News Release

Nonsyndromic epidermal differentiation disorders: New classification and nomenclature based on disease-associated genes leading to targeted therapy

Key Points

- **Experts on inherited keratinization disorders from around the world came together to carry out a comprehensive and fundamental revision of the names of diseases caused by genetic abnormalities of epidermal differentiation.**
- **With this revision, each disease has been reclassified according to the function of the pathogenic molecule, and the name of the disease-related gene has been incorporated into each disease name.**
- **All terms that could be considered derogatory, such as ”ichthyosis” and ”harlequin” have been removed from the new disease names.**
- **It is expected that new disease names incorporating the names of causative genes will contribute to the development of new etiological targeted therapies.**

Summary

The Reclassifying Epidermal Differentiation Disorders Initiative (REDDI) Task Force, consisting of experts on inherited keratinization diseases from around the world, including Professor Masashi Akiyama of the Department of Dermatology, Nagoya University Graduate School of Medicine, and representatives of patient groups, has comprehensively and radically revised the international nomenclature of diseases caused by genetic abnormalities of epidermal differentiation. In this revision, all previous names such as ”ichthyosis” and ”palmoplantar keratoderma” have been abolished, and all diseases caused by genetic epidermal differentiation defects, including many diseases other than ichthyosis, have been named ”Epidermal Differentiation Disorder (EDD)”. EDD has been divided into nonsyndromic EDD (nEDD), whose lesions are limited to the skin; syndromic EDD (sEDD), whose symptoms are also seen in organs other than the skin; and palmoplantar EDD (pEDD), whose lesions are mainly on the palms and soles of the feet. The papers covered in this press release are about nEDDs, which include many important EDDs such as ichthyosis. There are 53 types of nEDDs, including the diseases previously called ichthyosis, porokeratosis, Hailey-Hailey disease and Darier disease. The new disease names are based on the causative genes (e.g., *FLG*-nEDD (previous name, ichthyosis vulgaris)). This classification based on the function of the

causative molecules and the new disease names including the causative genes will enable patients to better understand their own condition and medical professionals to provide more appropriate treatment. In addition, the new disease names completely eliminate terms that are unpleasant for patients and their families, such as ”ichthyosis” and ”harlequin”, as well as eponyms. It is expected that the clarification of the causative genes by the new disease names will lead to the development of new treatments. The results of the present project were published in the online advance edition of the British medical journal ”British Journal of Dermatology” on May 1, 2025. In addition to this paper, the task force has already published three other papers on the project in the same journal (an overall review paper, a paper on sEDD, and a paper on pEDD).

Research Background

Inherited keratinization disorders are a group of diseases in which white, brown, or black scales are observed over a wide area or in some parts of the skin due to genetic defects of epidermal differentiation. In recent years, great progress has been made in elucidating the pathogenic gene variants of these diseases. In addition, progress has been made in elucidating the mechanisms of phenotype formation caused by these gene variants. In many skin diseases, new treatments have been developed, including biologics, small molecular targeted agents, and gene therapy, as understanding of the pathogenic mechanisms has improved. For inherited keratinization disorders, classifying the disease based on the function of the pathogenic gene product may pave the way for new targeted therapies. However, the nomenclature of inherited keratinization disorders remains very diverse, with numerous synonyms and misnomers, and it cannot be said that it is adequately classified based on the pathogenic mechanism, and is not fully useful for developing treatments. Therefore, there was a need to revise the international disease name and disease type classification of inherited keratinization disorders to reflect the newly discovered knowledge of the etiology and pathology.

Research Results

We, the Reclassifying Epidermal Differentiation Disorders Initiative (REDDI), consisting of experts on inherited keratinization disorders from around the world, have been working for the past three years to revise the international nomenclature and classification of inherited keratinization disorders to reflect new findings on the etiology and pathology. In this revision, all diseases caused by epidermal differentiation defects that are broader than the traditional

inherited keratinization disorders have been named Epidermal Differentiation Disorders (EDDs). In this new classification and nomenclature system that encompasses all EDD, EDD has been divided into nonsyndromic EDD (nEDD), in which lesions are limited to the skin; syndromic EDD (sEDD), in which symptoms are seen in organs other than the skin; and palmoplantar EDD (pEDD), in which lesions are mainly seen on the palms and soles of the feet. We will be publishing four papers (an overall review paper, a paper on nEDD, a paper on sEDD, and a paper on pEDD) regarding this disease name revision, and the paper covered by this press release is the paper on nEDD, which includes many important EDDs such as diseases previously called “ichthyosis”. There are 53 types of nEDD, including diseases previously known as ichthyosis, porokeratosis, Hailey-Hailey disease, and Darier disease. The new disease names are based on the causative genes (e.g., *FLG*-nEDD (old name, ichthyosis vulgaris)). The new disease names completely eliminate terms that are unpleasant for patients and their families, such as ”ichthyosis” and ”harlequin”, as well as eponyms. In addition, it is expected that the classification based on the function of the causative molecule and the new disease names including the causative genes will enable patients to better understand the etiology and pathophysiology of their own diseases, and medical professionals to provide more appropriate treatment.

Research Summary and Future Perspective

Classification of nEDDs according to the function of the pathogenic molecules and the related pathways, and clarification of the disease-related genes of each disease are expected to lead to the development of new treatments and the repurposing of drugs developed for other diseases. For the time being, patients in countries and regions where genetic testing is not available will be diagnosed with unspecified nEDD, but we hope that this revision of the disease name will be the beginning of eliminating countries and regions where genetic testing is not available.

Publication

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