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Overexpression of DNA methyl-transferase 3B in colorectal adenoma increase the risk of adenoma recurrence during colonscopy surveillance

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Background & Aim: Colorectal cancer is the leading incident cancer and the major cause of cancer death world-widely. Colonoscopy with polypectomy is current standard to prevent cancer development and decrease cancer associated morbidity and mortality. Current surveillance strategies were majorly based on adenoma size; number and pathology found in baseline index colonoscopy, but still unexpected high-risk colorectal adenoma or cancer were revealed despite earlier surveillance. Thus, additional risk factors to facilitate an earlier adenoma recurrence should exist. The goal of this study is to find potential biomarkers to help these patients with higher risk of adenoma recurrence, including cyclooxygenase (COX-2), an important marker in inflammation and concretization process, and DNA methyl-transferase 3B (DNMT3B), as an important enzyme influencing DNA methylation and epigenetic modification in cancer development.

Methods: The study consecutively enrolled 138 patients who received surveillance colonoscopy to establish previous colonoscopy findings as "index" colonoscopy and surveillance interval. In addition to clinical/ demographic/colonoscopy findings, immunohistochemistry staining was also performed for index colon polyps to determine whether overexpression of COX-2 or DNMT3B is associated surveillance outcomes.

Results: In mean surveillance interval of 24.9 months, the surveillance colonoscopy disclosed 29% of cases with high risk adenoma (HRA). In univariate and multivariate COX regression, senile age, the presence of index adenoma with high grade dysplasia and index polyp with DNMT3B overexpression were independent risk factors for HRA development during surveillance. Especially for patients without high risk adenoma in baseline colonoscopy, DNMT3B overexpression, but not COX-2 over-expression, can be associated with an increased risk.

Conclusions: DNMT3B overexpression in baseline colorectal polyps is associated with high risk adenoma occurrence during surveillance and may serve as a potential biomarker for high risk patients to receive earlier colonoscopy surveillance.

Kaplan-Meier survival analysis of potential biomarkers for high risk adenoma (HRA) occurrence during surveillance in patients without HRA in index colonoscopy: a) by COX-2 overexpression (p=0.191); b) by DNMT3B overexpression status (p=0.008)

The box plots of the total DNMT3B expression score (the sum of the expression score in the upper, middle, and lower third of the colonic mucosa) were shown for the different pathology types. Hp, hyperplastic polyp; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma; VA, villous adenoma; AdenoCa, adenocarcinoma.

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