

## Department of Surgery

### Division of Digestive Surgery

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### General Summary

Research is an important mandate for academic surgical divisions, and such activities are the mainstays of academic surgeons. However, the increasing demands of clinical practice and administrative duties may reduce the time available for surgical research. As a result, there is growing concern that research activity in the current healthcare climate is becoming increasingly difficult. To compare our research productivity from April 1, 2009, to March 31, 2010, with that of the University of Tokyo and Keio University, we performed an advanced Internet search (Medline). During this period, The Jikei University, the University of Tokyo, and Keio University produced 178, 506, and 597 English papers, respectively. Adding “surgery” to the search as a key word resulted in 72, 19, and 156 publications, respectively. The contribution of surgery to the research activities of The Jikei University appears relatively high, although search results do not mean that the article in the field of surgery came exclusively from the departments of surgery. To maintain this level of research activity, further efforts are necessary.

### Research Activities

#### *Upper gastrointestinal surgery*

We evaluate the pathogenesis of primary esophageal motor functional disorders, especially achalasia and gastroesophageal reflux disease, using manometry and multichannel intraluminal impedance pH-metry, and we perform many laparoscopic operations. For esophageal cancer, we continue to assess the viability of the gastric tube using an intraoperative thermal imaging system. The correlation between suitable construction techniques and postoperative complications of esophageal substitutes was then investigated. In new research, we are trying to clarify the mechanism of deglutition disorders after esophagectomy from the viewpoint of esophageal motility. Basic research in esophageal cancer led us to identify molecular markers indicating patients' prognoses. We aim to investigate the significance of small ubiquitin-like modifier 1 expression as a prognostic factor in esophageal cancer.

For early gastric cancer, we studied the validity of the limited operation using sentinel lymph node surgery by infrared endoscopy. Sentinel lymph node surgery for gastric cancer was approved as an advanced medical technique in June 2009 by the Ministry of Health, Labour and Welfare and its indications have been extended to include remnant gastric cancer and duodenal neoplasms. Studies of postoperative chemotherapy for advanced gastric cancer are continuing as a Stomach Cancer Adjuvant Multi-institutional Trial Group trial, a competitive examination about the effectiveness of TS-1+ lentinan, and a study of the effectiveness of intraperitoneal injection of paclitaxel. In addition, for patients who show a good response to TS-1, we are performing pathological research on gene expression to explore effective individualized treatments. Postgastrectomy syndrome impairs quality of life. We have been performing function-preserving gastrectomy, reconstruction with a substitute stomach, and limited gastric resection to minimize postgastrectomy syndrome. We have also developed multiple postoperative gastrointestinal function tests to evaluate various gastrectomy procedures and to obtain helpful information for diagnosing or treating postgastrectomy syndrome.

#### *Colorectal surgery*

To improve the quality of laparoscopic operations, we are evaluating the usefulness and reliability of the Virtual Reality Surgical Simulator (VRSS) for laparoscopic colectomy. Comparative studies of stress between open and laparoscopic surgery are ongoing. For chemotherapy, we are participating in national multicenter trials to provide new evidence to the world. Moreover, our original regimen is being developed in collaboration with the Division of Oncology/Hematology, Department of Internal Medicine. For the diagnosis of colorectal cancer, a joint project was started with the Department of Radiology, and the usefulness of diffusion magnetic resonance imaging for detection of lymph node metastasis has been reported.

There has been no breakthrough in basic research on various antibodies in relation to cancer. However, we can report the following. 1) The efficacy of indoleamine 2, 3-dioxygenase (the enzyme that leads to cancer immunotolerance) as a useful factor for predicting the recurrence of early colorectal cancer has been reported. 2) We are using enzyme-linked immunosorbent assays to examine the relationship between the reactions of various immunoglobulins in the serum of patients with cancer and several other factors relevant to cancer stage. 3) In joint research with the Department of Urology, we are developing proteomic methods to identify cancer-associated proteins in colorectal, esophageal, gastric, pancreatic, and liver cancers.

Injections of aluminum potassium sulfate and tannic acid have been used to treat anorectal diseases. Functional analysis of anorectal function with stationary 3-dimensional manometry has been introduced for the first time in Japan, and a systemic treatment strategy for anorectal diseases is being developed.

#### *Hepatobiliary and pancreatic surgery*

Our main areas of research are as follows: 1) living donor liver transplantation (LDLT) and regenerative medicine, 2) chemotherapy for pancreatic and biliary cancer, 3) expansion of surgical indications for multiple hepatic tumors, 4) laparoscopic surgery for the

liver, gallbladder, pancreas, and spleen, and 5) navigation surgery for liver surgery. The first LDLT was successfully performed for a patient with postnecrotic cirrhosis and hepatocellular carcinoma on February 9, 2007. Our eighth LDLT was performed for a patient with primary sclerosing cholangitis on October 2, 2009. All 8 recipients were discharged in good condition 15 to 33 days after surgery, and all donors were discharged 9 to 13 days after surgery and have returned to their preoperative status. We are planning to extend the indications of LDLT to include acute hepatic failure and ABO-incompatible cases. Our ongoing research on regenerative medicine, such as artificial bile duct made with cultured human bile duct epithelium, may be extended further for preclinical studies. We have carried out a translational research study of combination chemotherapy with gemcitabine and a new protease inhibitor, FUT-175, which is associated with both nuclear factor  $\kappa$ B inhibition and apoptosis induction in pancreatic cancer cell lines. Other clinical and experimental trials are ongoing after being approved by the Ethics Committee of The Jikei University.

## Publications

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