Research Center for Medical Sciences
Core Research Facilities for Basic Science
(Division of Molecular Genetics)

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General Summary

Recent advances in technologies and study designs have unveiled the genetic components of human diseases. The aim of our project is to explore genetic factors of allergic and immunological diseases. Interdisciplinary research is necessary to identify the molecular targets and improve our understanding of diseases.
Gene therapy has become an attractive procedure to cure diseases. We contribute to gene therapy by developing methods of regulating gene expression and of genome editing.
We also maintain the following experimental devices, which are commonly used: next-generation sequencing systems, 3130XL sequencer (Applied Biosystems, Life Technologies, Carlsbad, CA, USA), MoFlo XDP cell sorter (Beckman Coulter, Fullerton, CA, USA), flow cytometer, X-ray irradiation research system, and the quantitative real-time polymerase chain reaction. We also support experiments with these devices.

Research Activities

Genetics of inflammatory diseases
Psoriasis is an inflammatory skin disease histologically characterized by epidermal hyperplasia, inflammatory cell infiltration, and vascular changes. A dysregulated cutaneous immune response occurs in genetically susceptible individuals. We have collaborated with Osaka University and Nippon Medical University for researching inflammatory skin diseases. We have recruited patients with psoriasis and conducted an association study of psoriasis and of loci for psoriasis discovered with a genome-wide association study (GWAS). We also perform GWASs, next-generation sequencing analysis, and metabolome analysis of psoriasis.
Recent GWASs have identified genetic variants of the thymic stromal lymphopoietin (*TSLP*) locus which are associated with susceptibility to asthma- and allergy-related phenotypes. We conducted an association study of chronic rhinosinusitis with nasal polyps and aspirin-exacerbated respiratory disease using *TSLP* variants and observed a significant association of rs1837253 with these diseases. Our functional study with a super-shift binding assay suggested an allele-specific influence of rs1837253 on affinity for transcription factors, upstream stimulatory factors (USF) 1 and 2 in nasal fibroblasts. The manuscript containing those findings is under submission.
Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a severe food allergy that usually develops after the ingestion of wheat products followed by physical exercise.

Hydrolyzed wheat gluten protein (HWP) is used as an additive for facial soap. Most patients seemed to be sensitized to an HWP (Glupearl 19S® (Katayama Chemical, INC.) through the use of the facial soap "Cha-no-shizuku (Yuuka Co., Ltd)." Glupearl 19S® is a degraded gluten made from the direct resolution of wheat by hydrochloric acid. We conducted a GWAS including 464 patients with WDEIA induced by HWP-containing facial soap and 3,099 control subjects. Single nucleotide polymorphisms at a region on chromosome 6 were associated with WDEIA induced by HWP-containing facial soap. The manuscript containing these findings is under submission.

An effective strategy for the research of allergic and immunological diseases

Professor Tamari has served as a principal investigator of a group established to make plans for the next 10 years of allergy and clinical immunology research. This work is supported by Health Science Research Grants from the Ministry of Health, Welfare and Labour of Japan. We compiled a report on an effective strategy for research on allergic and immunological diseases and made a brochure explaining the research plans.

Development of the adenovirus vector systems

Because adenovirus vectors (AdVs) are attractive tools for expressing genes and regulating expression, they are applied to many areas of research. The AdVs are also a useful tool to transduce the purpose gene in hepatocytes. We have developed a protocol for curing hepatitis B virus (HBV) infection with an AdV. We established the efficient detection system of HBV genome replication applying AdVs (HBV103-AdV system). We performed high-throughput screening of anti-HBV drugs using this system. As a result, we identified several promising compounds and analyzed what mechanism showed the antiviral effect Furthermore, we succeeded in efficient cleavage of the HBV genome using CRISPR/Cas9 and have developed a hepatocyte-specific genome editing system. In addition, we have constructed AdVs for repairing the beta-glucuronidase (*GUSB*) gene of Sly's disease by genome editing.

Publications

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Reviews and Books

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