IMSUT Hospital

Department of Rheumatology and Allergy
アレルギー免疫科

Associate Professor Motohisa Yamamoto, M.D., D.M.Sc.
Assistant Professor Masaaki Uehara, M.D., D.M.Sc.

准教授 博士(医学) 山 本 元 久
助 教 博士(医学) 上 原 昌 晃

Founded in 2001, our department is dedicated to advancing the understanding and treatment of systemic autoimmune and inflammatory diseases, including rheumatoid arthritis, systemic lupus erythematosus, and IgG4-related disease. We provide personalized, evidence-based medical care grounded in cutting-edge clinical and translational research.
In particular, our department has played a pioneering role in the establishment, clinical characterization, and global standardization of IgG4-related disease, spanning basic science, clinical research, international collaboration, and health policy.
As part of an elite academic medical center, our mission extends beyond patient care to fostering the next generation of academic physicians, biomedical scientists, and clinician-educators who will lead the fields of rheumatology, immunology, and translational medicine.

1. Clinical Activities at IMSUT Hospital

Yuta Ichii, Masaaki Uehara, Motohisa Yamamoto

Our division provides state-of-the-art diagnostic and therapeutic services for patients with systemic autoimmune and inflammatory diseases, managing approximately 3,000 patients annually. Our rheumatologists integrate advanced clinical care with active basic and clinical research, while also playing a central role in the education and training of future rheumatology specialists.

Rheumatologic services at IMSUT Hospital include:

- Comprehensive outpatient consultations
- Specialized outpatient care for complex rheumatic diseases
- Inpatient consultation services
- Patient and physician education on rheumatic diseases and therapies
- Structured training programs for residents and early-career physicians
- Investigator-initiated and industry-sponsored clinical trials
- Contributions to community-based rheumatology care

2. Establishment of a Novel Registry and Development of Innovative Diagnostic and Therapeutic Strategies for IgG4-Related Disease

Yuta Ichii, Masaaki Uehara, Motohisa Yamamoto

IgG4-related disease (IgG4-RD) is a recently established disease entity, characterized as a chronic fibro-inflammatory disorder with elevated serum IgG4 levels and dense infiltration of IgG4-positive plasma cells, leading to progressive organ fibrosis. Dr. Motohisa Yamamoto is one of the physicians who played a central role in establishing the disease concept of IgG4-RD, contributing decisively to its recognition as a unified systemic disorder rather than a collection of organ-specific diseases.

Although the precise autoimmune nature of IgG4-

RD remains to be fully elucidated, referrals to rheumatologists have rapidly increased due to its multisystem involvement and complex immune dysregulation. To systematically address these challenges, we established a comprehensive patient registry for IgG4-RD—the TOMORROW Registry—and initiated prospective enrollment of patients.

This registry functions as a core clinical and research infrastructure and is operated in close alignment with national health policies. Dr. Yamamoto currently plays a leading role within AMED-funded research programs, including responsibilities for registry governance and serving as chair of dedicated subcommittees, thereby contributing not only to academic research but also to the formulation of national strategies for rare and intractable diseases. Data from the TOMORROW Registry are shared with the Rare Disease Data Registry of Japan (RADDAR-J), established by AMED, strengthening nationwide data integration and policy-driven research.

Through this registry-based approach, we aim to precisely characterize the clinical spectrum, disease course, and treatment outcomes of IgG4-RD, ultimately enabling more accurate diagnostic criteria and optimized therapeutic strategies.

Furthermore, leveraging blood and tissue samples obtained through the registry, we are conducting comprehensive multi-omics analyses. These include RNA sequencing of salivary gland tissues and peripheral blood mononuclear cells, salivary microbiome profiling, and analyses of HLA associations with treatment response. By integrating these molecular data with detailed longitudinal clinical information, we are promoting the development of AI-driven personalized medicine, capable of predicting therapeutic response and long-term prognosis.

In parallel, we are actively engaged in international collaborative clinical trials and the development of global clinical practice guidelines for IgG4-RD, positioning our department as a hub for translational and regulatory science in this field. These efforts also support the identification of novel therapeutic target molecules and accelerate drug discovery, with the ultimate goal of improving outcomes for patients worldwide.

3. Development of AI-Based Diagnostic, Therapeutic, and Prognostic Algorithms for Rheumatic Diseases

Masaaki Uehara, Motohisa Yamamoto

The diagnosis and management of rheumatic diseases traditionally rely on pattern-based criteria integrating clinical, laboratory, and imaging findings. Treatment decisions further require careful assessment of disease burden and functional impairment. To enhance precision and objectivity in this process, we have developed an artificial intelligence–based diagnostic algorithm for IgG4-related disease using multicenter clinical data, and successfully reported its clinical utility.

Building on this achievement, and in collaboration with Showa Medical University, we are currently developing advanced AI algorithms to predict therapeutic response, complications, and long-term prognosis in patients with rheumatoid arthritis. These efforts aim to support clinical decision-making and promote truly personalized treatment strategies.

4. Development of Preventive Strategies for Glucocorticoid-Induced Myopathy and Osteonecrosis

Masaaki Uehara, Motohisa Yamamoto

Glucocorticoids remain indispensable in the treatment of many rheumatic diseases but are frequently complicated by glucocorticoid-induced myopathy. We previously demonstrated that supplementation with branched-chain amino acids (BCAA) ameliorates skeletal muscle loss, particularly in slow-twitch muscle fibers. Moreover, we identified specific serum amino acid profiles that correlate with improvements in slow-twitch muscle function. Based on these findings, we propose fiber-type–specific recovery strategies and are currently investigating optimal interventions for both slow- and fast-twitch muscle preservation.

In addition, high-dose glucocorticoid therapy used for remission induction is associated with an increased risk of osteonecrosis of the femoral head, a severe complication for which no established preventive strategy exists. In collaboration with the Department of Orthopaedic Surgery at Sapporo Medical University School of Medicine, we are developing novel preventive approaches. Several candidate drugs have already been identified, and associated clinical trials have been completed, marking an important step toward risk reduction in vulnerable patients.

Publications

1. Yamamoto M, Kamekura R, Uehara M, Ichii Y, Tanaka T, Aochi S, Takano K. Submandibular gland tissue RNAseq and spatial transcriptome analyses in IgG4-related disease. Rheumatology (Oxford). 2025; 64: 2265-2271.
2. Kanda M, Nagahata K, Moriyama M, Takano KI, Kamekura R, Yoshifuji H, Tsuboi H, Yamamoto M, Umehara H, Umeda M, Sakamoto M, Maehara

T, Inoue Y, Kubo S, Himi T, Origuchi T, Masaki Y, Mimori T, Dobashi H, Tanaka Y, Nakamura S, Takahashi H and Japanese Study Group for IgG4-related Dacryoadenitis and Sialadenitis, Research Program for Intractable Disease by the Ministry of Health, Labour and Welfare (MHLW), Japan. The 2023 revised diagnostic criteria for IgG4-related dacryoadenitis and sialadenitis. Mod Rheumatol. 2025; 35: 542-547.

3. Yamamoto M, Kamekura R, Uehara M, Ichii Y, Tanaka T, Takano K. Comprehensive analysis of cytokine and chemokine gene expression in IgG4-related disease by spatial transcriptomics. Allergol Int. 2025; 74: 476-478.
4. Yamamoto M, Kanda M, Mizushima I, Atsushi K, Umemura T, Ikeura T, Kodama Y, Dobashi H, Tanaka Y, Masamune A, Moriyama M, Saeki T, Matsui S, Origuchi T, Masaki Y, Asada M, Umehara H, Seno H, Naitoh I, Yamamoto S, Iwasaki E, Kubota K, Tanoue S, Nishino T, Tsuboi H, Matsumoto Y, Isayama H, Goto H, Notohara K, Uchida K, Kawabe K, Yamada K, Kasashima S, Takahira M, Sato Y, Kawachi I, Yamaguchi I, Okazaki K, Nakamura S, Matsuda F, Ishikawa H, Kawano M, and Patient Registry Committee, Research Program for Intractable Disease by the Ministry of Health, Labour and Welfare (MHLW), Japan. Clinical profile of IgG4-related disease in Japan based on the rare disease data registry. Immunol Med. 2025; 48: 192-202.
5. Zhang Y, Iwasaki T, Kawaguchi T, Takahashi H, Kawaguchi S, Kanno A, Yamaguchi I, Kubota K, Dobashi H, Nagasaki M, Yamamoto M, Takahashi M, Shimizu M, Ikeura K, Matsui S, Kanda M, Nakamura K, Yokoyama K, Azumi A, Masaki Y, Mizushima I, Kurita Y, Seno H, Origuchi T, Yazumi S, Hirano K, Masamune A, Mizuno N, Shimada H, Moriyama M, Hori Y, Kodama Y, Saeki T, Kin T, Kawanami C, Asada M, Akamizu T, Nakamura A, Oshima K, Tanaka Y, Yoshifuji H, Kanzawa T, Kimura T, Umehara H, Ishikawa H, Chiba T, Okazaki K, Minori T, Nakamura S, Kawano M, Matsuda F, on behalf of the Japanese IgG4-Related Disease Working Consortium. Whole-genome sequencing analysis of IgG4-related disease in the Japanese population. Lancet Rheumatol. 2026; 8: e11-e22.