Research Activities

**Alimentary Tract**

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 score, and Matts’ grade (histologic activity) for PEG-MUM (0.93, 0.90, and 0.89, respectively) were each higher than for C-reactive protein (0.73, 0.77, and 0.75, respectively). Compared with the C-reactive protein level, the PGE-MUM level demonstrated greater sensitivity for reflecting ulcerative colitis activity, especially in cases of histologic inflammation, and thus seems to be a better evaluator of mucosal healing.

2. **Infliximab is effective at preventing restenosis after the endoscopic balloon dilatation therapy in patients with Crohn’s disease**
   The aim of this study was to evaluate the efficacy and safety of infliximab for preventing restenosis after endoscopic balloon dilatation. We performed the endoscopic balloon dilatation therapy for 14 patients with Crohn’s disease. Ten patients had no restenoses when infliximab was administered. Our results suggest that infliximab is useful for preventing restenosis after the endoscopic balloon dilatation therapy in patients with Crohn’s disease.

3. **Development of optical molecular imaging for gastrointestinal cancer and image-guided phototherapy**
   We have developed photoimmunotherapy, a type of molecular target-specific phototherapy that uses monoclonal antibodies conjugated to the near-infrared phthalocyanine dye. We have recently established a molecular target-specific phototherapy that uses imaging-guided and fluorescence molecular imaging methods in a mouse model of human gastric cancer.

4. **Photodynamic surveillance of colitis-associated dysplasia in patients with ulcerative colitis and in mice by visualization following oral 5-aminolevulinic acid sensitization**
   Photodynamic surveillance with autofluorescent endoscopy after 5-aminolevulinic acid sensitization offers the possibility of detecting low-grade dysplasia in ulcerative colitis by
characteristic fluorescent enhancement. Our data, including our results in mice, suggest this procedure with autofluorescent endoscopy following sensitization by administration of 5-aminolevulinic acid is a promising surveillance method for detecting dysplastic lesions which will be useful for detecting precancerous lesion during ulcerative colitis surveillance.

5. Clinicopathological investigation of predictors of lymph-node metastasis in superficial esophageal squamous cell carcinoma with a focus on evaluation of lymphovascular invasion
Statistical analysis of risk factors for lymph-node metastasis of esophageal superficial carcinoma showed that the strongest risk factor was vascular invasion evaluated with a special staining procedure.

Liver
1. Clinical characteristic of primary biliary cirrhosis and autoimmune antibodies
Antimitochondria antibodies, antinuclear antibodies, and anti-gp 210 antibodies were estimated in a case of primary biliary cirrhosis. The pattern of autoimmune antibodies was compared with the clinical course, outcome, and histological findings.
2. Pathogenesis of minimal hepatic encephalopathy
We found that psychometric testing was a useful method for the early diagnosis of minimal hepatic encephalopathy. We are developing a new nutritional support system for patients with liver cirrhosis.
3. Nutritional imbalance of patients with liver cirrhosis
We examined the nutritional status of patients with liver cirrhosis. The nutritional background was analyzed with a food frequency questionnaire based on food groups. We could easily evaluate the relation between nutritional imbalance and morbidity.
4. Nutritional evaluation in nonalcoholic fatty liver disease
The pathogenesis of nonalcoholic fatty liver disease resembles metabolic syndrome. We evaluated nutritional conditions in detail in nonalcoholic fatty liver disease and metabolic syndrome. We have tried the possibility of new nutrition supports system with accuracy.
5. Insulin resistance in the liver is critical for the pathogenesis of nonalcoholic steatohepatitis
We applied the fasting $^{13}$C-glucose breath test as a noninvasive assessment of hepatic insulin resistance in patients with nonalcoholic steatohepatitis and determined the role of hepatic insulin resistance in the pathogenesis of nonalcoholic steatohepatitis. Additionally, we published reports of a case of hepatic tuberculosis presenting as multiple hepatic masses and a case of peripancreatic tuberculous lymphadenitis diagnosed with endoscopic ultrasound-guided fine-needle aspiration.
A useful prognostic factor in cases of hepatocellular carcinoma. The Glasgow Prognostic Score system based on inflammation criteria and including only serum C-reactive protein and albumin shows a correlation with prognosis in cases of hepatocellular carcinoma.
6. Treatment response rate of antiviral analogue nucleic acids in chronic hepatitis B virus injection
Resistant viral mutations are an urgent remedial problem in chronic hepatitis B virus (HBV) infection treated with antiviral analogue nucleic acids. The viral gene sequence
analysis and the treatment response were performed. We consider the possibility of a new concurrent therapy for chronic HBV injection.

7. Long-term adefovir-dipivoxil therapy for active chronic HBV infection may provoke chronic renal failure/osteomalacia

We found that the elevation of the serum concentration of bone-specific alkaline phosphatase preceded the elevation of the serum creatinine level and the development of osteomalacia. Therefore, monitoring of bone-specific alkaline phosphatase is useful for predicting and preventing the development of chronic renal failure/osteomalacia.

8. The clinical background of cases of acute HBV infection

We found that the differences in clinical characteristics depend on the viral genotype. Cases of infection with the genotype A virus were more likely to be severe, to be prolonged, and to be treated with an antiviral nucleic acid analogue.

9. Intrahepatic natural killer T-cell kinetics in a mouse model of autoimmune hepatitis

Natural killer T-cell kinetics is a significant reaction in autoimmune hepatitis. Natural killer T-cells and several cytokine profiles were examined in a mouse model of autoimmune hepatitis. Changes in immunoreactions were analyzed in knock-out models.

10. Treatment for chronic hepatitis C virus infection

Predictive factors for the success of treatment with pegylated interferon + ribavirin for chronic infection with genotype 1b hepatitis C virus (HCV) were an increased cholesterol/triglyceride ratio in very low-density lipoprotein and a high level of apolipoprotein B-100 along with a major genotype of interleukin 28B. Interleukin 28B single nucleotide polymorphism remained an informative predictor of a sustained virological response. For chronic infection with genotype 2 HCV, prolongation of combination therapy with pegylated interferon + ribavirin from 24 weeks to 36 weeks allowed patients who did not achieve a virological response at 4 weeks to achieve it at 8 weeks.

Pancreas

Wilm’s tumor protein 1 (WT1) vaccine in combination with gemcitabine was well tolerated by patients with advanced pancreatic cancer. Delayed-type hypersensitivity-positivity to WT1 peptide and a higher frequency of memory-phenotype WT1-specific cytotoxic T lymphocytes could be useful prognostic markers for survival after combination therapy with gemcitabine and WT1 vaccine.

Publications


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Epub 2013 Nov 29.


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