Editorial

Genodermatoses: dermatologist in the era of molecular diagnosis

Newborn and infant skin conditions can run a transient or benign course such as in erythema toxicum neonatorum or naevus simplex. On the other hand, they can be precursors of underlying internal disease or genetic alterations. Genetic alterations causing skin disorders, collectively known as genodermatoses, are composed of a broad spectrum of disorders that can have a significant impact on the well-being and quality of life in infants. Some of these conditions are life-threatening; examples are Harlequin ichthyosis and generalised junctional epidermolysis bullosa (Herlitz type). It is not difficult to understand when a newborn presents with a severe type of genodermatosis, the psychological stress and devastating effect on the parents. Therefore, a timely and accurate diagnosis of the condition is of paramount importance to both the infant and parents.

Before the turn of the century, obtaining the genetic diagnosis of genodermatoses was lengthy and costly. In the 1990s, the disease gene was found by either linkage studies or from candidate gene approaches, which had a slow turnover. The next step of detecting mutations in the disease gene was even more tedious, although it is the most important landmark for an accurate diagnosis, providing a basis for genetic counselling, defining the disease mechanism, and then the construction of a disease model and finally the development of therapy. The availability of next generation sequencing (NGS) since 2005 represents a major advance and has revolutionised diagnosis in genodermatoses. Not only can the disease gene can be identified in a much shorter period of time, the cost for such testing has also greatly decreased in recent years. In addition, NGS is expected to act as a powerful tool in prenatal diagnosis and screening for genetic disease. However, there are always two sides to the story. The most important question being asked regarding the detection of enormous amount of gene mutations by NGS is whether they are pathogenic and how are they correlated with the clinical phenotypes.

In this issue of the Journal, Koh gives us a comprehensive and practical review of the clinical approach to some common and rare genodermatoses. The basic concept and approach to arrive at the molecular diagnosis is also elucidated. The review also emphasised the importance of identification of clinical phenotype for clinical correlation in the diagnosis of genodermatoses, pointing out that it is as important as genetic testing due to the current shortcomings of NGS.[1] Therefore, as dermatologists, we have not yet been replaced in this era by molecular diagnostics and can still play our role in deciphering the puzzle.

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Reference

1. Sarig O, Sprecher E. The molecular revolution in cutaneous biology: Era of next-generation sequencing. J Invest Dermatol 2017;137:e79-e82.