INTRODUCTION

The skin and its blossoms—fertile soil for clinical science

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Dermatology has its origins in eighteenth century France, and until this day, skin manifestations are traditionally called “efflorescences”, which translates from French to the process of blossoming. This issue is a selected garland of current advances in dermatology, and we are content to have obtained brand-new insights from each leader in the respective field.

Efflorescence most fittingly describes the rapid changes that can be induced by inflammatory skin conditions, which can produce skin changes of vivid pink, red, yellow, and white. Subsequently, these fleeting “blossoms” wither away to scaly brown, gray, or transparent secondary lesions that slowly disappear or leave largely irreversible scarring in their wake.

Utilizing this common-place observation that each skin disease has a distinct temporal development, dermatological research has begun to describe the different stages in temporal evolution of skin lesions. In psoriasis, atopic dermatitis, and possibly many other dermatoses, these stages loosely correspond to initial activity of the innate immune system that subsequently evolves in cutaneous pathology driven by adaptive immune reactions. This issue of Seminars in Immunopathology aims to give an overview on the current insights on the mechanisms producing the most important immune-mediated dermatoses. In addition, our authors address

treatment strategies and how they relate to the understanding of pathogenetic mechanisms in dermatology.

Kamran Ghoreschi and Martin Röcken are widely known immune dermatologists and have originally introduced the concept of active immune reprogramming in dermatology. Their contribution gives the reader a concise primer on the immunology of the skin and introduces the various key players and the complex interactions that result in efficient orchestration of the immune response.

Jonathan Barker, Satveer Kaur Mahil, and Francesca Capon, two of whom were deeply involved in the elucidation of the genetics of psoriasis since the early days, give us an insight on current understanding of this common but recalcitrant condition. They point out that the most important players in the immunopathology of psoriasis such as IL-23 and its receptor were found both in functional experiments as well as in genome-wide association studies, validating these latter studies as rich source of information for understanding of pathogenetic mechanisms. Interestingly, IL-22 was not pinpointed as important factor by genetic studies, which was later shown to correspond to clinical trials. The role of the innate immune system is important as well, as physical trauma can induce antimicrobial peptides by keratinocytes, which activates autoreactive T cells and mediates the breakdown of immune tolerance to self-nucleic acids. This instigates interferon type I responses, which is thought to be the first step towards the development of psoriasis.

While psoriasis is traditionally understood to be a Th1/Th17 disease, atopic dermatitis is thought to depend on Th2 cytokines. Tilo Biedermann and colleagues have contributed an article that widens our perspective here, introducing the role of innate signaling in this common condition. Microbiota and the host immune system are in permanent contact and communication via the skin. Commensals contribute to the alertness of the immune system and to immune tolerance.

This is the introduction for Advances in Immunodermatology - Drs. Lars French and Alexander Navarini

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Because of the impaired skin barrier, atopic dermatitis patients develop both impaired innate and adaptive immune responses.

Navarini et al. address the question of whether there is an overlap between neutrophil dermatoses and autoinflammatory conditions. The former were described purely on the level of clinical features, the latter were identified more recently based on genetic data. However, both groups are clinically closely related, produce primarily neutrophil granulocytic infiltrates, and have largely similar cytokine profiles of the interleukin 1 group. Thus, both groups could be merged in a new group of “innate immune disorders”.

Autoimmune bullous diseases are among the best studied skin conditions, but have still not yielded all their secrets. Borradori and colleagues review in detail the HLA class II-associated genetic susceptibility to pemphigus, pathogenic desmoglein (Dsg) antibodies, and pathogenic Dsg-specific B and T cells. Surprisingly, intracellular signaling following antibody binding is required for keratinocyte dissociation in pemphigus vulgaris—thus, a potential role for intracellular kinase inhibitors in therapy could be the future of autoimmune bullous conditions.

Subsequently, Hötzenecker and French rigorously review the field of drug-associated exanthema, a field that was influenced greatly by French’s finding of Fas-FasL interactions in toxic epidermal necrolysis. More recently, Th17 T cells were identified as well in severe but not in mild drug rashes, suggesting that neutrophils might play a role as well those critical reactions.

The three following reviews address the classic collagenoses or autoimmune skin conditions, namely scleroderma, lupus erythematosus, and dermatomyositis. Localized

and systemic sclerodermas require the expertise of both dermatologists and rheumatologists. Cozzio and Distler review the current field, new approaches based on modulation of TGF- β , serotonin as well as biologics against classical proinflammatory cytokines. Kuhn and coworkers address recent advances in lupus erythematosus. This multifactorial condition is investigated with increasingly large cohorts and genome-wide association studies. The improved understanding of pathophysiology revealed that the clinical expression of LE is predisposed by susceptibility genes and that environmental factors such as UV light are driving the abnormal immune response that includes an important role for interferon type I. Thirdly, Callen and Wright review the current understanding and treatment of dermatomyositis in the age of the biologics.

The final article in the issue addresses the future of targeted therapies in dermatology. The discovery that cytokine patterns vary according to the development stage in each lesion of psoriasis, eczema, and other diseases could be exploited for prevention as well as for therapy. Schlapbach and Navarini also discuss the utility analyzing publications of off-label use of targeted therapies to understand the pathogenesis of rarer skin diseases, the potential future of combination therapies and immune deviation strategies to stably reprogram the pathogenic immune response.

Taken together, the present issue is a glance in the present and future of immunodermatology and shows a field yielding high-impact insights and creative approaches that will increasingly result in earlier, more efficacious and better tolerated therapies for our patients.