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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3158
Title: Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles
Reviewer code: 00004187
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-04-11 20:15
Date reviewed: 2013-07-06 05:52

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

The work is good and I recommend its publication. Better define groups of 120 and 58 patients Add a Table. ? You must specify the 120 unrelated patients with hereditary. How many had Amsterdam II criteria, Bethesda, first-degree relatives with CRC? In each subgroup How many had MSI or MSS or not analyzed. All MSI became germline mutations study? ? Clarify pacietnes 58. What types and number of polyps had the 35 patients? Had MUTYH-PAF?? Of the other 23 How many Amsterdam II criteria met, Bethesda or had first-degree relatives with CRC? In each subgroup had few MSI or MSS or not analyzed. All MSI became germline mutations study? 120 58 Amsterdam - MSI o Mutation o No mutation o Unknown - MSS - Unkonwn Bethesda - MSI o Mutation o No mutation o Unknown - MSS - Unknown First-degree relatives with CRC - MSI o Mutation o No mutation o Unknown - MSS - Unknown Polyps (> 10 polyps) o Mutyh o Positive o Negative o Unknown o FAP o Positive o Negative o Unknown - MSI o Mutation o No mutation o Unknown -MSS - Unknown ? In results, do not add 120 (37 +50 +34 = 121). The family with 3 diffuse gastric cancer or intestinal Was? Defining what is "Likely Lynch syndrome" and "syndrome X" In the abstract to express the confidence intervals

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3158
Title: Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles
Reviewer code: 00502983
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-04-11 20:15
Date reviewed: 2013-07-08 19:31

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[Y] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

"Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles ", by KüRY et al. July 8th 2013 This paper attempt to replicate a study from Coisseux et al. who inferred a major role of the UNC5C gene in the predisposition to familial forms of colorectal cancer (CRC) based on higher frequency of the A628K variant in the patient population than in a control population. In this paper, with samples from independent patient populations, authors conclude that variation observed in exon 11 UNC5C alleles confer only a low risk for both familial and sporadic forms of CRC. These results imply medical and technical implication. I therefore think that this study is appropriate for publication.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3158
Title: Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles
Reviewer code: 00180990
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-04-11 20:15
Date reviewed: 2013-07-15 17:29

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

ESPS Manuscript NO: 3158 (15.07.2013) Title: Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles by Kury et al. This manuscript presented a well performed study assessing the role of rare genetic variant in the UNC5C gene, in particular the A628K missense mutation in 11 exon of UNC5C in familial colorectal cancer genetic predisposition. The authors also evaluated the relation between this rare variant and sporadic CRC. The methodology used in this investigation is suitable for reaching the results and it is well described; the findings are clearly presented; the analysis and interpretation of data seem appropriate and competent, but too wasteful. The study presented interesting and seemingly controversial results, concerning role of A628K substitution in UNC5C receptor gene that has been studied before from Coissieux et al, 2012. No doubt that expression of the netrin-1 dependence receptor UNC5C is reduced in many colorectal tumors and has a role in triggering apoptosis which prevent tumor cell survival. An explanation of differences in the results of Coissieux et al, and data presented here could be due to statistically interpretation. Indeed rare variant frequencies reported by the two investigators teams are approximately close: range 0.1 to 0.9 of Coissieux et al. and range 0.18 to 0.56 of Kury et al. Moreover in too studies the frequency of variant is enhanced in CRC then control, particularly for familial CRC. All these frequency are too small and less than 1% which show that A628K missense is more like mutation then polymorphic variant. It should be noted that statistical analysis is designed preferentially for normally distributed polymorphic allele. I believe that the authors should discuss their results as not preclude the significance of the mutation as a rare genetic anomaly distributed in distinct family. The author should take in consideration the above mentioned and appropriate interpreted the data observed in their study. Section Discussion and related areas require substantial processing in

connection with the foregoing

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 3158
Title: Evaluation of the colorectal cancer risk conferred by rare UNC5C alleles
Reviewer code: 02461836
Science editor: Zhai, Huan-Huan
Date sent for review: 2013-04-11 20:15
Date reviewed: 2013-07-17 01:09

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
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the foregoing