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# Department of Pathology and Diagnostic Pathology

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**Homepage <http://pathol.umin.ac.jp/>**

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## Introduction and Organization

This department was re-organized in 2003, uniting Department of Human Pathology and Department of Diagnostic Pathology. It is responsible for the practice of diagnostic pathology, education, and research in conjunction with Division of Diagnostic Pathology of the University Hospital. Our aim is the construction of “pathology as clinical medicine” as

well as “next-generation pathology for translational research”.

In 2007, Lecturer Dr. Kashima and Associate Dr. Goto have started their research as a visiting scientist in UK and USA, respectively. New members of Associate were Drs. Ishikawa, Hino, and Morikawa. Dr. Nakaya was taken in as Program Associate of Cancer Profession Training Program, which has started in October.

Three postgraduate students finished the course and received Ph.D. In the new fiscal year, 2008, there are ten postgraduates (including one foreign student).

The research is mainly based on morphology, targeting human diseases. On the other hand, we take charge of General pathology course for the 1<sup>st</sup> grade students in collaboration with Department of Molecular Pathology, and Systematic pathology, Clinical clerkship, and Bedside-learning (BSL) for the 2<sup>nd</sup>–4<sup>th</sup> grade students.

## **Clinical activities (diagnostic pathology and autopsy)**

Together with Division of Diagnostic Pathology, we are responsible for the pathologic diagnosis and autopsy in the University Hospital (see the corresponding section of Division of Diagnostic Pathology).

Clinico-pathological conferences (CPCs) for the two autopsy cases are held every month in the hospital. They serve to the education of clinical residents in addition to the weekly autopsy conferences. Surgical pathology conferences are regularly held with each clinical division, and discusses the cases of various tumors, including thorax, upper gastrointestinal tract, neurosurgery, liver, pancrea-biliary tract, urology, gynecology, breast, and orthopedics, as well as biopsy cases of liver, kidney and skin.

## **Teaching activities**

We take on General Pathology course for the 1<sup>st</sup> grade of undergraduate students, especially in its morphological field. The course program and lecture notes are open to public and available in UT Open Course Ware (<http://ocw.u-tokyo.ac.jp/>) .

Each class of Systematic Pathology course and the exercise is held in parallel with that of Systematic Medical course. Such integrated classes are expected to promote the practical understanding of systemic pathology for students. Handouts are available in every half course of the pathological

exercises. Furthermore, all slides used in the course are now transformed to virtual slides, and are accessible on our website.

Clinical clerkship for the 3<sup>rd</sup> grade, and BSL for the 4<sup>th</sup> grade are carried out. In BSL, following courses are included; autopsy pathologic practices including presentation of each case for paired students, surgical pathologic practice using various tumor sections, and a tour of the pathology laboratory.

The past examinations for the second grade students and for graduation are also referred on the web.

We will start the lecture series of tumor pathology for the Cancer Profession Training Program in postgraduate school, and have written the textbook for them (Bunkodo, 2008).

## **Research activities**

The first major theme is “chronic inflammation and neoplasms”, for which various investigations are developed, including Epstein-Barr virus associated neoplasms (gastric carcinoma), lung carcinoma and scar formation, and carcinogenesis in pulmonary fibrosis.

The second main theme is the search of target molecules for cancer therapy by global analysis of expression profiles of various cancers, in collaboration with Research Center for Advanced Science and Technology, the University of Tokyo.

We hosted the 4<sup>th</sup> Epstein-Barr Virus Conference on June 29, 2007.

## **References**

1. Abe T, Fukushima N, Brune K, Boehm C, Sato N, Matsubayashi H, Canto M, Petersen GM, Hruban RH, Goggins M. Genome-wide allelotypes of familial pancreatic adenocarcinomas and familial and sporadic intraductal papillary mucinous neoplasms. Clin Cancer Res 2007 Oct 15;13(20):6019-25.
2. Fujii K, Ishikawa S, Uchikawa H, Komura D, Shaperro MH, Shen F, Hung J, Arai H, Tanaka Y,

- Sasaki K, Kohno Y, Yamada M, Jones KW, Aburatani H, Miyashita High-density oligonucleotide array with sub-kilobase resolution reveals breakpoint information of submicroscopic deletions in nevoid basal cell carcinoma syndrome. *Hum Genet.* 2007 Dec;122(5):459-66.
3. Fukushima N, Fukayama M. Mucinous cystic neoplasms of the pancreas: pathology and molecular genetics. *J Hepatobiliary Pancreat Surg.* 2007;14(3):238-42.
  4. Fumimura Y, Ikemura M, Saito Y, Sengoku R, Kanemaru K, Sawabe M, Arai T, Ito G, Iwatsubo T, Fukayama M, Mizusawa H, Murayama S. Analysis of the adrenal gland is useful for evaluating pathology of the peripheral autonomic nervous system in lewy body disease. *J Neuropathol Exp Neurol.* 2007 May;66(5):354-62.
  5. Hashimoto T, Kitayama J, Hidemura A, Ishigami H, Kaizaki S, Fukushima N, Miyata T, Nagawa H. Ume (Japanese Apricot)-Induced Small Bowel Obstruction with Chronic Radiation Enteritis. *Case Rep Gastroenterol* 1:184-189, 2007.
  6. Hibi Y, Fukushima N, Tsuchida A, Sofuni A, Itoi T, Moriyasu F, Mukai K, Aoki T. Pancreatic juice cytology and subclassification of intraductal papillary mucinous neoplasms of the pancreas. *Pancreas.* 2007 Mar;34(2):197-204.
  7. Inamura K, Shimoji T, Ninomiya H, Hiramatsu M, Okui M, Satoh Y, Okumura S, Nakagawa K, Noda T, Fukayama M, Ishikawa Y. A metastatic signature in entire lung adenocarcinomas irrespective of morphological heterogeneity. *Hum Pathol.* 2007 May;38(5):702-9.
  8. Ishida K, Mitoma H, Wada Y, Oka T, Shibahara J, Saito Y, Murayama S, Mizusawa H. Selective loss of Purkinje cells in a patient with anti-glutamic acid decarboxylase antibody-associated cerebellar ataxia. *J Neurol Neurosurg Psychiatry.* 2007 Feb;78(2):190-2.
  9. Itoi T, Sofuni A, Fukushima N, Itokawa F, Tsuchiya T, Kurihara T, Moriyasu F, Tsuchida A, Kasuya K. Ribonucleotide reductase subunit M2 mRNA expression in pretreatment biopsies obtained from unresectable pancreatic carcinomas. *J Gastroenterol.* 2007 May;42(5):389-94.
  10. Kaji Y, Oshika T, Takazawa Y, Fukayama M, Takata T, Fujii N. Localization of D-beta-aspartic acid-containing proteins in human eyes. *Invest Ophthalmol Vis Sci.* 2007 Sep;48(9):3923-7.
  11. Kaji Y, Nagai R, Amano S, Takazawa Y, Fukayama M, Oshika T. Advanced glycation end product deposits in climatic droplet keratopathy. *Br J of Ophthal.* 2007 Jan;91(1):85-8.
  12. Kako S, Kanda Y, Sato T, Goyama S, Noda N, Shoda E, Oshima K, Inoue M, Izutsu K, Watanabe T, Motokura T, Chiba S, Fukayama M, Kurokawa M. Early relapse of JAK2 V617F-positive chronic neutrophilic leukemia with central nervous system infiltration after unrelated bone marrow transplantation. *Am J Hematol.* 2007 May;82(5):386-90.
  13. Kunita A, Kashima TG, Morishita Y, Fukayama M, Kato Y, Tsuruo T, Fujita N. The platelet aggregation-inducing factor aggrus/podoplanin promotes pulmonary metastasis. *Am J Pathol.* 2007 Apr;170(4):1337-47.
  14. Maeda D, Fujii A, Yamaguchi K, Tominaga T, Fukayama M, Mori M. Sarcomatoid carcinoma with a predominant basaloid squamous carcinoma component: the first report of an unusual biphasic tumor of the ureter. *Jpn J Clin Oncol.* 2007 Nov;37(11):878-83.
  15. Matsumoto L, Yamamoto T, Higashihara M, Sugimoto I, Kowa H, Shibahara J, Nakamura K, Shimizu J, Ugawa Y, Goto J, Dalmau J, Tsuji S. Severe hypokinesia caused by paraneoplastic anti-Ma2 encephalitis associated with bilateral intratubular germ-cell neoplasm of the testes. *Mov Disord.* 2007 Apr 15;22(5):728-31.
  16. Minaguchi T, Nakagawa S, Takazawa Y, Nei T, Horie K, Fujiwara T, Osuga Y, Yasugi T, Kugu K, Yano T, Yoshikawa H, Taketani Y.

- Combined phospho-Akt and PTEN expressions associated with post-treatment hysterectomy after conservative progestin therapy in complex atypical hyperplasia and stage Ia, G1 denocarcinoma of the endometrium. *Cancer Lett.* 2007 Apr 8;248(1):112-22.
17. Morikawa T, Goto A, Tomita K, Tsurumaki Y, Ota S, Kitamura T, Fukayama M. Recurrent prostatic stromal sarcoma with massive high-grade prostatic intraepithelial neoplasia. *J Clin Pathol.* 2007 Mar;60(3):330-2.
  18. Morikawa T, Sugiyama A, Kume H, Ota S, Kashima T, Tomita K, Kitamura T, Kodama T, Fukayama M, Aburatani H. Identification of Toll-like receptor 3 as a potential therapeutic target in clear cell renal cell carcinoma. *Clin Cancer Res.* 2007 Oct 1;13(19):5703-9.
  19. Moriyama A, Kii I, Sunabori T, Kurihara S, Takayama I, Shimazaki M, Tanabe H, Oginuma M, Fukayama M, Matsuzaki Y, Saga Y, Kudo A. GFP transgenic mice reveal active canonical Wnt signal in neonatal brain and in adult liver and spleen. *Genesis.* 2007 Feb;45(2):90-100.
  20. Murata K, Ota S, Niki T, Goto A, Li CP, Ruriko UM, Ishikawa S, Aburatani H, Kuriyama T, Fukayama M. p63 - Key molecule in the early phase of epithelial abnormality in idiopathic pulmonary fibrosis. *Exp Mol Pathol.* 2007 Dec;83(3):367-76.
  21. Nakajima J, Goto A, Takamoto S, Murakawa T, Fukami T, Kusakabe M. Invasive lymphangioma of the lung manifesting as a large pulmonary mass with hemoptysis: report of a case. *Surg Today.* 2007;37(5):418-22.
  22. Nakajima J, Morota T, Matsumoto J, Takazawa Y, Murakawa T, Fukami T, Yamamoto T, Takamoto S. Pulmonary intimal sarcoma treated by a left pneumonectomy with pulmonary arterioplasty under cardiopulmonary bypass: report of a case. *Surgery Today.* 2007;37(6):496-9.
  23. Nakamura Y, Niki T, Goto A, Morikawa T, Miyazawa K, Nakajima J, Fukayama M. c-Met activation in lung adenocarcinoma tissues: an immunohistochemical analysis. *Cancer Sci.* 2007 Jul;98(7):1006-13.
  24. Nakamura Y, Matsubara D, Goto A, Ota S, Sachiko O, Ishikawa S, Aburatani H, Miyazawa K, Fukayama M, Niki T. Constitutive activation of c-Met is correlated with c-Met overexpression and dependent on cell-matrix adhesion in lung adenocarcinoma cell lines. *Cancer Sci.* 2008 Jan;99(1):14-22.
  25. Nakao K, Watanabe K, Fujishiro Y, Ebihara Y, Asakage T, Goto A, Kawahara N. Olfactory neuroblastoma: long-term clinical outcome at a single institute between 1979 and 2003. *Acta Otolaryngol Suppl.* 2007 Dec;(559):113-7.
  26. Nohara H, Furuya K, Kawahara N, Iijima A, Yako K, Shibahara J, Kirino T. Lymphoplasmacyte-rich meningioma with atypical invasive nature. *Neurol Med Chir (Tokyo).* 2007 Jan;47(1):32-5.
  27. Sano A, Kage H, Sugimoto K, Kitagawa H, Aki N, Goto A, Fukayama M, Nakajima J, Takamoto S, Nagase T, Yatomi Y, Ohishi N, Takai D. A second-generation profiling system for quantitative methylation analysis of multiple gene promoters: application to lung cancer. *Oncogene.* 2007 Oct 4;26(45):6518-25
  28. Sato N, Fukushima N, Hruban RH, Goggins M. CpG island methylation profile of pancreatic intraepithelial neoplasia. *Modern Pathol.* 2008 Mar;21(3):238-44.
  29. Shi C, Fukushima N, Abe T, Bian Y, Hua L, Wendelburg BJ, Yeo CJ, Hruban RH, Goggins MG, Eshleman JR Sensitive and quantitative detection of KRAS2 gene mutations in pancreatic duct juice differentiates patients with pancreatic cancer from chronic pancreatitis, potential for early detection. *Cancer Biol Ther.* 2007 Dec 2;7(3).
  30. Soda M, Choi YL, Enomoto M, Takada S, Yamashita Y, Ishikawa S, Fujiwara S, Watanabe H, Kurashina K, Hatanaka H, Bando M, Ohno S, Ishikawa Y, Aburatani H, Niki T, Sohara Y, Sugiyama Y, Mano H. Identification of the transforming EML4-ALK fusion gene in non-small-cell lung cancer. *Nature.* 2007 Aug2;448(7153):561-6.

31. Suzuki S, Kitazawa T, Ota Y, Okugawa S, Tsukada K, Nukui Y, Hatakeyama S, Yamaguchi D, Matsuse S, Ishii T, Matsubara T, Yamauchi C, Ota S, Yahagi N, Fukayama M, Koike K. Dengue hemorrhagic shock and disseminated candidiasis. Intern Med. 2007;46(13):1043-6.
32. Ushiku T, Chong JM, Uozaki H, Hino R, Chang MS, Sudo M, Rani BR, Sakuma K, Nagai H, Fukayama M. p73 gene promoter methylation in Epstein-Barr virus-associated gastric carcinoma. Int J Cancer. 2007 Jan 1;120(1):60-6.
33. Yamauchi C, Hasebe T, Iwasaki M, Imoto S, Wada N, Fukayama M, Ochiai A. Accurate assessment of lymph vessel tumor emboli in invasive ductal carcinoma of the breast according to tumor areas, and their prognostic significance. Hum Pathol. 2007 Feb;38(2):247-59.
34. Wang T, Niki T, Goto A, Ota S, Morikawa T, Nakamura Y, Ohara E, Ishikawa S, Aburatani H, Nakajima J, Fukayama M. Hypoxia increases the motility of lung adenocarcinoma cell line A549 via activation of the epidermal growth factor receptor pathway. Cancer Sci. 2007 Apr;98(4):506-11.