# ANNUAL PUBLICATIONS

# Department of Oral Pathology

1993.1.-2000.3.

#### I. Staffs and Students (April, 1999)

Professor Minoru Takagi Associate Professor Teruo Kayano Research Associate Ken-ichi Katsube

Kei Sakamoto

Technical Staff Shoko Shiraki

Miwako hamagaki

Hisae Honda

Graduate Student Hiroko Mega

Wang Lihong Yi Hongfang Michiko Tanaka Kazuhide Kato Jiang Wei-wen

Fernanda Pittella Da Silva

Chuai Manli Mai Nishioka Yen-chun Liu Ayataka Ishikawa

Kazuyo Kurose

Research Student Hisae Ichikawa

Hiroshi Adachi Aya Misaki

# II. Educational Outline of Graduate Course

The medical science seeks the scientific method to maintain the human health and to cure the disease and the pathology contributes to understand the origin, the cause, initiation and the process of the disease. The main object of the dentist in clinical work is the caries and the periodontal disease, but it is necessary to understand systematically the origin and the cause of the disease. Pathology gives the essential knowledge both in medicine and the odontology and it is also important both in basic medicine and the clinical medicine.

### Educational goal

### Pathology

We divide this course into the general and the systemic pathology. The general pathology is to understand the general rules and the criteria concerning the morphological changes due to the disease and the teratology in any organ and tissue. Systemic pathology is to understand the disease and the teratology in each organ and tissue (pathology of the lung, liver etc.). The general pathology is emphasized in this subject and some principal diseases are taken out from the systemic pathology and lectured in the general pathology.

### Oral pathology

Oral pathology is lectured after the course of pathology and is focused on the diseases in the oromaxillofacial areas. Observation and investigation of the pathological specimens are also held.

#### Educational course

Pathology and oral pathology are lectured from 3rd trimester in D3 class to 3rd trimester of D4 class. Pathology and oral pathology are lectured continuously. The lecture and observation of pathological specimens are combined in the course. Sometimes the top researchers in this field are invited to do the special lecture. On some occasion, pathological autopsy is demonstrated to the students to understand the practical pathology. Student clinico-pathological conference (CPC) is held in the last trimester of D6 class in

association with oral surgery Department.

### III. Research Subjects

To investigate the mechanism, diagnosis and the prevention of the oral diseases, we perform the research in the themes as followed.

- 1 ) Molecular biology of the mechanism of the oral disease Etiologic study of human papilloma virus in the oral tumor
- 2 ) Analysis of the genes related to the neurogensis
- 3 ) Notch signaling system in the neurogenesis
- Etiologic study of the human papilloma virus in the oral tumors.
  by Minoru TAKAGI

Human papilloma virus (HPV) is considered to be related to the tumorigenesis in cervical area and in oral tumors, the HPV is also highlighted. Immunohistochemistry study, *in situ* hybridization and PCR were performed to detect the HPV in the oral tumors. Some differentiation makers were also investigated because the HPV is related to the differentiation stage of the epithelial cells.

2. Analysis of the genes related to the neurogensis-The roles of the Nau/sTOP, one of the Microtubule associated proteins (MAPs) in neurogenesis

by Ken-Ichi KATSUBE

Nau gene was identified as a related gene to the neuronal differentiation and was turned out to be a STOP like gene, a MAP gene identified in rat nervous system. It had a characteristic sequence in 3' untranslated region and it might be related to its mRNA axonal transport. Its role in axonogenesis was investigated.

### 3. The analysis of the Notch signaling

Kei SAKAMOTO and Ken-IchiKATSUBE

Notch signaling genes regulates various cell differentiation like lateral inhibition. In vertebrate, their equivalents were identified as a consequence of the genetic evolution and multiplication. We investigated to identify these gene and discovered one of the homologues of the Serrate and Fringe genes. Their expression pattern during embryogenesis was specific evoking their particular roles in neurogenesis. We investigated their roles by in ovo electroporation technique and found the interrelationship with other Notch signaling genes.

# IV. Publications (January, 1993-March, 2000)

#### A. Original Articles

- 1 ) Frnzen P., Ichijo H., Miyazono K.: Different signals mediate transforming growth factor 1-induced growth inhibition and extracellular matrix production in prostatic carcinoma cells. Exp.Cell Res. 207: 1-7, 1993.
- 2 ) Franzen P., ten Dijke P., Ichijo H., Yamashita H., Schulz P., Heldin C.-H., Miyazono K.: Cloning of a TGF- type receptor that forms a heteromeric complex with the TGF- type receptor. Cell 75: 681-692, 1993.
- 3 ) Ichijo H., Hellman U., Wernstedt C., Gonez L.J., Claesson-Welsh L., Heldin C-H., Miyazono K.: Molecular cloning and characterization of ficolin, a multimeric protein with fibrinogen-and collagen-like domains. J.Biol.Chem. 268: 14505-14513, 1993.
- 4 ) Ichijo H., Yamashita H., ten Dijke P., Heldin C.-H., Miyazono K.: Characterization of in vivo autophosphorylation activity of activin type receptor. Biochem.Biophys.Res.Commun. 194: 1508-1514, 1993.
- 5 ) Miyazono K., Ichijo H., Heldin C.-H.: Transforming growth factor- : latent forms, binding proteins and receptors. Growth Factors 8: 11-22, 1993.
- 6 ) ten Dijke P., Ichijo H., Franzen P., Schultz P., Saras J., Toyoshima H., Heldin C.-H., Miyazono K.: Activin receptor like kinases; a novel subclass of cell surface receptors with predicted serine/threonine kinase activity. Oncogene 8: 2879-2887, 1993.
- 7 ) Ishii N., Takagi M., Tuchida N.: Analysis of the expression of p53 in oral squamous cell carcinoma. J. Stomatological Society 60:1, 1993 (in Japanese).
- 8 ) Iimura T., Oida S., Ichijo H., Goseki M., Maruoka Y., Takeda K., Sasaki S.: Modulation of responses to TGF- by 1,25 Dihydroxyvitamin D3 in MG-63 osteoblastic cells. Biochem.Biophys.Res.Commun. 204: 918-923, 1994.
- 9 ) Ishisaki A., Oida S., Momose F., Amagasa T., Rikimaru K., Ichijo H., Sasaki S.: Identification and characterization of an autocrine motility factor-like activity in oral squamous cell carcinoma cells. Int.J.Cancer 59: 783-788, 1994.

- 10 ) Miyazono K., ten Dijke P., Ichijo H., Heldin C.-H.: Receptors for transforming growth factor—superfamily. Advances in Immunology 55: 181-220, 1994.
- 11) Taketazu F., Kato M., Gobl A., Itoh J., Ichijo H., ten Dijke P., Itoh J., Kyougoku M., Ronnelid J., Miyazono K., Heldin C.-H., Funa K.: Distribution of TGF- and TGF- type receptor in the synovial tissues of patients with rheumatoid arthritis. Lab.Invest. 70: 620-630, 1994.
- 12) Takeda K., Oida S., Ichijo H., Iimura T., Maruoka Y., Amagasa T., Sasaki S.: Molecular cloning of rat bone morphogenetic protein(BMP) type A receptor and its expression during ectopic bone formation induced by BMP. Biophys.Res.Commun. 204: 203-209, 1994.
- 13) ten Dijke P., Yamashita H., Ichijo H., Franze P., Laiho M., Miyazono K., Heldin C.-H.: Characterization of type receptors for TGF- and activin. Science 264: 101-104, 1994.
- 14) ten Dijke P., Yamashita H., Sampath K., Reddi H., Riddle D., Ichijo H., Heldin C.-H., Miyazono K.: Identification of type receptors for osteogenic protein01 and bone morphogenetic protein-4. J.Biol.Chem. 269: 16985-16988, 1994.
- 15) ten Dijke P., Franzen P., Yamashita H., Ichijo H., Heldin C.-H., Miyazono K.: Serine/threonine kinase receptors. Progress in Growth Factor Research 5: 55-72, 1994.
- 16) Yamamoto N., Nomura K., Kayano T., Kitagawa T.: Carcinogen daily dose-dependence of the biological features and development rate of hepatocellular carcinomas induced by 3'-methylaminoazobenzen in rat. Cancer Letters 83: 59-68, 1994.
- 17) Yamashita H., Ichijo H., ten Dijke P., Grimsby S., Moren A., Miyazono K.: Endoglin forms a heteromeric complex with the signaling receptors for transforming growth factor- . J.Biol.Chem. 269: 1995-2001, 1994.
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- 19) Li T., Takikawa K., Yoshizawa K., Sakatsume M., Aoki H.: Reaction of Hydroxyapatite-sol in bone marrow. Bio-Medical Materials and Engineering 5(2): 83-92, 1995.
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- 21) Saitoh M., Nishitoh H., Amagasa K., Miyazono M., Takagi M., Ichijo H.: Identification of important regions in the cytoplasmic juxamembrane domain of type receptor that separate signaling pathways of transforming growth factor- . J.Biol.Chem. 271: 2769-2775, 1996.
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- 23) Miyamoto I.: Characterization of cementic lesion of jaw bone. J. Stomatological Society 63(2): 354-374, 1996 (in Japanese).
- 24) Flores M.G.: Immunohistochemical study of type , , collagen in salivary pleomorphic adenoma. J. Stomatological Society 63(1): 122-130, 1996 (in Japanese).
- 25) Chen K.: Study of agranulocytosis induced by Vesnarinone. J. Stomatological Society 63(1): 8-17, 1996.
- 26) Sakamoto K., Yan L., Takagi M., Nabeshima Y., Takeda S., Katsube K.: Identification of a chick homologue of Fringe and C-Fringe 1: Involvement in the neurogenesis and the somitogenesis. Biochem.Biophys.Res.Commun. 234: 754-759, 1997.
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- 29) Sakamoto, K., Nakamura, H., Takagi, M., Takeda, S., Katsube, K.: Epitopic expression of lunatic Fringe leads to downregulation of Serrate-1 in the developing chick neural tube; analysis using in ovo electroporation transfection technique. FEBS Letters. 426: 337-341, 1998.
- 30) Li, T., Takagi, M.: Tissue reaction of hydroxyapatite sol to rat molar pulp. J. Materials Science: Materials in Medicine 9: 1-12, 1998.
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- 34) Chen Y., Shiraki S., Takagi M.: Synovial cyst of the temporomandibular joint: report of a case. Oral Med. & Pathol. 3: 97-99, 1998.

- 35) Terai M., Sata T., Natsukura T., Takagi M.: Human papillomavirus (HPV) in papilloma, leukoplakia, squamous cell carcinoma of the oral cavity. Oral Med. & Pathol. 4: 18-23, 1999.
- 36) Chen Y., Kayano T., Takagi M.: Dysregulated expression of bcl-2 and bax in oral carcinomas: evidence of post-transcriptional control. J. Oral Pathol. Med. 29: 63-9, 1999.
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- 41) Hirata Y., Iwaki H., Amagasa T., Wadamori T., Uzawa N., Isobe M., Nagaoka S., Yamada T., Sakamoto K., Takagi M.: Clinical and pathological studies of cemento-ossifying fibroma. Jpn. J. Oral Maxillofac. Surg. 45(12): 823-825, 1999 (in Japanese).
- 42) Yin H., Okada N., Takagi M.: Comparison study of clinicopathological features of extranodal oral non-Hodgkin's lymphoma (NH) and Maxillofacial Nodal NHL. Oral Med. & Pathol. 4:55-62, 2000.
- 43) Yin H., Okada N., Takagi M.: Prognostic evaluation of apoptosis and tumor growth factors in mucoepidermoid carcinoma of the oral minor salivary glands. Pathol. Int. 50: 603-609, 2000.
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#### B. Books

- 1) Takagi M.: Color Atlas of Histopathology and Differential Diagnosis. Ishiyakusyuppan Tokyo, p.109-134, 1994 (in Japanese).
- 2 ) Takagi M.: Melanoma. Bunkoudou, Tokyo, p.156-167, 1994 (in Japanese).
- 3 ) Takagi M.: Surgical Pathology. Bunkoudou, Tokyo, p.81-127, 1994 (in Japanese).
- 4 ) Takagi M.: Atlas of Cancer Histopathology, Nankoudou, Tokyo, 1995 (in Japanese).
- 5 ) Kayano T.: Atlas of Cancer Histopathology, Nankoudou, Tokyo, 1995 (in Japanese).
- 6 ) Takagi M.: Atlas of tumor Pathology-Borderline Cases and Differential Diagnosis-. Ishiyaku Pub. Tokyo, p.45-59, 1997 (in Japanese).
- 7) Takagi M.: Handy Pathology & Oral Pathology. Gakkensyoin, Tokyo, p.77-92, 190-195,233-248, 1997 (in Japanese).

# C. Review Articles

- 1 ) Miyazono K., Ichijo H., Yamashita H.: Knock out of TGF- superfamily genes and their receptor system. Jikkenigaku, 11, p.74-77, 1993 (in Japanese).
- 2 ) Ichijo H., Miyazono K.: Structure and mechanism of TGF- receptor system. Jikkenigaku, 12, p.27-34, 1994 (in Japanese).
- 3 ) Ichijo H.: Prevention of atherosclerosis: TGF- . Mebio, 11, 1994 (in Japanese).
- 4 ) Nishitou H., Ichijo H.: TGF- family receptors. BIO Clinica, 9, p.57-60, 1994 (in Japanese).
- 5 ) Ichijo H., Takagi M.:TGF- superfamily and oral diseases. Kokubyogakkaishi 62(1), 152, 1995 (in Japanese).
- 6 ) Takagi M., Nikai H., Shimono M.: Pathology in Dentistry. Shikaitennbou: Dental Olympia 95, 1996 (in Japanese).