Project to elucidate hereditary skin diseases

Research overview

1. Development of a new genetic diagnosis method

We are developing a rapid and inexpensive genetic diagnostic method for congenital and hereditary diseases that are difficult to diagnose. Specifically, we analyzed all coding regions of approximately 500 genes that have already been found to cause hereditary skin diseases using next-generation sequencers, and developed a system for definitive diagnosis based on the gene mutations found and clinical symptoms. We expect that genetic testing will enable the diagnosis of cases that were previously difficult to diagnose based on clinical symptoms, which will not only enable patients to receive appropriate treatment at an early stage but also enable early detection and prevention of complications.

2. Elucidation of new diseases, causative genes, and pathological mechanisms

We are searching for causative genes using exome analysis for hereditary diseases for which the causative gene is unknown and cases for which the cause cannot be determined by the above-mentioned screening methods. Specifically, we used next-generation sequencing to analyze all exonic regions of approximately 25,000 genes that directly encode proteins in our genomic DNA to identify mutations. In 2013, we used this method to analyze genomic DNA from patients with palmoplantar keratosis of the long island type, the cause of which was previously unknown, and found that SERPINB7 deficiency is the cause of the disease (Am J Hum Genet 2013). In 2017, we first identified GJA1 as the gene responsible for inflammatory linear Verrucous epidermal nevus (ILVEN) (JID 2017), and in 2019, we found that linear sweat pore keratosis and sunlight-disseminated sweat pore keratosis are caused by a single second hit in fetal life and numerous second hits in mature life, respectively. In 2020, we reported a novel progeria/diverse aneuploidy mosaic syndrome with CDC20 as the causative gene (Aging Cell 2020). In 2020, we reported a novel progeria/variegated aneuploidy mosaic syndrome caused by CDC20 (Aging Cell 2020), and in 2021, we revealed that acrochordons/skin tags that appear on the neck and axillae with aging are caused by keratinocytes with gene mutations in the same spectrum as those of seborrheic keratoses, which appears on the face and back (JID 2021).

3. Development of disease-specific therapies

We are currently developing new therapeutic methods based on molecular pathology. We are also focusing on tailor-made treatments for rare diseases. We have been studying the mechanism of hand and foot odor, which is a common problem in patients with palmoplantar keratosis, and have been developing topical treatments to reduce odor. We are also treating the congenital hemidysplasia with ichthyosiform erythroderma and limb defects syndrome (CHILD syndrome) by topical application of a mixture of statin and cholesterol ointment. We have been treating the skin rash of the CHILD syndrome with topical statin and cholesterol ointment.

Publications

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