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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 (UC). Areas under the receiver operating characteristic curves of simple clinical colitis activity index, Mayo endoscopic scoring, and Matts' grading (Histologic Activity) for PEG-MUM were each higher than for CRP.

The main advantage of PGE-MUM appears to be differentiation of colonoscopic or histologic remission from active disease in UC. On the other hand, this maker of UC patients in remission was lower compared to healthy volunteers. By comparison to CRP level, PGE-MUM level demonstrated better sensitivity for reflecting UC activity, especially in cases of histologic inflammation, and thus seems to be a better evaluator of mucosal healing.

According to this result, we have conducted a comparison trial to detect a most reliable marker for detecting endoscopic mucosal healing in UC patients among immunochemical fecal occult blood test, fecal calprotectin, and PGE-MUM.

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

Levels of procalcitonin (PCT) are relevant to immunologic responses that contribute to systemic inflammation responses and septic shock. PCT demonstrated activity of chronic inflammatory and autoimmune diseases like Wegener's granulomatosis. Herein, we hypothesized the serum PCT level might be helpful to predict the disease activity of inflammatory bowel disease (IBD); Crohn's disease (CD), ulcerative colitis (UC) or intestinal Behcet's disease (Int/BD). The Serum PCT levels were correlated to activity of CD, Int/BD, not UC. These levels were helpful to distinguish severe active to fulminant CD from mild to moderate active CD, and may serve as a new serological marker of disease activity as well as CRP.

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

We have developed a method for boosting HER2-specific cancer theranostics utilizing

near-infrared light and HER2-specific monoclonal antibody-photoabsorber conjugates.

3. Nutritional treatment for inflammatory bowel disease

The intake of n-3 PUFA and the subsequent associated efficacy for the maintenance of remission may be achieved by understanding the importance of n-3 diet therapy.

4. A lymph node metastatic risk factor of the esophageal superficial carcinoma

Performing statistical analysis about a lymph node metastatic risk factor of the esophageal superficial carcinoma, a vascular invasion evaluation using the special staining procedure was the strongest risk factor.

Liver

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

The only curative treatments for primary liver cancers are surgical resection for early-stage patients. However, most patients are diagnosed at advanced stages 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 1) SALL4 regulates cell fate decision in hepatic stem/progenitor cells during normal liver development 2) SALL4 is indicative of aggressiveness and 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 future therapeutic strategy against liver cancers.

2. Pathogenesis, mRNA and miRNA expression profiling of primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH)

The pathogenesis is unknown in autoimmune liver disease. To investigate the pathogenesis and identify novel therapeutic targets, we analyzed mRNA and miRNA expression in CD4+ T cells derived from 14 PBC patients using microarray analyses. We found that decreased expression of four miRNAs (miR-425, -181a, -181b, -374b) which dysregulate TCR signaling in PBC-CD4 T+ cells. Especially, the decreased miR-425 expression strongly induced inflammatory cytokines via N-Ras upregulation in the TCR signaling pathway, suggesting that the restoration of decreased miR-425 or the suppression of N-Ras may be a promising immunotherapeutic strategy against PBC.

3. The relationship between nutritional condition and neuropsychological test results in liver cirrhosis patients

Liver cirrhosis (LC) cases complicate minimum hepatic encephalopathy (MHE) and have caused some traffic accidents and communication problems. Neuropsychological disturbance is typical of MHE. However, the diagnostic criteria for MHE have not yet been clarified. We studied the pathophysiological findings of MHE using a neuropsychological test (NPT) and food frequency questionnaire (FFQg). 17% of LC patients were Digit Symbol Test (DST)-abnormal. DST-abnormal was related to Child-Pugh score, serum albumin, Branched chain amino acid & Tyrosine Ratio (BTR), nutrient intake as usual energy intake, and fat energy ratio. Thus, NS using the FFQg may be a useful method to prevent MHE.

4. The investigation of Frailty index in elderly digestive disease patients

We evaluate whether simplified Frailty Scores are associated with clinical outcomes or adverse outcomes after treatments in elderly patients over 80 years old with digestive disease.

Gall bladder and Pancreas

1. The investigation of Wilm's tumor protein 1 (WT1)-pulsed dendritic cell vaccines for the advanced pancreatic cancer patients

Prolonged low levels of plasma IL-6/-8 in pancreatic ductal adenocarcinoma (PDA) patients may be a prognostic marker for the clinical outcomes of chemoimmunotherapy.

2. The trend of disease of the hepatobiliary system in super-aging society

There has been a dramatic increase in the average life expectancy in Japan. Therefore, the opportunities to examine super-elderly patients over 80 years old with digestive disease have significantly increased in our hospital. Thus, we investigate the clinical characteristics and outcomes of super-elderly patients over 80 years old with digestive disease, including hepatocellular carcinoma, pancreatic cancer, chronic hepatitis C and acute cholecystitis.

3. The investigation of the relationship between biliary tract disease and inflammation-based prognostic scores

Inflammation-based prognostic scores have been reported to have prognostic value in patients with various types of cancer. These inflammation-based prognostic scores have also been shown to correlate with outcomes or disease severity in patients with, sepsis, acute heart failure, and Crohn's disease. Therefore, we evaluate whether the inflammation-based prognostic scores are associated with disease severity in patients with acute cholecystitis or acute cholangitis.

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