Department of Laboratory Medicine

Tomokazu Matsuura, *Professor*
Hiroshi Yoshida, *Professor*
Kenichi Sugimoto, *Professor*
Yoji Ogasawara, *Associate Professor*
Yoshihiro Mezaki, *Assistant Professor*
Midori Kouno, *Assistant Professor*
Ken Kaito, *Professor*
Hironari Sue, *Professor*
Kouji Nakada, *Professor*
Takahiro Masaki, *Assistant Professor*
Sae Ochi, *Assistant Professor*
Setuko Akizuki, *Assistant Professor*

General Summary

We performed a wide range of research in clinical laboratory medicine, including practical studies of infectious disease tests, biochemical tests, blood tests, physiological function tests, and clinicopathological tests. In addition, future subjects of our department will be of the development of collection methods of clinical information, medical safety measures, the new development of brain function tests, application to clinical tests of mass spectrometry, and functional tests using stable isotope ^{13}C-labeled compounds.

Research Activities

Clinical microbiology

We participated in medical education programs to provide basic clinical skills training for medical students. In addition, we were appointed to be examiners of objective structured clinical examinations for students in years 4 and 6. Basic and clinical research on viral hepatitis and liver fibrosis was conducted, and our manuscript about transforming growth factor β and liver fibrosis was published in the journal *Heliyon*. We also investigated the effects of metoformin, a widely used pharmacotherapeutic agent for type 2 diabetes, on intestinal microflora in mice. We attempted to perform the chromatographic analysis of volatile organic compound patterns in exhaled breath from patients with inflammatory diseases.

Clinical chemistry

We studied gastric emptying and fat digestive and absorptive function after various types of gastrectomy by ^{13}C-breath tests. Function-preserving gastrectomy attenuated rapid gastric emptying, which is usually seen after conventional gastrectomy. This attenuation might, in part, explain the mechanism of ameliorating postgastrectomy syndromes, such as diarrhea and dumping.

Professor Yoshida and others demonstrated that the diet therapy of the weight-loss program decreased chylomicron cholesterol and decreased cholesterol/alpha tocopherol of lipoprotein(a) (unpublished data). In the meantime, we have reported that angiotensin II can enhance matrix metalloproteinase 2, mainly through angiotensin II receptor type 2, in endothelial cells (J Cardiovasc Pharmacology 2018; 71: 233-9).

Safety management in clinical laboratories

Because accidents occurring in a laboratory sometimes have harmful results, software and hardware must be improved and safety measures, based on an understanding of human thought, must be ensured. We analyzed situation monitoring, situation awareness, and action to complete the safer work. When accidents occurred in our department, they were due to inadequate observation and confirmation, 80%; communication errors, 11%; and poor procedures, 9%. Most of the accidents were derived from heuristics brought by quick thought after recognition of the target. To avoid the judgment by heuristics, basic confirmation practices should be customarily performed.

Clinical hematology

We are studying the pathophysiology of bone marrow failure syndrome. To assess the optimal treatment for acquired aplastic anemia we analyzed the clinical and laboratory data of patients with aplastic anemia who received immunosuppressive therapy at our hospital.

Clinical psychiatry

We discussed a patient with nonconvulsive status epilepticus and psychic problems. We have conducted a study of epilepsy in adult patients taking Resilience into consideration and a study of the reconsideration of rational antiepileptic drug polypharmacy. We held the 12th Kanto-Koushinetsu regional epilepsy meeting in June. We are planning to establish the Epilepsy Center of The Jikei University Hospital.

Clinical physiology

Research was conducted on the accuracy of automatic electrocardiogram analysis for diagnosing arrhythmia. In the clinical area, we continued research related to catheter ablation of atrial fibrillation and reported the results in several journals.

Clinical pathology and clinical cell biology

Vitamin A is needed for many physiological functions, including vision, reproduction, embryonic development, and maintenance of epithelia. We have analyzed cellular retinol-binding protein I and lecithin:retinol acyltransferase in polar bear liver, which contained a large amount of vitamin A, and found a strong co-localization of these 2 proteins.

Publications

Katagiri S, Hosono K, Hayashi T, Kurata K, Mizobuchi K, Matsuura T, Yoshitake K, Iwata T, Nakano T, Hotta Y. Early onset flecked retinal dystrophy associated with new compound heterozygous RPE65 variants. *Mol Vis.* 2018; **24:** 286-96. eCollection 2018.

Uchiyama K, Aiki H, Matsumura A, Saruta K, Yuasa A, Ito Z, Takami S, Saito K, Ohtaki Y, Suzuki S, Hayashi S, Koido S, Yoshida H, Ohkusa T, Saruta M. The efficacy of the consumption of n-3 polyunsaturated fatty acids for the maintenance of remission in patients with inflammatory bowel disease. *Food Nutri Sci.* 2018; **9:** 105-18.

Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S, Umemoto S, Egusa G, Ohmura H, Okamura T, Kihara S, Koba S, Saito I, Shoji T, Daida H, Tsukamoto K, Deguchi J, Dohi S, Dobashi K, Hamaguchi H, Hara M, Hiro T, Biro S, Fujioka Y, Maruyama C, Miyamoto Y, Murakami Y, Yokode M, Yoshida H, Rakugi H, Wakatsuki A, Yamashita S; Committee for

Epidemiology and Clinical Management of Atherosclerosis. Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017. *J Atheroscler Thromb.* 2018; **25:** 846-984.

Kinami S, Takahashi M, Urushihara T, Ikeda M, Yoshida M, Uenosono Y, Oshio A, Suzukamo Y, Terashima M, Kodera Y, Nakada K. Background factors influencing postgastrectomy syndromes after various types of gastrectomy. *World J Clin Cases.* 2018; **26:** 1011-120.

Narui R, Yamane T, Tokuda M, Ikewaki H, Okajima E, Sato H, Oseto H, Isogai R, Tokutake K, Yokoyama K, Kato M, Ito K, Tanigawa SI, Yamashita S, Inada K, Matsuo S, Miyanaga S, Sugimoto K, Yoshimura M. Atrial fibrillation diagnosed by a medical checkup is associated with a poor outcome of catheter ablation. *Heart Vessels.* 2018; **33:** 770-6.

Mezaki Y, Nagatsuma K, Yokoyama H, Park JH, Nakamura M, Masaki T, Blomhoff R[1], Senoo H[2], Matsuura T ([1]Oslo Univ, [2]Akita Univ). Biochemical and histochemical analyses of lecithin: retinol acyltransferase from polar bear (Ursus maritimus) livers. *Polar Biol.* 2018; **41:** 805-15.

Sato R, Hiraishi C, Yoshida H. Effect of angiotensin II on matrix metalloproteinase-2 secretion in human umbilical vein endothelial cells. *J Cardiovasc Pharmacology.* 2018; **71:** 233-9.

Suzuki K, Kobayashi N, Ogasawara Y, Shimada T, Yahagi Y, Sugiyama K, Takahara S, Saito T, Minami J, Yokoyama H, Kamiyama Y, Katsube A, Kondo K, Yanagisawa H, Aiba K, Yano S. Clinical significance of cancer-related fatigue in myeloma patients. *Int J Hematol.* 2018; **108:** 580-7.

Murayama A, Fujiwara K, Yamada N, Shiina M, Aly HH, Masaki T, Muramatsu H, Wakita T, Kato T. Evaluation of antiviral effects of novel NS5A inhibitors in hepatitis C virus cell culture system with full-genome infectious clones. *Antiviral Res.* 2018; **158:** 161-70.

Qin XY, Suzuki H, Honda M, Okada H, Kaneko S, Inoue I, Ebisui E, Hashimoto K, Carninci P, Kanki K, Tatsukawa H, Ishibashi N, Masaki T, Matsuura T, Kagechika H, Toriguchi K, Hatano E, Shirakami Y, Shiota G, Shimizu M, Moriwaki H, Kojima S. Prevention of hepatocellular carcinoma by targeting MYCN-positive liver cancer stem cells with acyclic retinoid. *Proc Natl Acad Sci U S A.* 2018; **115:** 4969-74.

Yokoyama H, Masaki T , Inoue I, Nakamura M, Mezaki Y, Saeki C, Oikawa T, Saruta M, Takahashi H, Ikegami M, Hano H, Ikejima K, Kojima S, Matsuura T. Histological and biochemical evaluation of transforming growth factor-β activation and its clinical significance in patients with chronic liver disease. *Heliyon.* 2019; **5:** e01231.

Nomoto H, Maehashi H, Shirai M, Nakamura M, Masaki T, Mezaki Y, Park J, Aizawa M, Ohkawa K, Yoshida K, Matsuura T. Bio-artificial bone formation model with a radial-flow bioreactor for implant therapy-comparison between two cell culture carriers: porous hydroxyapatite and β-tricalcium phosphate beads. *Hum Cell.* 2019; **32:** 1-11.

Ishikawa T, Yokoyama H, Matsuura T, Fujiwara Y. Fc gamma RIIb expression levels in human liver sinusoidal endothelial cells during progression of non-alcoholic fatty liver disease. *PLoS One.* 2019; **14:** e0211543.

Reviews and Books

Yoshida H. An Intriguing and Important Concept Relevant to Oxidized Low-Density Lipoprotein and Atherogenesis is Still Problematic for its Contribution to the Better Understanding of Clinical Atherosclerosis. *J Atheroscler Thromb.* 2018; **25:** 1007-8.

Yanai H, Yoshida H. Beneficial Effects of Adiponectin on Glucose and Lipid Metabolism and Atherosclerotic Progression: Mechanisms and Perspectives. *Int J Mol Sci.* 2019; **20**. pii: E1190.