Over the past 20 years, the discovery that keratinocytes are immunologically active cells has reinforced the concept that the skin is an active immune organ. It is clear that the epidermis can function as an immunologic tissue. This is critically important to its function as a barrier to external toxins and microbes. Moreover, recent findings on the roles of antimicrobial peptides, Toll-like receptors, antigen-presenting cells, regulatory T (Treg), and interleukin-17 (IL-17)-producing T helper (Th17) cells in maintaining the skin functions and leading to various skin disorders also encourage the development of immunologically active biologic therapies for skin diseases. In this special issue, important recent findings on skin immunity are comprehensively reviewed by the experts.

Galectins are a family of lectins containing one or two conserved carbohydrate-recognition domains that preferentially bind β-galactosides. Galectins may work extracellularly in an autocrine or paracrine manner to modulate cell status or functions, e.g., activation of cells, mediation of cell–cell–cell–extracellular matrix interactions, and promotion of cell migration. Intracellularly, galectins can function in a carbohydrate-independent manner to regulate cell apoptosis, migration, and responses to stimuli. Several galectins such as galectin-1, -3, and -9 have been found to be important regulators in cutaneous immune disorders. In this issue, Chen et al review the importance of galectins in cutaneous immunity and skin diseases, especially contact dermatitis, psoriasis, and atopic dermatitis (AD).

Chemokines are structurally related, small (8–14 kDa) polypeptide signaling molecules that bind to and activate a family of seven transmembrane G protein-coupled receptors, the chemokine receptors. Chemokines are known for their ability to stimulate the directional migration of all classes of leukocytes. In the skin, chemokines from various skin cells mediate trafficking of different subsets of inflammatory cells to bind to the corresponding chemokine receptors, forming a pro-inflammatory response. In this special issue, Lee and Hwang examine two diseases as examples where the roles for chemokines and their receptors have been demonstrated through human and experimental animal studies. The understanding of how chemokine receptors participate in various skin disorders provides a promising rationale for the use of receptor inhibitors or anti-chemokine receptor antibodies as novel therapeutic agents.

The recent discovery of the roles of Th17 cells in the pathogenesis of psoriasis is a major breakthrough in psoriasis management. Activated dendritic cells produce cytokines, including IL-23, IL-12, and tumor necrosis factor (TNF)-z, and drive naïve T cells to undergo Th17 cells differentiation in the presence of transforming growth factor (TGF)-β and IL-6. Th17 cells produce IL-17, IL-22, and have other important downstream pro-inflammatory effects in skin. Clinically, expression of Th17-related cytokines is markedly increased in psoriatic lesions, and successful therapy is associated with restoration of the expression of Th17-associated genes to near-normal levels. A summary of the current knowledge about Th17 cells and new therapeutic agents targeting the effector functions of Th17 cells for psoriasis is also presented in this special issue.

AD is a chronic relapsing skin disease characterized by eczematous skin lesions and intense pruritus. It is one of the most frequent chronic inflammatory skin diseases, affecting at least 15% of children and 2–10% of adults in industrialized countries and its prevalence appears to be increasing. There is a long debate around what is the primary cause of AD, the barrier dysfunction or the allergy/immunology abnormalities. Recently, the discovery of a link between the incidence of AD and loss-of-function mutations in filaggrin suggests that barrier dysfunction occurs first, followed by allergy/immunology abnormalities. The atopic inflammatory response can induce an acquired barrier defect to create a positive feedback loop by acting in a highly interdisciplinary manner in the development of AD. In this scenario, epicutaneous (EC) sensitization of protein antigens, which induces predominant Th2, marginal Th1, and significant Th17 and Treg responses, might be one of the important routes of allergen sensitization for AD. It has been shown that EC sensitization with ovalbumin induced a predominant Th2 and a marginal Th1 response with high immunoglobulin E (IgE) production in mice. EC sensitization with house dust mite Ag was also shown to elicit a Th2-dominant cytokine response. It is common to find adult AD patients with serum IgE even higher than 10,000 IU/mL. Omalizumab, designed to bind to free IgE but not to IgE bound by the high-affinity IgE-Fc receptors (FcεRI) on mast cells and basophils, can neutralize IgE and block IgE binding to FcεRI. Omalizumab has been approved in the USA, the European Union, and many other regions for the treatment of patients 12 years and older with moderate-to-severe or severe allergic asthma. However, its role in treating AD is still controversial. In the past several years, many reports investigating the therapeutic effects of omalizumab in patients with moderate-to-severe or severe AD have been published. Based on the above observations, Chen et al proposed a novel pharmacological mechanism in omalizumab in which the rapidly accumulated IgE:anti-IgE immune complexes may trap allergens. Whether this effect is present in high-IgE patients...
with AD needs further investigation in order to provide the theoretical basis for using omalizumab for the treatment of this disease.

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