Implications of Inflammatory and Oxidative Tissue Damage in Gastrointestinal Carcinogenesis

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Current evidences have expanded the concept that chronic inflammation might play a crucial role in the development and progression of several gastrointestinal (GI) cancers. For instances, many cancers originated from GI tissues are closely associated with chronic, persistent, perpetuated, repetitive in its degree like relapse and remission, inflammations, clinical presentation as chronic *Helicoabcter pylori* infected gastritis, Barrett's esophagitis, ulcerative colitis, chronic viral hepatitis or non-alcoholic steatohepatitis (NASH), and cholangitis, all of which are associated with gastric cancer, Barrett associated adenocarcinoma of esophagus, colitic cancer, hepatocellular carcinoma, and cholaniocarcinoma, respectively. Here, in the current symposium, we will discuss the molecular evidence and preventive way that chronic inflammation is capable of inducing cancer and procancer microenvironment favorable for the survival of cells and their growth in *H. pylori*-associated gastric cancer model and ulcerative colitis-associated colon cancer model.

1) *H. pylori*-associated gastric cancer model with chemoprevention

In 1994, WHO-IARC (World Health Organization-International Agency on Research about carcinogenesis), Lyon, defined *H. pylori* as class I, that is, definite, carcinogen, which was further proved by the 12 years cohot study by Uemura N *et al* that patients infected with *H. pylori* developed gastric cancer, whereas none developed gastric cancer in patients with no evidence of *H. pylori* infection. Before this evidence, several animal models served as cancer model after *H. pylori* infection. This year, Prof. B. Marshall got the lucky to receive Novel prize, based on the works that *H. pylori* is the pathogen either for gastritis and peptic ulcer disease or precancerous lesions in the stomach. We have established the mice model with *H. pylori* infection, showing the diverse pathologies, including chronic gastritis, chronic atrophic gastritis, and even gastric cancer and explored the underlying molecular mechanisms. Recently we can prevent *H. pylori*-associated gastric carcinogenesis with several anti-inflammation or antioxidant agents, suggesting that early and appropriate intervention can prevent the disaster of *H. pylori* infection since the eradication of *H. pylori* do not privilege the efficacy of cancer prevention in cohort study.

2) Ulcerative colitis-associated colon cancer model with chemoprevention

Ulcerative colitis (UC)-associated cancer develops from dysplasia lesion caused by chronic inflammation. However, the specific mechanistic link between chronic inflammation and carcinogenesis in colon has not been integrated into molecular understanding. In this study, we established experimental animal model of human UC and to identify proteins involved in development of UC-associated colorectal cancer, proteomics based on 2-dimensional electrophoresis and MALDI-TOF MS was employed. 5 weeks C57BL/6J mice were exposed to 15 cycles of dextran sodium sulfate (DSS) that each cycle comprised of 0.7 % DSS for a week followed by distilled water for the subsequent 10 days. Colorectal tumors developed in 22 out of 24 repeated colitis-induced mice (91.6 %) and the tumor multiplicity was 1.58 per a tumor-bearing mouse. Comparative 2DE analysis showed 38 protein spots differentially expressed in colon tumor. 27 proteins including GRP94, HSC70, enolase, prohibitin, and transgelin were identified. Transgelin out of 27 identified spots significantly reduced in mouse colon tumor documented by Western blot and immunohistochemistry analysis. Down expression of transgelin was noted in neoplasms of human colon compared to abundant expression in adjacent non-tumorous tissues. These results suggest that loss of transgelin could be a candidate for biomarker of repeated colitis-associated colon cancer.