Oncogenic viruses in gastrointestinal cancer

REVIEW OF LITERATURE:

ARTICLES ON ONCOGENIC VIRUSES IN GASTROINTESTINAL CANCER:

1. Author Nima Khalighinejad et al. worked on " Adenoviral gene therapy in gastric cancer". Gastric cancer is one of the most common malignancies worldwide. With current therapeutic approaches the prognosis of gastric cancer is very poor, as gastric cancer accounts for the second most common cause of death in cancer related deaths. Gastric cancer like almost all other cancers has a molecular genetic basis which relies on disruption in normal cellular regulatory mechanisms regarding cell growth, apoptosis and cell division. Thus novel therapeutic approaches such as gene therapy promise to become the alternative choice of treatment in gastric cancer. In gene therapy, suicide genes, tumor suppressor genes and anti-angiogenesis genes among many others are introduced to cancer cells via vectors. Some of the vectors widely used in gene therapy are Adenoviral vectors. In this work, the scientists elucidated the new developments in adenoviral cancer gene therapy including strategies for inducing apoptosis, inhibiting metastasis and targeting the cancer cells.

2. Author M Ohashi, et al. worked on " Adenovirus mediated p53 tumor suppressor gene therapy for human gastric cancer cells in vitro and in vivo". Gastric cancer is one of the most prevalent forms of cancer in East Asia. Point mutation of the p53 gene has been reported in more than 60% of cases of gastric cancer and can lead to genetic instability and uncontrolled cell proliferation. The purpose of this investigation was to evaluate the potential of p53 gene therapy for gastric cancer. The responses of human gastric

cancer cell lines, MKN1, MKN7, MKN28, MKN45, and TMK-1, to recombinant adenoviruses encoding wild type p53 were analysed in vitro. The efficacy of the AdCAp53 treatment for MKN1 and MKN45 subcutaneous tumours in nude mice was assessed in vivo. He observed the p53-specific growth inhibition in vitro in two of four gastric cancer cell lines with mutated p53, but not in the wild type p53 cell line. He was found the gastric cancer cells by AdCAp53, by flow cytometric analysis and detection of DNA fragmentation, to be apoptosis. In vivo studies showed that the growth of subcutaneous tumours of p53 mutant MKN1 cells was significantly inhibited by direct injection of AdCAp53, but no significant growth inhibition was detected in the growth of p53 wild type MKN45 tumours. Adenovirus mediated reintroduction of wild type p53 is a potential clinical utility in gene therapy for gastric cancer.

3. Author Darryl Shibata, et al. worked on “ Epstein-Barr Virus-associated Gastric Adenocarcinoma”. The Epstein-Barr virus has been detected in certain types of lymphoma and some epithelial neoplasms including nasopharyngeal lymphoepithelioma and rare lymphoepithelioma-like carcinomas occurring in a variety of organs including, most recently, the stomach. He investigated the possibility that EBV may be present not only in the rare gastric cancers that resemble nasopharyngeal lymphoepithelioma, but also in typical gastric adenocarcinoma. EBV sequences were detected in 22 of 138 (16%) cases of typical gastric adenocarcinoma by polymerase chain reaction and in situ hybridization (ISH) techniques. The EBV genomes were specifically present within the gastric carcinoma cells in an even distribution. The EBV genomes were also present in adjacent dysplastic epithelium but were absent in surrounding lymphocytes, other normal

stromal cells, intestinal metaplasiag and normal gastric mucosa. EBV was most often detected in gastric tumors from men (21%) compared with women (3%). Thus some cases of gastric adenocarcinoma are EBV associated.

4. Author M. A. H Lee, et al. worked on " Epstein-Barr virus associated gastric cancer and its clinical characteristics". Epstein-Barr virus is associated with a variety of lymphoproliferative disorders. Recently, many authors reported the association between EBV and gastric cancer, but it is not well known about characteristics of EBV associated gastric cancer. They observed the EBV in gastric cancer by using in situ hybridization(ISH) with tissue microarray and reviewed the patients' chart to determine special characteristics of EBV associated gastric cancer. Formalin-fixed and paraffin-embedded blocks from 380 surgically resected gastric specimens were studied by using ISH with tissue microarray. All patients were diagnosed with gastric cancer between January 1998 and March 2003 at kangnam St. Mary's hospital of Korea. Clinical data was obtained from clinical record. It was observed EBV in 20 of 380 cases (5. 3%) with gastric cancer by ISH. In EBV-positive gastric cancer, median age was 58. 5 years. Most common symptom was epigastric pain (55%). Most lesions were at upper portion of stomach. Fourteen cases (70%) were located at body, five cases (25%) at antrum, and one case (5%) at cardia. According to histologic grade, 10 patients (50%) had moderate differentiated adenocarcinoma, and 9 patients (45%) had poorly differentiated adenocarcinoma. Most of patients with EBV-positive gastric cancer had early gastric cancer by gastrofiberscopic classification (80%). Although its incidence is very low, EBV associated gastric cancer has

tendency to be diagnosed at early stage. They observed several protein expressions to determine how EBV plays a role in carcinogenesis in gastric cancer.

5. Author Sook-Kyoung Heo, et al. worked on “ The presence of high level soluble herpes virus entry mediator in sera of gastric cancer patients”. The development of gastric cancer is closely related to chronic inflammation caused herpes virus entry mediator is a receptor expressed on the surface of leukocytes that mediates potent inflammatory responses in animal models. They observed that the interaction of HVEM on human leukocytes with its ligand LIGHT induces intracellular calcium mobilization, which results in inflammatory responses including induction of proinflammatory cytokine production and anti-bacterial activities. In this study, they report that leukocytes from GC patients express lower levels of membrane HVEM and have lower LIGHT-induced bactericidal activities than those from healthy controls. In contrast, levels of soluble HVEM in the sera of GC patients were significantly higher than in those of HC. He found that monocyte membrane-bound HVEM is released into the medium when cells are activated by proinflammatory cytokines such as TNF-α and IL-8, which are elevated in the sera of GC patients. mHVEM level dropped in parallel with the release of sHVEM, and release was completely blocked by the metalloprotease inhibitor, GM6001. He indicated that mHVEM on leukocytes and sHVEM in sera may contribute to the development and progression of GC.

6. Author Eva Serup-Hansen, et al. worked on “ Human Papillomavirus Genotyping and p16

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Stages I to III Carcinoma of the Anal Canal". Carcinomas of the anal canal are strongly associated with the human papillomavirus. Expression of p16 is used as a surrogate marker of HPV infection. In a retrospective study, They evaluated HPV genotyping and p16 expression as prognostic markers of overall survival and disease-specific survival in patients diagnosed with American Joint Committee on Cancer stages I to III carcinoma of the anal canal. It was observed HPV16 in 81. 0% of the tumors, followed by HPV33 (5. 1%), HPV18 (2. 2%), and HPV58 (0. 7%). p16 positivity was found in 92. 9% of the tumors. It was observed the p16 positivity is an independent prognostic factor for OS and DSS in patients with AJCC stages I to III carcinoma of the anal canal.

7. Author Kamangar F, et al. " Human papillomavirus serology and the risk of esophageal and gastric Cancers". Esophageal and gastric cancers cause more than 900, 000 deaths worldwide. Human papilloma virus, especially type 16, has been suggested to have a role in the etiology of esophageal cancer, however, the results of previous seroepidemiological studies have not been consistent. They conducted a large prospective study to examine the association between serum antibodies to HPV 16, HPV 18 and HPV 73 and subsequent development of esophageal squamous cell carcinoma, gastric cardia adenocarcinoma (GCA), and gastric noncardia adenocarcinoma (GNCA) in a high-risk population for these cancers in Linxian, China. Case and control subjects for this study was selected from the 29, 584 participants of the Linxian General Population Trial. Prediagnostic serum samples from 99

cases of ESCC, 100 cases of GCA, 70 cases of GNCA, and 381 age- and sex-matched controls were selected for this study. The presence of antibodies to HPV virus-like particles was determined by type-specific enzyme-linked immunosorbent assays.