AUTOIMMUNE BULLOUS DISEASES

HLA ASSOCIATIONS AND AUTOIMMUNE BLISTERING DISEASE: GENERALITY AND HETEROGENEITY

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Background: Autoimmune blistering diseases (AIBDs) are a group of rare acquired blistering skin diseases, which are divided into five major subtypes based on the clinical appearance and pathology: pemphigus diseases, bullous pemphigoid (BP), epidermolysis bullosa acquisita (EBA), dermatitis herpetiformis (DH) and Linear IgA bullous dermatosis (LigA). Current understanding has been greatly increased by genetic investigations mainly focus on the HLA in various populations. We have conducted the HLA association studies on different subtypes of AIBDs in Chinese population by using Next-generation (NGS) based HLA typing methods.

Objective: Upon these data, we aimed to investigate the generality and heterogeneity in different disease subtype and population.

Materials and Method: A total number of 369 pemphigus (210 PV and 159 PF), 575 BPs, 36 DHs, 33 LigAs, 17 EBAs and 976 healthy controls were inrolled in the study. Genome-wide association studies were performed in the pemphigus and BPs. Associations study of HLA were conducted on the results of NGS based HLA typing.

Results: We have identified different associations for subtypes of AIBDs. For pemphigus, we confirmed HLA-DQB1*05:03 to be the strongest association with PV and PF. In addition, HLA-DRB1*14 was demonstrated to be a second independent variants for PV, while HLA-DRB1*04:06 was demonstrated to be the second independent signal for PF. For pemphigoid, HLA-DQB1*03:01 were confirmed to be the strongest association, especially for the BP180-positive group. For DH, HLA-B*08:01 and HLA-DRB1*03:01 were confirmed to be independent associations. None significant HLA associations were identified for EBA and LigA. Population heterogeneity analysis revealed effect of HLA associations on different subtype of AIBDs, especially for DH.

Conclusions: The investigation of AIBD subtypes advanced the understanding the genetics of AIBD susceptibility and offers molecular insight into the pathophysiological mechanisms.