

Department of Internal Medicine

Division of Gastroenterology and Hepatology

Hisao Tajiri, *Professor*
Mikio Zeniya, *Professor*
Ichiro Takagi, *Professor*
Hirokazu Nishino, *Professor*
Tomohisa Ishikawa, *Associate Professor*
Mika Matsuoka, *Assistant Professor*
Satoshi Suto, *Assistant Professor*

Mario Itsubo, *Professor*
Toshifumi Okusa, *Professor*
Yoshio Aizawa, *Professor*
Shigeo Koido, *Associate Professor*
Atsushi Hokari, *Associate Professor*
Kazuhiko Koike, *Assistant Professor*
Yoshinari Miyagawa, *Assistant Professor*

Research Activities

Alimentary tract

We analyzed the efficacy of polaprezinc enema in the treatment of ulcerative colitis. Endoscopic and clinical findings showed that the addition of polaprezinc enemas produced significant improvement in patients with moderate to severe ulcerative colitis. Significant improvements were detected with endoscopy in the rectum and sigmoid colon, which are the areas exposed to polaprezinc enemas. A polaprezinc enema may become a useful new add-on treatment to accelerate mucosal healing in ulcerative colitis.

In a double-blind placebo-controlled multicenter trial, 2-week triple antibiotic therapy produced improvement, remission, and steroid withdrawal in active ulcerative colitis more effectively than did a placebo.

The efficacy and safety of endoscopic balloon dilatation for the treatment of intestinal strictures were studied. A single-balloon enteroscopy system was used to perform 222 enteroscopic procedures.

The subjects who underwent endoscopic balloon dilation were 12 patients with Crohn's disease and 1 patient with a nonspecific ulcer of the small intestine. The procedures allowed surgery to be avoided in 10 patients (76.9%). Complications developed in only 1 of the 13 patients (7.7%). Endoscopic balloon dilatation appears to be safe and extremely useful, allows surgical resection to be avoided, and maintains patients' quality of life.

Statistical analysis showed that the strongest risk factor for metastasis of superficial carcinoma of the esophagus to the lymph nodes is vascular invasion, as evaluated with a special staining procedure.

Intestinal Behçet's disease is rare. The diagnosis and management of intestinal Behçet's disease is sometimes difficult and controversial. We reported 5 cases, including a case complicated by myelodysplastic syndrome, and discussed therapeutic strategies.

Liver

Clinicopathological study of autoimmune hepatitis: The prediction of resistance to immunosuppressive therapy and of recurrence despite immunosuppressive therapy were weighed against pathological findings of continuance in liver biopsies specimens in cases of autoimmune hepatitis (AIH).

Intrahepatic natural killer T-cell kinetics in AIH model mice: The profiles of natural killer (NK) T-cells and several cytokines were examined in AIH model mice. Changes in immunoreactions were analyzed in knock-out model mice.

Treatment response of antiviral analogue nucleic acids in chronic hepatitis B infection: Analyses of the viral gene sequence and treatment response were performed. We considered the possibility of a new concurrent therapy for chronic hepatitis B.

Nutritional evaluation in nonalcoholic fatty liver disease: The nutritional background in nonalcoholic fatty liver disease may be evaluated by using a food frequency questionnaire based on food groups and indirect calorimetry.

Sleep apnea syndrome and imbalance of hepatic metabolism: Cases of sleep apnea syndrome were complicated by severe hypoxia and liver dysfunction. We analyzed the respiratory quotient with indirect calorimetry.

Study of hepatitis C virus: The initial immune response to the hepatitis C virus (HCV) was studied in transgenic mice. We found that NK cells participate in the elimination of core-expressing hepatocytes in the innate immune response during the acute phase of HCV infection.

In a study with HCV transgenic mice, the HCV core protein stimulated immune response to lymphocytes at liver parenchyma. NK cells participate in the elimination of core-expressing hepatocytes in the innate immune response during the acute phase of HCV infection.

Multiregression analysis revealed that serum levels of apolipoprotein B and amino-acid substitution at position 70 of the HCV core region are independent factors associated with the efficacy of pegylated interferon plus ribavirin therapy for chronic HCV G1b infection. In addition, the usefulness of this response-guided therapy on chronic hepatitis C was verified in our cohort.

Magnetic resonance imaging assessment of hepatocellular carcinoma: The magnetic resonance imaging properties with contrast enhancement were related to prognosis and clinical characteristics.

Examination of the molecular mechanisms of the differentiation of hepatic stem cells: Transcription of the marker factor *Sall4* regulated cell-fate decisions in fetal hepatic stem/progenitor cells. This molecule has the potential for clinical application.

The fasting ¹³C-glucose breath test: The area under the curve until 360 minutes (AUC₃₆₀) of the kinetic curve for ¹³C excretion of the fasting ¹³C-glucose breath test (FGBT) reflects the efficiency of energy production in the liver. The AUC₃₆₀ of healthy subjects was consistently higher than that of patients. FGBT is a novel glucose metabolic test that can be used to conveniently and safely evaluate the balance of glucose metabolism in the liver. The FGBT test has excellent sensitivity for diagnosing alterations in hepatic glucose metabolism.

Latency-associated protein of tumor necrosis factor β degradation products: We have developed a novel quantitative and specific assay of plasma latency-associated proteins (LAPs), which are produced during proteolytic activation of tumor necrosis factor (TNF) β . The LAP degradation products would be novel markers in blood and tissues reflecting fibrogenetic activity but not the amount of accumulated fibrosis in patients, especially those with chronic HCV or AIH, and can be used to estimate the early stage of fibrosis,

when TNF- β activation and hepatic stellate cell activation are more frequent, and to assess the effects of treatment.

Pancreas

Gemcitabine enhances Wilms' tumor gene WT1 expression and sensitizes human pancreatic cancer cells with WT1-specific T-cell-mediated antitumor immune responses.

Fusions of dendritic cells from healthy donors and plasma protein fraction-dependent pancreatic cancer cells were effective for inducing antitumor immunity. However, fusions from patients with metastatic pancreatic cancer induced increased expression levels of TGF- β 1 in CD4⁺ CD25-high T cells and induced low levels of CTLs of cytotoxic T lymphocytes with decreased interferon γ production.

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