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Research Activities

Alimentary tract

1. Examination of new biomarkers to assess disease activity in inflammatory bowel disease

1) Prostaglandin E-major urinary metabolite as a reliable surrogate marker for mucosal inflammation in ulcerative colitis

We evaluated whether prostaglandin E-major urinary metabolite (PGE-MUM) can be used as a biomarker for ulcerative colitis. Areas under the receiver operating characteristic curves of the simple clinical colitis activity index, Mayo endoscopic scoring, and Matts' grading (histologic activity) for PEG-MUM were each higher than for C-reactive protein.

The main advantage of PGE-MUM appears to be differentiation of colonoscopic or histologic remission from active disease in ulcerative colitis. On the other hand, this marker of patients with ulcerative colitis in remission was lower compared to healthy volunteers. Compared with the C-reactive protein level, the PGE-MUM level demonstrated better sensitivity for reflecting ulcerative colitis activity, especially in cases of histologic inflammation, and thus seems to be a better evaluator of mucosal healing.

2) The clinical benefit of procalcitonin to assess disease activity and severity in inflammatory bowel disease

Levels of procalcitonin are relevant to immunologic responses that contribute to systemic inflammation responses and septic shock. Procalcitonin demonstrates the activity of chronic inflammatory and autoimmune diseases, such as Wegener's granulomatosis. Herein, we hypothesized that the serum procalcitonin level is helpful for predicting the disease activity of inflammatory bowel diseases: Crohn's disease, ulcerative colitis, or intestinal Behcet's disease. The serum procalcitonin levels were correlated to the activity of Crohn's disease and intestinal Behcet's disease but not ulcerative colitis. These levels were helpful to distinguish cases of Crohn's disease that are severely active to fulminant from cases that are mildly to moderately active and may serve as a new serological marker of disease activity, as does C-reactive protein.

2. The development of treatment with a phototherapeutic effect based on fluorescence molecular imaging

We have developed a method for boosting cancer theranostics utilizing near-infrared light and monoclonal antibody-photoabsorber conjugates, both specific for human epidermal growth factor receptor 2.

3. A genetic factor associated with drug-induced leukopenia in Japanese patients with inflammatory bowel disease

The 94C>A mutation of the inosine triphosphate gene (*ITPA*) and genetic factors have been suggested to be involved in the onset of thiopurine-induced leukopenia in Japanese patients with inflammatory bowel disease.

4. The investigation of efficacy and adherence to an omega-3 diet for remission maintenance in patients with inflammatory bowel disease

The intake of omega-3 polyunsaturated fatty acids and the subsequent associated efficacy for the maintenance of remission may be achieved by understanding the importance of omega-3 diet therapy.

5. Clinical features of patients with early colonic cancer treated with endoscopic submucosal dissection

We evaluated the clinical features of patients with early colonic cancer treated with endoscopic submucosal dissection.

Liver

1. The development of targeting therapy for cancer stem cells in liver cancers

The only curative treatment for patients with primary liver cancers is surgical resection at an early stage. However, cancers are diagnosed in most patients at an advanced stage, by which time extant therapies are ineffective. Therefore, the identification of novel molecules that can become targets for future therapies is urgently needed. We have reported that spalt like transcription factor 4 (*SALL4*) regulates cell fate decision in hepatic stem/progenitor cells during normal liver development, is indicative of aggressiveness and a poor prognosis, and maintains the stemness of cancer stem cells in liver cancers. Further analyses on cancer stem-cell-mediated mechanisms may provide a novel therapeutic strategy against liver cancers.

2. The relationship between lipoprotein profile and cholesteryl ester transfer protein in patients with chronic hepatitis C

The concentration of cholesteryl ester transfer protein was significantly high in patients with chronic hepatitis C, and hepatitis C virus (HCV) infection was extracted as an independent factor. An examination of lipoprotein profiles of patients with HCV infection found that low concentrations of low-density lipoprotein-cholesterol and apolipoprotein C-II are associated with liver fibrosis and that a high concentration of apolipoprotein E is associated with the HCV genotype.

3. Clinical characteristics of autoimmune hepatitis

We evaluated clinical characteristics among 78 patients with autoimmune hepatitis onset before 2006 and 59 patients with onset since 2006. No significant differences were found between the groups.

4. Diseases of the hepatobiliary system in superelderly patients

The mean life expectancy in Japan has dramatically increased. Therefore, the opportunity to examine superelderly patients (80 years or older) who have diseases of the digestive

tract has significantly increased in our hospital. Thus, we have investigated the clinical characteristics and outcomes of superelderly patients with diseases of the digestive tract, including hepatocellular carcinoma, pancreatic cancer, chronic HCV infection, and acute cholecystitis.

5. Investigation of the Frailty Index in elderly patients with diseases of the digestive tract
We evaluated whether simplified Frailty Index scores are associated with clinical outcomes or adverse outcomes after treatment in elderly patients (older than 80 years) with diseases of the digestive tract.

6. The efficacy of tolvaptan in patients with cirrhosis and refractory ascites

Tolvaptan, a novel oral arginine vasopressin V2 receptor antagonist, has been available since September 2013 for treating patients with hepatic edema. We evaluated the therapeutic efficacy and safety of tolvaptan administration in patients with cirrhosis and refractory ascites.

Pancreas

1. The investigation of Wilm's tumor protein 1-pulsed dendritic cell vaccines for patients with advanced pancreatic cancer

Prolonged low plasma levels of interleukin 6 and interleukin 8 in patients with pancreatic ductal adenocarcinoma may be a prognostic marker for the clinical outcome of chemoimmunotherapy.

Publications

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