

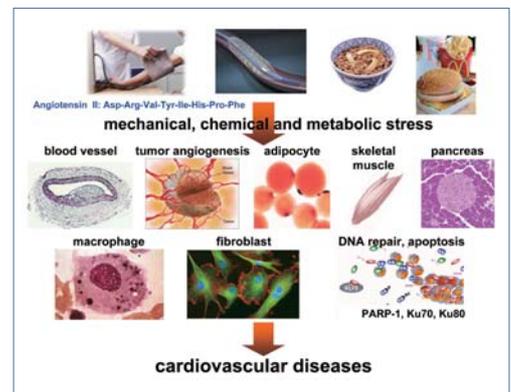
Internal Medicine

Cardiovascular Medicine

<http://plaza.umin.ac.jp/~utok-card/>

We are investigating the pathogenesis, pathophysiology, diagnostic methods, and novel therapeutic measures of various cardiovascular diseases (ischemic heart disease, heart failure, cardiomyopathy, arrhythmias, atherosclerosis, hypertension, etc.) using a variety of research tools (from molecular biology to epidemiology, bioinformatics).

- Transcriptional regulation of various genes in cardiovascular development and pathogenesis
- Cardiac hypertrophy and heart failure: analyses of pathogenic mechanisms and developments of novel therapies (gene therapy, etc.)
- Immunological basis of cardiovascular diseases
- Imaging techniques (echocardiography, MRI, CT, RI, NOGA) in cardiovascular diseases
- Mechanisms of anti-arrhythmia therapy
- Molecular mechanisms of ischemia-reperfusion injury
- Genetic polymorphisms and risk factors in cardiovascular disease
- Differentiation of smooth muscle cells (atherosclerosis and restenosis after vascular interventions)
- Mouse genetic models of cardiovascular diseases and vascular development
- Neurohumoral factors in cardiovascular diseases

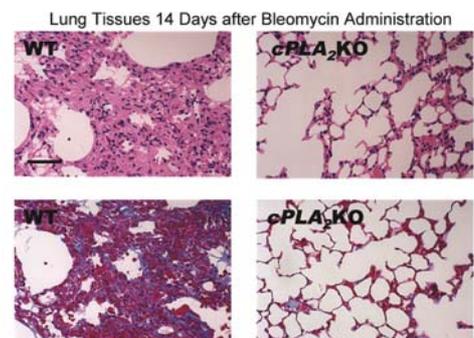


Respiratory Medicine

<http://kokyuki.umin.jp/>

Based on the fact that a number of patients with respiratory diseases including lung cancer and COPD is tremendously increasing, fruitful results of respiratory research are more and more expected in the 21st century. In this era, we are conducting basic and clinical researches for wide variety of respiratory disorders including lung cancer, asthma and COPD. Especially, we have been intensively studying the molecular mechanisms underlying the pathogenesis of lung disorders. Our research goal is to develop novel therapeutic tools to manage these pulmonary diseases.

- Clinical studies of lung cancer, COPD, bronchial asthma and pulmonary fibrosis
- Epidemiological studies of diffuse panbronchiolitis (DPB) and interstitial lung disease
- Molecular mechanisms underlying the pathogenesis of acute lung injury or ARDS
- Molecular mechanisms underlying the pathogenesis of pulmonary fibrosis (as shown in Figure)
- Analysis of disease models using genetically-engineered mice
- Effects of air pollutants such as diesel exhausts on airway hyperresponsiveness
- Roles of chemokines/cytokines and eicosanoids on airway epithelial cells, smooth muscle cells and eosinophils.
- DNA methylation and lung cancer
- Establishment of conditional vectors for hairpin siRNA knockdowns
- Establishment of CpG island searcher



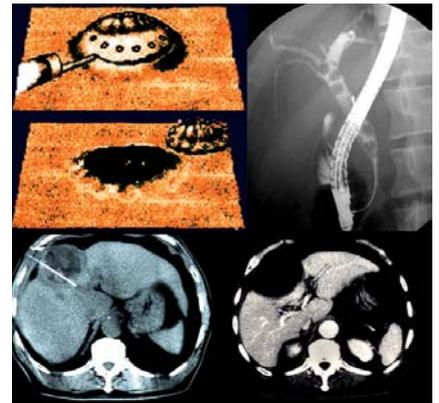
Murine model of pulmonary fibrosis

Gastroenterology

<http://www.h.u-tokyo.ac.jp/gastro/>

Our Department of Gastroenterology is one of the top institutions in the world in the treatment of hepatocellular carcinoma by unique ablation(RFA) and gastrointestinal/pancreatobiliary cancer/stone by endoscopic manipulation(ESD&ERCP). The goal of our department is to accurately diagnose and give the best available treatment to these patients, and to this end, we are performing a wide variety of basic as well as clinical research.

- Development of better therapeutic strategy for hepatitis B and C
- Elucidation of hepatocarcinogenesis mechanism in viral hepatitis
- Development of a better therapeutic modality for hepatocellular carcinoma & metastatic liver tumor
- Elucidation of gastric injury mechanisms by *Helicobacter pylori*
- Clarification of colon disease, especially right-sided colon carcinogenesis
- Development of therapeutic strategy for advanced pancreatobiliary cancer
- Development of a better endoscopic therapeutic modality for pancreatobiliary cancer/stone
- Development of better diagnostic & therapeutic strategy for chronic pancreatitis
- Development of an endoscopic *en bloc* resection method for early gastric, esophageal and colonic cancer
- Elucidation of the mechanisms of metabolism-associated liver diseases
- Development of better diagnostic & therapeutic strategy for small intestinal diseases

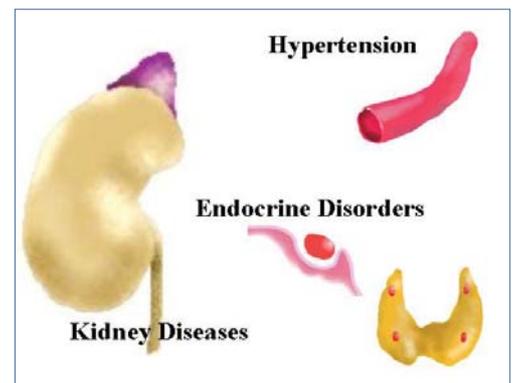


Nephrology / Endocrinology

<http://plaza.umin.ac.jp/~kid-endo/top.html>

We are investigating the pathophysiology of renal and endocrine disorders for the development of innovative diagnostic and therapeutic tools. Hypertension is our special interest because not only it is a serious medical problem which impairs many vital organs and the QOL of our patients, but also we have the great advantage of organizing the strategic research approach since hypertension is closely related to both nephrology and endocrinology.

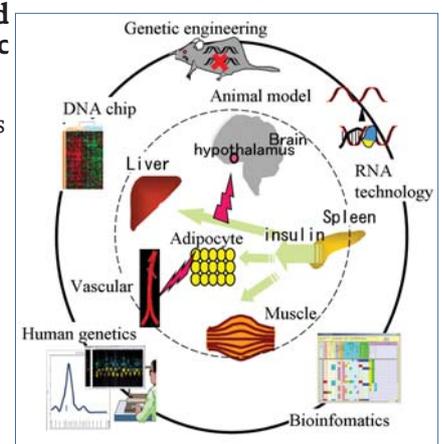
- Renal physiology and morphology
- Pathophysiology of immune-mediated renal injury
- Analysis of pathophysiology and prognostic factors of chronic renal failure
- Endothelial injury and vascular biology in kidney disease
- Role of nitric oxide and oxidative stress in renal disease and hypertension
- Clinical and basic investigation of bone and mineral disorders
- Mechanism of action of nuclear hormone receptors
- Pathophysiology of hypertension and roles of adrenomedullin
- G protein signaling in health and disease



Nutrition and Metabolism

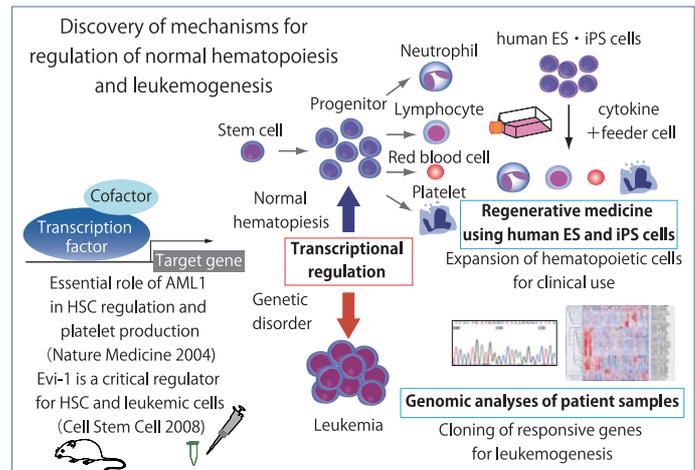
We are investigating to reveal the molecular mechanisms underlying the development of metabolic diseases (diabetes mellitus, lipid metabolic disorders, obesity, metabolic syndrome and atherosclerosis) using interdisciplinary approaches and state-of-the-art technology including genetically engineered model animals, DNA chip, epigenetics, RNA technology, human genetics, clinical epidemiology and bioinformatics. Our major goal is to develop mechanism-based fundamental treatment and prevention strategies for the metabolic diseases.

- Molecular mechanism of insulin resistance linked to obesity focusing on adipokines
- Transcriptional regulation of insulin resistance and obesity by nuclear receptors and cofactors
- Molecular mechanism of insulin signal transduction
- Molecular mechanism of insulin secretory defect in type 2 diabetes
- Genetic susceptibility and risk factors of type 2 diabetes
- Development of accurate diagnostic algorithm for type 2 diabetes
- Molecular mechanism of adipogenesis and obesity
- Transcriptional regulation of lipid metabolism
- Molecular mechanism of atherosclerosis
- Mouse genetic models of diabetes, lipid metabolism disorder and atherosclerosis



We are investigating the pathogenesis, diagnostic methods, and novel therapeutics of hematological disorders by making comprehensive use of research technologies in molecular biology, developmental biology, and immunology. Studies about transcriptional regulation and signal transduction in hematopoiesis and analyses of regulation of hematopoietic stem cells are performed. We are also performing basic and clinical studies based on genomics, regenerative medicine, and transplantation medicine, which aim at application to therapeutic strategies.

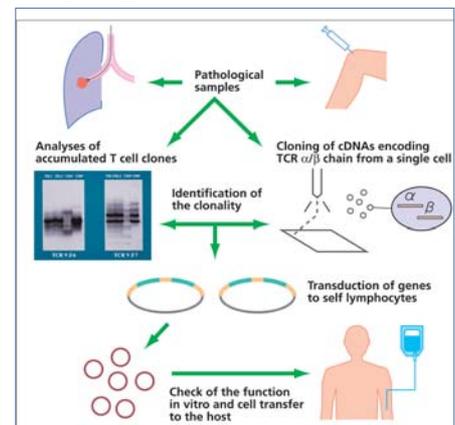
- Self renewal and differentiation of hematopoietic stem cells
- Genome-wide analyses of hematological malignancies
- Identification of molecular pathogenesis of leukemia
- Analyses of the immune system by developmental biology
- Regenerative medicine of hematopoietic cells using human ES and iPS cells



Allergy and Rheumatology

Allergy and rheumatic diseases are immune mediated disorders. We are investigating the fine mechanisms of such disorders. One of our final purposes is to establish novel therapies which control pathological immune disorders but do not suppress other physiologically important immune functions. We are combining recent findings in basic immunology and our own viewpoints base on our clinical experience.

- Clonal analyses of T cell receptor (TCR) , *in vitro* reconstitution of the TCR function using such information and antigen specific immunotherapy
- Mechanisms of oral tolerance and application to therapeutic strategies
- Mechanism of immunological tolerance to autoantigens and immunoregulation
- Development and induction of regulatory T cells and their applications
- Intracellular signaling in immune disorders
- Genomic analyses of rheumatic diseases
- Development of molecular targeting immunosuppressive reagents
- Airway hypersensitivity and remodeling of bronchial asthma
- Mechanisms of IgE mediated allergic disorders and applications for therapies
- Involvement of chemokines in allergic diseases and applications to therapeutic strategies

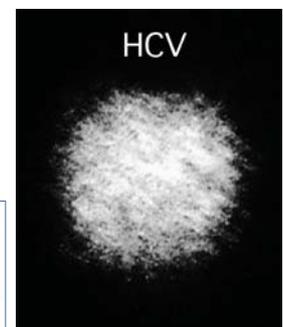
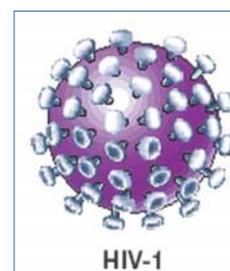


Clonal analyses of T cell receptor (TCR) and *in vitro* reconstitution of the TCR function for an antigen specific immunotherapy

Infectious Diseases

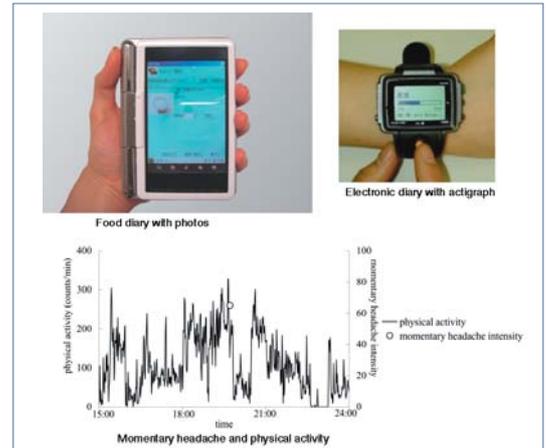
We are investigating both clinical and basic aspects in infectious diseases, in particular, on HIV infection and hepatitis viral infections, the latter of which is the major cause of liver disease worldwide. Our research topics cover the wide areas in microbiology, immunology and pathobiology of infectious diseases, including HIV and HCV infections.

- Clinical studies of HIV infection
- Development of new methods in infection control and treatment of viral hepatitis
- Molecular pathogenesis of hepatocellular carcinoma in HCV infection
- Pathogenesis of extrahepatic manifestations and its control in HCV infection
- Pathogenesis of progression of HIV infection
- Molecular pathogenesis of the mitochondrial disturbances in viral infections
- Molecular pathogenesis of hepatitis B viral infection
- Host defences to microorganisms
- Molecular analysis of innate immunity in microorganism infection
- New detection method and pathogenesis of opportunistic cytomegaloviral infection
- Mechanism of multi-drug resistant microorganisms



The targets of our laboratory include stress-related diseases such as primary headaches and lifestyle-related diseases, eating disorders and malignancies. The goals of our work are to determine the mechanisms of these conditions, to develop objective markers for diagnosis and severity, and to discover new treatment approaches using ecological momentary assessment (EMA), biochemical assessment of eating-related molecules, and physiological assessment of autonomic nervous function.

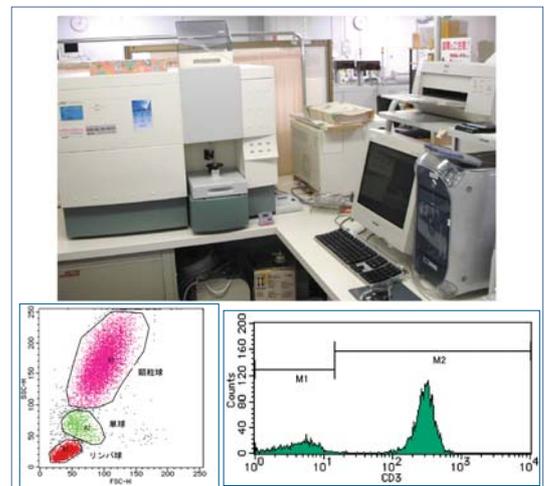
- We are using ecological momentary assessment (EMA) techniques to collect and evaluate subjective and objective data including physical activity and autonomic nervous function in natural settings in stress-related diseases. We are also developing new treatments using these methods.
- Investigation into the pathophysiology, psychopathology and neurobehavioral basis of stress-related diseases by use of ecological momentary assessment methods
- Using heart rate and blood pressure variability, we are investigating autonomic nervous function in eating disorders. This work uses non-linear analyses such as fractal analysis, as well as linear analysis.
- We have developed an egogram questionnaire, which we refer to as the TEG.



Clinical Laboratory Medicine

The main goal of our research projects, described below, is the development of new and useful laboratory tests, and elucidation of pathophysiology of diseases through laboratory tests.

- Elucidation of (patho)physiological roles of lysophospholipid mediators, and its application to laboratory medicine
- Platelet biology, Hepatology
- Genetic testing
- Research on bioactive peptides, especially adrenomedullin
- Oxidative stress and organ damage
- Cell surface analysis and quantification of cell surface antigens using flow cytometry
- Analysis of the ventricle functions using ultrasound
- Relationship between the respiratory function and various pathophysiological conditions
- Magnetoencephalographic (MEG) study on neural mechanisms for audiovisual integration



Flow cytometer and analysis patterns

Transfusion Medicine

Control, testing and supply of all blood products for transfusion are the main clinical activities of the department of transfusion medicine, which is responsible for the provision of safe blood products and the control of the transfusion practice in the hospital. It actively takes part in autologous blood collection, preservation, and supply for patients receiving routine surgery. In addition, apheresis procedures for collection of peripheral blood stem cells for transplantation, and of peripheral blood mononuclear cells for dendritic cell-based vaccine therapy of cancer patients are performed. Also, lymphocyte-based vaccine is prepared for the immunotherapy of recurrent abortion cases. Special laboratory testings, including HLA typing (serologic and DNA-based) for bone marrow and organ transplantations and the detection of anti-HLA, anti-platelet (HPA) and anti-granulocyte antibodies, as well as the phenotyping and genotyping of platelet- and granulocyte-specific antigens for patients with adverse reactions after transfusion, are performed. The research fields include 1) the development of immunological methods for antigen-antibody testing of red cells, lymphocytes, granulocytes, platelets and endothelial cells, 2) the development and clinical application of dendritic cell-based and other vaccines for immunotherapy of cancer, and 3) the development of new anti-thrombotic materials for clinical use.

- Detection of platelet alloantigens and alloantibodies / • Detection of leukocyte alloantigens and alloantibodies
- Detection of anti-endothelial cell antibodies and investigation on their clinical relevance
- Development of a novel method for the evaluation of platelet function
- Dendritic cell-based immunotherapy for malignant diseases
- Development of new anti-angiogenic strategies to treat cancer
- Development of new immunotherapeutic approaches to treat malignant diseases
- Development of new anti-thrombotic materials for clinical use / • Use of stem cells in regenerative medicine