June 29th, 2015

Dear reviewer,

Thank you for your advice on our ESPS manuscript NO: 18625. After we have revised the manuscript based on your suggestions, we are now sending the revised manuscript to you with the details of how the paper has been revised as follows. All of the revisions have been highlighted in the revised manuscript.

Suggestion 1: English must be polished a little.

Answer: Our manuscript has been polished by Jing-Yun Ma Editorial Office, which is a professional English language editing company recommended by WJG editorial office.

Suggestion 2: I suggest include another table with the information of each polymorphism mentioned: chromosome location, location with respect the gene, type of mutation, wild type and mutated allele, etc.

Answer: We added Table 2 with the information of all studied single nucleotide polymorphisms, including their gene, chromosome, SNP, wild allele, mutated allele, contig position, and location in gene in our revised manuscript as follows. In addition, since it is hard to describe the exact location of VNTR at chromosome, moreover, each VNTR has a lot of alleles, and it is also hard to define which is wild allele, as well as which is mutated allele, we did not describe the details of studied VNTR in Table 2.

Page 4, last line and page 5, first line, Details of the studied single nucleotide polymorphisms (SNPs) in mucin genes are described in Table 2.

Table 2 Description of the studied SNPs in mucin genes

Gene	Chromosome	SNPs	Wild	Mutated	Contig	Location[b]

			alleles	alleles	position[a]	
MUC1	1q21	rs4072037	A	G	12007689	T22T
		rs2070803	C	T	12000652	3'flanking region
		rs6427184	A	G	11965720	3'flanking region
		rs4971052	C	T	11968955	3'flanking region
		rs4276913	A	G	11974610	3'flanking region
		rs4971088	T	A	11985820	3'flanking region
		rs4971092	T	C	11986883	3'flanking region
		rs2990245	T	C	12043084	5'flanking region
		rs9628662	T	G	12051963	5'flanking region
		rs9426886	T	A	11994691	3'flanking region
		rs3814316	C	T	11992655	3'flanking region

		rs1045253	T	C	12046857	5’flanking region
MUC5AC	11p15.5	rs1541314	G	A	1182293	3’flanking region
		rs2014486	A	G	1177573	3’flanking region
		rs2075859	C	T	1169258	3’flanking region
		rs2672785	C	T	1165711	3’flanking region
		rs2735733	C	T	1180410	3’flanking region
		rs7118568	C	G	1162850	3’flanking region
		rs868903	T	C	1161460	3’flanking region
		rs4963049	A	G	1155197	3’flanking region
		rs3793966	C	T	1221718	3’flanking region
		rs3793964	C	T	1220752	3’flanking region

		rs3750919	G	A	1211601	3’flanking region
		rs5743942	C	T	1232798	3’flanking region
		rs4963062	G	A	1245411	3’flanking region
		rs885454	C	T	1162161	3’flanking region
		rs6578810	T	G	1209349	3’flanking region
		rs11040869	G	A	1203382	3’flanking region
		rs7118481	G	C	1267108	3’flanking region
		rs7105198	G	C	1086133	5’ flanking region
MUC6	11p15.5	rs1128413	C	T	950694	3’flanking region
		rs4077293	C	T	936522	3’flanking region
		rs7483870	C	T	916019	3’flanking region

	rs7943115	G	A	913885	3’flanking region
	rs11602663	C	T	960778	Intronic
	rs11605303	G	A	978110	5’ flanking region
	rs10902076	G	C	1006044	5’ flanking region
	rs2071174	C	T	1013712	5’ flanking region
	rs11245936	G	A	1026266	5’ flanking region
	rs10794359	C	T	991715	5’ flanking region
	rs7112267	C	T	996981	5’ flanking region
	rs12574439	G	C	997948	5’ flanking region
	rs7119740	C	G	1000419	5’ flanking region
	rs11601642	C	A	1002509	5’ flanking region
	rs4076950	C	T	955021	Intronic

		rs7481521	G	A	967811	V619M
		rs11246384	C	T	970448	Intronic
		rs6597947	G	T	977029	5’ flanking region
		rs9794921	G	T	979867	5’ flanking region
MUC2	11p15.5	rs10902073	C	A	1000934	5’ flanking region
		rs10794281	C	T	1003149	5’ flanking region
		rs2856082	C	G	1011562	5’ flanking region
		rs2071174	C	T	1013712	5’ flanking region
		rs7396030	C	T	1025368	Intronic
		rs11245936	G	A	1026366	G832S
		rs7944723	C	G	1039802	P1832P
		rs6421972	G	A	1042586	I2154T
		rs10794293	C	T	1045031	Intron

	rs11245954	A	G	1047170	V2459V
	rs7480563	G	A	1047741	T2524P
	rs7126405	G	A	1049388	Q2653P
	rs3924453	G	A	1051898	3'flanking region
	rs4077759	C	T	1052068	3'flanking region
	rs2856111	T	C	1015747	L58P
	rs11825977	A	G	1015920	V116M

[a] Based on contig NT_004487.20 for *MUC1* gene, and contig NT_009237.19 for *MUC5AC*, *MUC6* and *MUC2* genes.

[b] SNP location relative to each gene in the region.

Suggestion 3: In page 7: which are the polymorphisms cited by the authors in this sentence? "Furthermore, Marin et al. [49] reported that three tested tagSNPs in MUC1 gene were not associated with precursor lesions of GC in a high-risk area in Spain".

Answer: We have added the id of mentioned SNPs on page 7, line 16-17, which is: Marin *et al*[49] reported that three tag SNPs (rs3814316, rs9426886 and rs1045253) in *MUC1* were not associated with precursor lesions of GC in a high-risk area of Spain.

Suggestion 4: Page 10: plesse rephrase this paragraph, it sounds a little confusing: "Their results indicated that three SNPs (including rs10794293, rs3924453, and rs4077759) at the 3'-moiety in *MUC2* gene were associated with a decreased risk of progression of the lesions, while another four SNPs (including rs10902073,

rs10794281, rs2071174, and rs7944723) at the 5'-moiety were significantly associated with regression of the lesions, and the effect of all associated SNPs with GC precursor lesions was found to be stronger in *H. pylori* infected patients."?

Answer: We have rephrased this paragraph on page 10, line 12-22, which is: Marin *et al*[49] have investigated the association of 14 tag SNPs in *MUC2* with evolution of GC precursor lesions in 387 patients with 12.8 years follow-up. According to the diagnosis at recruitment and after follow-up, the patients were divided into three groups, that is, those with no change in lesions, progression of lesions, and regression of lesions. The results indicated that three SNPs (rs10794293, rs3924453 and rs4077759) at the 3' moiety in *MUC2* were associated with a decreased risk of lesion progression. In contrast, another four SNPs (rs10902073, rs10794281, rs2071174 and rs7944723) at the 5' moiety were significantly associated with lesion regression. The association of SNPs with GC precursor lesions was stronger in patients with *H. pylori* infection.

Suggestion 5: Authors could consider include this work in their review: Frank et al. Eur J Cancer, 2012; 48(1):114-20.

Answer: We had included this work in our original manuscript as ref. 48.

We have also made some modifications in the format throughout the text according to the editor's suggestions, which is highlighted in the revised manuscript.

We wish the quality of our revision has been adequate and will be delighted should our manuscript be acceptable for your World Journal of Gastroenterology.

We are looking forward to hearing from you soon.

Sincerely yours,

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