Author's response to reviews

Title: Genetic risk factors for intestinal metaplasia in a high risk Singapore-Chinese population: a cohort study

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We thank Drs. Rabkin and Zambon for considering our revisions complete.

Dr. Hamajima is indeed correct that \textit{IL10} -819T/C and \textit{NQO1} 609C/T are not in HWE. Upon review, we found this highlighted in one of our earlier drafts (not sent) but it unfortunately was missed in our many consolidations of co-author drafts. The sentence “All polymorphisms were in Hardy-Weinberg equilibrium (P>0.05), with the exception of \textit{IL10} -819T/C, \textit{NQO1} 609C/T and \textit{TP53} Arg72Pro” on page 8 has been modified (changes underlined) to address this. We are very confident with the genotyping. Pyrosequencing is an established method, and positive controls were included in every run. In principle, HWE only can be expected in healthy populations, so it is not unexpected that some of the genotypes were not in HWE in this higher-risk population.

We have performed multivariate analysis to identify the factors associated with IM in the “HP+ or IM+” (that is, subjects that were either HP-/IM+ or HP+/IM- or HP+/IM+, denoted as “revised HP+”) subgroup. The sentence “As it is possible that IM+/HP- cases in this study had prior unrecorded HP infection[30], subgroup analysis on cases with a “revised HP+” status (either HP+/IM-, HP+/IM+ or HP-/IM+) was also performed. Age (OR = 2.10, 95%CI: 1.24–3.56, P=0.006) and \textit{IL-10} -819 C allele (OR=1.82, 95%CI: 1.07–3.08, P=0.027) were the only significant variables in this subgroup.” has been added to the end of Results on page 9 to address this. In the previous report on the “HP+” subgroup, Age, \textit{IL-10}-819, \textit{NQO1}+609, and \textit{PTPN11} rs2301756 GA/AA were significant, so \textit{NQO1}+609, and \textit{PTPN11} rs2301756 GA/AA have been lost with the “revised HP+” definition.