



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 27954

**Title:** Aging related methylation influences the gene expression of key control genes in colorectal cancer and adenoma linked

**Reviewer's code:** 03381915

**Reviewer's country:** United States

**Science editor:** Jing Yu

**Date sent for review:** 2016-06-24 12:42

**Date reviewed:** 2016-08-10 02:41

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

This manuscript describes or rather reaffirms a relationship between aging and cancer. There is nothing new but authors provide additional data. I did not see any major problem with the manuscript. However, I have following comments to be addressed by the authors. a. In Materials and Methods, simply saying that statistical review was performed by so and so is not enough. the methods employed for these analyses must be described. The validity of data depends on this. b. In the results section, "other genomic regions" mentioned on page 9 must be described. c. there are multiple language problems. Since lines are not numbered by the authors, I'll submit few examples and strongly suggest that that whole manuscript should be carefully reviewed. 1. Reference "Horvath et al" on page 3 (abstract) is not mentioned in the References. There is Hovath S, but not et al. I therefore suggest that authors should go thru each reference to make sure it is in the text. 2. Sentences should not start with numbers (Example: page 10, line 5) 3. Abbreviations used in the abstract for the first time (CRC etc.) must be defined when used for the first time.



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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 27954

**Title:** Aging related methylation influences the gene expression of key control genes in colorectal cancer and adenoma linked

**Reviewer’s code:** 03437591

**Reviewer’s country:** China

**Science editor:** Jing Yu

**Date sent for review:** 2016-06-24 12:42

**Date reviewed:** 2016-08-05 11:23

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

1. The authors should provide the demographic details of the samples included in this investigation.
2. How did the authors obtain the the Encode ChromHMM results of nine human cell lines and identify genomic elements such as promoters, enhancers and insulators?
3. How to identify the differnetially methylated genes?
4. The authors showed many calculated results but lacked further analyses.
5. How did the authors ensure that the alterations of methylation levels of the age-related ‘epigenetic clock’ genes in cancer samples were caused by aging or tumor genesis?
6. The influence of promoter methylation level of SFRP1 on its expression need further validation by experiments.
7. Some errors in sentences like “The expression of several genes including SYNE1, CLEC3B, LTBP3 and SFRP1 was similarly” should be corrected.

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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 27954

**Title:** Aging related methylation influences the gene expression of key control genes in colorectal cancer and adenoma linked

**Reviewer's code:** 00505564

**Reviewer's country:** United States

**Science editor:** Jing Yu

**Date sent for review:** 2016-06-24 12:42

**Date reviewed:** 2016-07-05 01:15

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

Galamb et al. is an attractive paper for this Journal. The authors analyzed DNA methylation alterations of age-related genes belonging to 353 epigenetic clock CpG sites during colorectal carcinogenesis and aging. They significantly found several age-related DNA methylation alterations that could be observed during CRC formation and progression affecting the mRNA expression of certain CRC- and adenoma-related key control genes such as hypermethylated secreted frizzled related protein 1 (SFRP1), spectrin repeat containing nuclear envelope protein 1 (SYNE1) and hypomethylated cell migration-inducing protein (CEMIP). Interestingly, for the first time they found significantly lower SFRP1 methylation levels in children (under 18 years) compared to healthy adult colonic tissues. Excellent observation. This is a well written detailed manuscript. The citations are adquetely presented. However, I need clarity of the followings (i) the difference between healthy and normal patient samples. Is healthy patient samples the same as normal patient samples or not. You investigated 8 healthy adults and 19 normal children, were those 8 healthy adults normal? And/or were the 19 normal children healthy? it is confusing. (ii) How was the informed consent done to



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children. The attached Institutional IRB letter is in Hungarian language and I am not able to understand it.