Innate Immunity in the Skin

Ulf Meyer-Hoffert

Department of Dermatology, University of Kiel, Kiel, Germany

Looking at the skin might evoke different associations and emotions among different spectators. The beauty of nature led some sometimes to forget the efficient and complex immunological organ in front of us. The skin protects us not only from water loss and physical damage, it is also our protective shield against microorganisms we have to face in this world. However, skin infections rarely occur. To combat microbial attacks, an efficient immune system is needed. It acts at different levels depending on how many resources are required to stay healthy – nature is not only beautiful but also economic. These different defense levels go hand in hand and complement each other.

First of all, the skin possesses a repertoire of antimicrobial substances on its surface. They are derived from keratinocytes and prebuilt during the differentiation process to fight surrounding microbes. The underlying epidermis functions not only as a ‘bricks-and-mortar’ barrier but also as a sensor to environmental hazards. Keratinocytes and epidermal dendritic cells (Langerhans cells) express different receptors to sense dangerous molecules. These innate immune receptors, some being located on the cell surface and others within the cell, initiate immune responses. These immune responses range from enhancement of antimicrobial activity by inducing antimicrobial production over the release of inflammatory cytokines to antigen presentation and control of adaptive immune responses. Research during recent years has revealed that this innate immune system is not involved in the direct fight against pathogens but turns

out to be crucial for many inflammatory processes centrally involved in dermatological diseases.

In the first review of this issue, de Koning et al. [1] summarize the current knowledge on pattern recognition receptors in immune disorders affecting the skin. They show that pattern recognition receptors like Toll-like receptors and members of the leucine-rich repeat-domain proteins participate in common cutaneous inflammatory diseases like psoriasis, atopic dermatitis and allergic contact dermatitis. Most has been learned from very rare diseases, which are monogenetic in their inheritance, like cryopyrin-associated periodic syndrome, NLRP12-associated periodic syndrome and Blau’s syndrome, which are all caused by specific defects in the inflammasome complex. This understanding has already changed the therapeutic approach in these patients, which are nowadays excellently treated by IL-1 antagonists. Due to this therapeutic breakthrough, there were great expectations for novel drugs targeting pattern recognition receptors and their specific pathways.

The other two papers in this issue deal with antimicrobial peptides, which are the effector molecules of the innate immune system. In their review, Simanski et al. [2] discuss the role of antimicrobial RNases in cutaneous defense mechanisms. RNase 7, for example, is a highly active antimicrobial peptide expressed in healthy human skin [3]. In contrast to other antimicrobial peptides, it has not attracted the same attention as defensins for instance, though its antimicrobial capacity and its expression in the human skin is comparable and even higher compared

with skin-derived defensins [4]. As shown in this review, RNase 7 expression in the human skin depends on its location, which implies that it is regulated by intrinsic and/or extrinsic factors. Understanding these control mechanisms might be of therapeutic benefit in the fight against bacterial diseases.

Finally, Leonard et al. [5] study canine β -defensin (CBD) 103 in their research paper. β -Defensins represent the oldest evolutionary subfamily, and they are found in diverse species, ranging from horseshoe crabs and birds to hominids. The genomes of some mammals, such as ruminants and carnivores, appear to encode exclusively

β -defensins. CBD103 mutations causes black coat color in domestic dogs [6]. Leonard et al. [5] provide more insight into antimicrobial activity and tissue expression in health and disease as well as breed variation in CBD103 and its common genetic polymorphisms.

In summary, this issue demonstrates the variety and sophistication of innate immune functions present in the skin. Understanding these mechanisms might likely give the answer to many unsolved pathological conditions and harbors novel therapeutic strategies. I hope that the reader will look at the skin from a different perspective.

References

- 1 de Koning HD, Simon A, Zeeuwen PL, Schalkwijk J: Pattern recognition receptors in immune disorders affecting the skin. *J Innate Immun* 2012;4:225–240.
- 2 Simanski M, Köten B, Schröder JM, Gläser R, Harder J: Antimicrobial RNases in cutaneous defense. *J Innate Immun* 2012;4:241–247.
- 3 Harder J, Schröder JM: RNase 7, a novel innate immune defense antimicrobial protein of healthy human skin. *J Biol Chem* 2002;29: 46779–46784.
- 4 Harder J, Dressel S, Wittersheim M, Cordes J, Meyer-Hoffert U, Mrowietz U, Fölster-Holst R, Proksch E, Schröder JM, Schwarz T, Gläser R: Enhanced expression and secretion of antimicrobial peptides in atopic dermatitis and after superficial skin injury. *J Invest Dermatol* 2010;130:1355–1364.
- 5 Leonard BC, Marks SL, Outerbridge CA, Af-folter VK, Kananurak A, Young A, Moore PF, Bannasch DL, Bevins CL: Activity, expression and genetic variation of canine β -defensin 103: a multifunctional antimicrobial peptide in the skin of domestic dogs. *J Innate Immun* 2012;4:248–259.
- 6 Candille SI, Kaelin CB, Cattanaach BM, Yu B, Thompson DA, Nix MA, Kerns JA, Schmutz SM, Millhauser GL, Barsh GS: A β -defensin mutation causes black coat color in domestic dogs. *Science* 2007;318:1418–1423.