Research Center for Medical Sciences
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 molecular targets and improve our understanding of diseases.
We are performing collaborative research with other institutions. We also support research projects, which are conducted in clinical departments of The Jikei University School of Medicine.

Research Activities

Genetics of inflammatory diseases
Recent genome-wide association studies (GWASs) have identified variants of the thymic stromal lymphopoietin gene (*TSLP*) locus that 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 those diseases. Our functional study using a super-shift binding assay suggested an allele-specific influence of rs1837253 on affinity for upstream stimulatory factors 1 and 2 in nasal fibroblasts. We reported those findings in *Allergology International* (2020 Jan; 69(1): 138-140).
Wheat-dependent exercise-induced anaphylaxis (WDEIA) is a severe food allergy that usually develops after 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 HWP (Glupearl 19S®) through the use of the facial soap "Chano-shizuku." Glupearl 19S® is a degraded gluten made from the direct resolution of wheat by hydrochloric acid. We conducted a GWAS of WDEIA induced by HWP-containing facial soap in 464 patients and 3,099 control subjects. Single nucleotide polymorphisms at a region on chromosome 6 were associated with WDEIA induced by HWP-containing facial soap. We reported those findings in the *Journal of Allergy and Clinical Immunology* (2019 Nov; 144(5): 1354-1363).
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 research on inflammatory skin diseases. We have recruited patients with psoriasis and performed an association study of psoriasis with GWAS-discovered loci for psoriasis. We also performed a GWAS, next-generation sequencing analysis, and metabolome analysis of psoriasis. In 2019, we exam-

ined whether polymorphisms of the genes tumor necrosis factor A (*TNFA*), TNF receptor superfamily member 1B (*TNFRSF1B*), and TNF alpha induced protein 3 (*TNFAIP3*) contribute the positive response to drug treatment in Japanese patients with psoriasis, but there was no significant association of the 3 single nucleotide polymorphisms with response to treatment against tumor necrosis factor β. We have submitted these findings to *Journal of Dermatology*.

An effective strategy for the research of allergic and immunological diseases

Professor Tamari has served as the principal investigator of a group established to make plans for the next 10 years of allergy and clinical immunology research. The hope is to establish a stable society in which people can have long, healthy lives, as free as possible from allergic and immunological diseases at each stage of life. This work is supported by Health Science Research Grants from the Ministry of Health, Welfare and Labour of Japan. We have reported a manuscript on an effective strategy for the research of allergic and immunological diseases (Arerugi 2020; 69(1): 23–33) and launched a website for the research plans, ENGAGE-TF toward 2030 (https://www.engage-tf.jp).

Publications

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