Reviewer’s report

Title: Prevalence and Spectrum of MLH1, MSH2, and MSH6 Pathogenic Germline Variants in Pakistani Colorectal Cancer Patients

Version: 0 Date: 10 Mar 2019

Reviewer: Andrzej Plawski

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VALID TERMINOLOGY

- Hereditary nonpolyposis colorectal cancer (HNPCC) refers to patients and/or families who fulfill the Amsterdam criteria

- Lynch syndrome refers to patients and families with a germline mutation in one of the DNA mismatch repair genes (MLH1, MSH2, MSH6, PMS2) or the EPCAM gene.

Those can’t be used interchangeably. Not all HNPCC may be named Lynch syndrome.

You wrote "HNPCC is caused by germline mutations in DNA mismatch repair” look on definition what is HNPCC. Lynch syndrome is caused by mutation of MMR genes

In manuscript it have to be corrected in all places

In small group of HNPCC and HNPCC suspected probants authors identified one recurrent mutation which led to diagnose over 8% of their families.

Interesting is novel substitution c.116+3A>T. Wasn't it possible to make cDNA and check the impact of the mutation on mRNA sequence. In this case it will clarify the doubts

This study confirming thesis that, checking HNPCC families for mutations in MMR genes increases the chances of success if compare to group not fulfilling HNPCC criteria.

It is nice report of examination of small group of HNPCC families from Pakistan

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Quality of written English
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