Author’s response to reviews

Title: The genetic basis of colonic adenomatous polyposis syndromes

Authors:

Bente Talseth-Palmer (Bente.Talseth-Palmer@newcastle.edu.au)

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Author’s response to reviews:

Bente Talseth-Palmer

Researcher

Norwegian University of Science and Technology (NTNU), Norway

University of Newcastle, Australia

Finlay Macrae

Editor

Hereditary Cancer in Clinical Practice (HCCP)

Re: Manuscript HCCP-D-16-00009

Thank you for your email on the 2nd November 2016 regarding the resubmission of manuscript HCCP-D-16-00009 entitled ‘Familial Adenomatous Polyposis Genetics’. The manuscript has been revised taking into account the minor revisions from reviewer 2 and I hope it is acceptable for publication in HCCP in its current form.

The manuscript has been appropriately altered according to the reviewers’ comments and I will, in point form, describe what has been edited. Track changes have been used in the main document.

Reviewer 2: Minor revisions

- Please ensure that throughout that the names of genes are in italics and their protein product in normal font. Gene names seem to appear in both italic and normal font.
o This has been taken care off. Thank you for the reminder.

• At the introduction to the section describing MAP, NAP, etc, you state that they are all recessively inherited. This is incorrect as PPAP is dominantly inherited.
  o This has been corrected from ‘‘All the recently…’’ to ‘‘Some of the recently…’’.

• Please include an age in your definition of attenuated FAP. As I mentioned before, a 10 year old with 80 adenomas is very different to a 60 year old with 80 adenomas. Most would use <100 adenomas at 25 years or older.
  o Mean age of polyp diagnosis in AFAP patient was already in the manuscript and referenced (44 years of age and reference 8). As I found no literature suggesting 25 years of age for the definition of attenuated FAP, I have included another reference (34) and changed the text to ‘‘…on average in fourth to fifth decade of life, with cancer developing 10-15 years later. Screening is suggested to start late teens to mid 20s’’.

• There are a number of grammatical/language errors littered throughout which need correcting.
  o The manuscript was sent to English editing and has been carefully corrected for errors in spelling, grammar and word choice. Track changes have been used throughout the manuscript to highlight the changes done to the manuscript.

• There is no mention of mosaicism and this is probably of more importance (given the diagnostic workup and the once discovered the possibility of predictive testing in FDRs) than the possibility of genetic modifiers, which have not be identified.
  o I would like to disagree when the reviewer who says genetic modifiers have not been identified (ref 65) and I also refer to a study that have shown that modifiers are associated with adenoma numbers in APC mutation carriers (ref 58).
  o Mosaicism is mention in the FAP Genetics section and referenced with two references (21 and 22).
I appreciate all the helpful comments from the reviewers and trust the manuscript is ready for publication in HCCP. I hope that the editor will make a fast decision on this manuscript considering it was first submitted in March 2016 and that this will be a 2016 publication.

Kind regards,

Bente Talseth-Palmer

Researcher

Norwegian University of Science and Technology (NTNU), Norway

University of Newcastle, Australia

T: +47 711 210 62
M: +47 480 53 009
E: Bente.Talseth-Palmer@newcastle.edu.au

Address:
Molde Hospital
Parkveien 84
6407 MOLDE
NORWAY