Commentary

Towards Understanding Mechanisms of Autoimmune Bullous Skin Diseases

Rafal P Krol, Atsushi Yasukochi, Takashi Hashimoto

Department of Dermatology, Kurume University School of Medicine, and Kurume University Institute of Cutaneous Cell Biology, Kurume, Fukuoka, Japan

Address for correspondence: Prof. Takashi Hashimoto, Department of Dermatology, Kurume University School of Medicine and Kurume University Institute of Cutaneous Cell Biology, 67 Asahimachi, Kurume, Fukuoka-830001l, Japan. E-mail: hashimot@med.kurume-u.ac.jp

Autoimmune bullous skin diseases are characterized by pathogenic autoantibodies targeting distinct adhesion molecules of the skin. Their clinical features are usually heterogeneous, and pathomechanism is believed to involve complex interactions between genetic, immunological, and environmental factors. Environmental causes are still poorly identified, and genetic components are probably multifactorial, with small penetrance.[1] The detailed mechanism of autoimmunity development is however still one of the big enigmas of immunology.

Endemic forms of pemphigus foliaceus present unique opportunity to study the pathology of autoimmunity development. They occur in well-defined restricted geographical regions and prevalence in local population is usually very high. Thus, they constitute an excellent model allowing detailed analysis of interactions between clinical, epidemiological, immunological, and environmental aspects of the disease.

Endemic pemphigus foliaceus is known for over a 100 years, since prototype was described in rural areas of Brazil. Recently, a new type of endemic pemphigus foliaceus was found in El Bagre, Colombia. The local population was extensively studied by Abreu Velez *et al*., who performed prospective fieldwork study for over 10 years. Several publications resulting from this study helped to elucidate many aspects of autoimmune bullous skin diseases, including autoantibody characterization, autoantigen identification, genetic factors, and exposure to environmental factors such as mercury, metalloids, and trace elements.[2]

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Induction of acantholysis and blister formation in pemphigus-type autoimmune bullous skin diseases is a complicated process triggered by interaction of autoantibodies with desmosomal target molecules. Several mechanisms, including various signaling pathways, were suggested for development of acantholysis by experimental evidences.[3] The article by Abreu Velez *et al*.,[4] published in this issue of North American Journal of Medical Sciences, describes a pilot study, the aim of which was further clarification of blister formation mechanism. The authors studied lesional skin from patients with endemic pemphigus and others autoimmune bullous diseases to clarify the involvement of novel signaling pathway, namely the presence of phosphorylated form of ribosomal protein S6.[4]

Previous attempts to clarify mechanism of acantholysis in immunobullous diseases suggested involvement of mammalian target of rapamycin (mTOR). This kinase protein has emerged as important regulator of cell size and protein synthesis. One of the downstream effectors of mTOR is ribosomal protein S6 kinase, primary substrate of which is ribosomal protein S6. Phosphorylation of ribosomal protein S6 was shown to be an important event in signaling pathways, which are involved in global protein synthesis, control of translation, cell size, cell proliferation, and glucose homeostasis.[5]

Autoimmune bullous skin diseases are still life-threatening dermatological conditions. Because of their heterogeneity, precise diagnosis is very important.

Constant efforts to elucidate pathomechanisms of diseases and to develop new therapies are needed to improve care quality for our patients.

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