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General Summary

Research activities in clinical medicine should be measured not by the number of abstracts accepted at scientific meetings and publications in the journals with a low impact factor, but by the number of publications in core clinical journals. Such journals in the field of digestive and general surgery include *Annals of Surgery*, *British Journal of Surgery*, *Journal of the American College of Surgeons*, *JAMA Surgery (*previously *Archives of Surgery)*, *Surgery*, *American Journal of Surgery*, and other subspecialty journals, such as *Transplantation*. In addition to successfully performing a study acceptable for publication in these journals, we must avoid scientific misconduct that could cause confusion in the field of surgical science. According to a recent article in *European Heart Journal*, William T. Summerlin, a transplant immunologist claimed in 1971 that rejection in skin grafts could be avoided, if the material is treated with a form of tissue culture before transplantation. This was a discovery that brought him a position at the Sloan-Kettering Institute in New York as the chief of transplantation immunology. Unfortunately, in New York, he could not replicate his previous experimental results — obviously this can happen, as any scientist knows. In desperation, he colored some of the grafts of his white mice with a black felt-tip pen. This misconduct was immediately discovered, and during the inquiry, doubts also fell on his previous work.
Scientific reports are based on empirical observation, precise wording, consistent statements about facts, and their interaction supported by appropriate statistics. Researchers should be familiar with medical statistics, and all authors should carefully read and approve the manuscripts they are involved with.

Research Activities

Upper gastrointestinal surgery
We began to use high-resolution manometry and multichannel intraluminal impedance

pH monitoring to study the pathogenesis of primary esophageal motor functional disorders, such as achalasia and gastroesophageal reflux disease. We investigated the significance of the expression of small ubiquitin-like modifier (SUMO) 1 as a prognostic factor in esophageal cancer. We found that overexpression of SUMO-1 correlated with malignancy-associated pathological findings and a poor prognosis. We continue to assess the viability of the gastric tube during esophagectomy using an intraoperative thermal imaging system; our findings suggest a correlation between optimal graft construction and postoperative complications. The sentinel lymph node navigation system may play a key role in limited surgery for early gastric cancer.

In 553 patients who underwent laparoscopic gastrectomy, gastric cancer recurred in 5 (0.9%) patients (3 patients with stage I disease, 1 patient with stage II disease, and 1 with stage III disease). Postgastrectomy syndrome comprises specific symptoms after gastrectomy and is a target for treatment. To decrease the incidence and severity of postgastrectomy syndrome and to maximize residual gastric function, several types of limited gastric resection with refined techniques of reconstruction have been attempted. In addition, multiple tests of postoperative gastrointestinal function are applied to patients who have undergone gastrectomy to evaluate various gastrectomy procedures and to inform the patients of the advantages and disadvantages of each procedure.

Lower gastrointestinal surgery

We are using a virtual reality surgical simulator to train surgical residents. We compared surgeons' stress between laparoscopic surgery and open surgery by measuring the serum levels of epinephrine, norepinephrine, dopamine, adrenocorticotropic hormone, and cortisol. We are analyzing the data to determine whether the measurement of such variables might contribute to the training of the next generation of laparoscopic surgeons.

We are preparing a collaborative study with the Department of Urology to use proteomics to identify novel cancer-related proteins in gastrointestinal cancers (including colon, esophageal, gastric, pancreatic, and liver cancers). The aim of this study is to identify tumor markers or possible target proteins via comprehensive protein analysis of biopsy specimens from cancerous tissue and noncancerous mucosa.

The relationships of copy number variation to recurrence and prognosis are evaluated after DNA is extracted from frozen specimens of colorectal cancer tissue, which have been stored in our department. For genes showing copy number variation, the intracellular gene expression varies significantly. This variable expression, therefore, may affect gene functions. In collaboration with the Department of Biochemistry, we have committed to constructing a complementary DNA library from surgical specimens of colorectal cancer to analyze the expression of intraocular signal molecules associated with the progression and growth of colorectal cancers. As a first step of this project, we have started to analyze the cell-cycle regulation and dual-specificity tyrosine-(Y)-phosphorylation-regulated kinase 2 in relation to c-Jun/c-Myc phosphorylation. In addition to these analyses, we will strengthen a platform for our future basic research through a complementary DNA library and a clinical database.

Hepatobiliary and pancreatic surgery

Our main research activities are as follows.

1. Living donor liver transplantation (LDLT) and regenerative medicine
2. Treatment for hepatocellular carcinoma (HCC) and control of recurrence
3. Chemotherapy for pancreatic and biliary cancer
4. Expansion of surgical indications for multiple hepatic tumors
5. Laparoscopic surgery for the liver, biliary tree, pancreas, and spleen
6. Navigation surgery for hepatobiliary and pancreatic diseases
7. Nutritional therapy for cancer patients
8. Control of surgical site infection in surgical patients
9. Effect of preoperative treatment of eltrombopag on splenectomy for idiopathic thrombocytopenic purpura
10. Genome-wide association study for donors and recipients in LDLT
11. Molecularly targeted therapy for advanced HCC
12. Analyses of new biological tumor markers for HCC

The first LDLT was successfully performed for a patient with postnecrotic cirrhosis and HCC on February 9, 2007. Our 13th LDLT was performed for a patient with primary biliary cirrhosis on May 31, 2013. All 13 recipients were discharged in good condition from postoperative days 15 to 55, and all donors were discharged on postoperative days 8 to 26 and have returned to their preoperative status. We are planning to extend the indications for LDLT to ABO blood type-incompatible patients and patients with acute hepatic failure. We have performed translational research for the combination chemotherapy of gemcitabine and a new protease inhibitor, FUT-175, which is associated with both nuclear factor κ-B inhibition and apoptosis induction in pancreatic cancer cell lines. We have started treatment with a new 3-drug combination chemotherapy comprising gemcitabine, TS-1, and FUT-175 for advanced pancreatic cancer. Navigation for liver resection is covered by the national health insurance system as of April 1, 2012, and the Vincent navigation system was introduced in July 2012. Biliary and pancreatic navigation surgery is performed with the Institute for High Dimensional Medical Imaging Research Center. Other clinical and experimental trials are ongoing regarding treatment of hepatic tumors and of laparoscopic surgery, nutritional therapy, surgical site infection, and eltrombopag as a pretreatment for laparoscopic splenectomy in cases of idiopathic thrombocytopenic purpura. Also, we are participating in multicenter studies of genome-wide associations, molecularly targeted therapy for advanced HCC, and new biological tumor markers for HCC.

Publications

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