Author's response to reviews

Title: Humoral immune response to MUC5AC in patients with colorectal polyps and colorectal carcinoma

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Answers to Reviewer I (Samuel B. Ho)

Major Compulsory Revisions

I- as the reviewer pointed out that the number of patients in our study was small. We cannot demonstrate statistical significance of the correlation of MUC5AC positivity with clinicopathological parameters although the percentage of them shows difference. Abstract was corrected according to reviewer's comments.

II-III The histology of polyps were specified and correlated with MUC5AC antibody level in the text and at table 3.

Although hyperplastic polyps have been generally believed to be non-neoplastic, several recent important studies have suggested their malignant potential, particularly in hyperplastic syndrome, as well as serrated adenoma. The known alterations include K-ras mutation, low and occasionally high level microsatellite instability, 1p LOH, and methylation of HPP1/TPEP (1). It is believed that with these mutations, serrated polyps (hyperplastic polyps, serrated adenomas) changed to carcinoma.

M Koike et al. demonstrated gastric foveolar cell-type expression (SH-9, Human Gastric Mucin, MUC5AC) in many cases of hyperplastic polyp and serrated adenoma, while it was relatively rare in tubular adenomas (2). Yao et al reported gastric-type colorectal carcinoma showing gastric foveolar cell-type differentiation. It was rather rare (only 2%) in colorectal carcinoma but these cases exhibited high grade malignancy (3-4). Biemer-Hutmann et al also demonstrated that MUC5AC expression increased in hyperplastic polyps and serrated adenomas (5). Koike M et al. showed that Human gastric mucin [(45M1) that we used in our study] was expressed in 88.9% at hyperplastic polyps (6). These ratios were also similar with our results.

5- Biemer-Hutman A, Walsh MD, McGuckin MA, Ajiko Y, Watanabe H, Leggett BA, Jass JR. Immunohistochemical staining patterns of MUC1, MUC2, MUC4 and MUC5AC mucins in hyperplastic polyps, serrated adenomas, and traditional adenomas of the colorectum.

Minor Essential Revisions

IV- Corrected

V- We made a new table that showing correlation of MUC5AC antibody positivity with clinicopathological parameters of colorectal carcinoma patients (Table-4). We thought that if we add the percentage of MUC5AC antibody positivity in each subgroup, Table 1 will a crowded and confusing table.

VI- OVS and DFS abbreviation were corrected.

VII- Reference 31 was given for data cited.

Answers to Reviewer two

Minor Essential Revisions

1- The reviewer suggestion is right. The sensitivity of ELISA may be increased by using at least 2 or more VNTR. It might provide epitopes to better recognition of antibodies present in the sera. The issues should
be examined in the future about improves the detecting MUC5AC antibody in sera.
2. We discuss the possibility of using different MUC5AC glycopeptides and monoclonal antibodies in this ELISA.