers of p. G338H polymorphism [9] we found no association with any of the following variables: synchronous adenomas (p=0.76) CRC (p=0.79) and family history (p=0.11) in this selected group. (Table 7).

**Author’s response:**

*Results:*

In relation to the 19 carriers of G338H polymorphism [9] we found no association with any of the following variables: synchronous adenomas (p=0.76) CRC (p=0.79) and family history (p=0.11) in this selected group. (Table 7).

*Discussion*

In the study of G338H non-pathogenic polymorphism (exon 12) our data indicate no association with attenuated familial adenomatus polyposis (MAP) in this selected group.

**Reviewer’s comment:**

- The last sentence of the background seems more appropriate for the beginning of the introduction, for example as the second sentence?

**Author’s response:**

“We also analyzed the prevalence of a non-pathogenic polymorphism, located in exon 12: G338H” as the second sentence of the introduction.

**Reviewer’s comment:**

- Page 9: Monoallelic MUTYH germline mutations in 7.3%, i.e. 6/82 carried monoallelic MUTYH germline mutations. Change this sentence in:

  Monoallelic MUTYH germline mutations were found in 7.3% (6/82)?

**Author’s response:**

Monoallelic MUTYH germline mutations were found in 7.3% (6/82) of the patients.
In contrast, classical FAP patients, as is described in the literature,[16][17][18], show a CRC onset 10 years earlier than MAP (mean ages at presentation 39 versus 53 respectively)[16].


We make every effort to fully address your comments during this revision, as it is the last one on which we are allowed to seek advice.
Cover letter

Dear editor,

In response to reviewers´comments:

Dear reviewer Milo Frattini:

**Reviewer´ comment:**
The paper was corrected on the basis of reviewers´ suggestions and comments. In my opinion, the paper can be accepted, but there are few errors in the text that must be changed:
- last sentence of the introduction: remove "? (penetration)"

**Author´s response:**
Biallelic *MUTYH* mutations have also been found to be appended with 93-fold excess risk of colorectal cancer, with practically complete penetrance by 60 years of age [1].

**Reviewer´ comment:**
- 2nd page of results: change the statement "several rounds..... in each exon" as follows: "Several rounds were carried out, as a confirmatory method and to set up the appropriate sensitivity of each exon"

**Author´s response:**
Several rounds were carried out, as a confirmatory method and to set up the appropriate sensitivity of each exon.

**Reviewer´ comment:**
- discussion: change "toll" to "method"
- add a blank row before the title "Conclusions"

**Author´s response:**
- Discussion: .... it to a gene not yet analyzed by this method.
- We added a blank row before the title “Conclusions”.

We make every effort to fully address your comments during this revision, as it is the last one on which we are allowed to seek advice.