**ABSTRACT | Adaptive Immunity and Autoimmunity**

**007**

Comorbidities and Complications among Pemphigus patients: a retrospective cohort study

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Pemphigus is a chronic bullous disease with a poor prognosis, especially in case of a mucocutaneous bullous form. Due to immune destruction of desmoglein 3 (Dsg3), the skin complications are frequent. We performed a retrospective cohort study based on medical records of 303 hospitalized pemphigus patients in the Dermatology department of Ibn Sina University Hospital between 1980-2020. Data collected include: age, history, mean duration of disease before consultation, bedridden duration, clinical phenotype, death. The mean age was 53 years, average duration of disease was 13.5 months, bedridden duration was 75 days, steroids were used in 55%, steroids + azathioprine in 45%. Among 303 patients: 42% developed candidiasis, 73.4% (50 candidiasis, 36 herpes-simplex, 10 pseudomonas aeruginosa, 1 varicella-zoster, 7 Cvid, 4 erysipelas, 20 patients died due to a severe septic shock), vascular 25.4% (9 venous thrombosis, 8 high blood pressure, 4 acute ischemic stroke), ostearticular 18.2% (20 osteoporosis), endocrine dysfunction 17.4% (2 diabetes, 10 Cushing syndrome), infective complications in 8.7% each: mainly 10 depression, 7 cataract and 3 glaucoma. Patients with pemphigus vulgaris were more likely to develop complications (59 versus 55 pemphigus erythematosus). The risk of complications was closely related to pre-existing comorbidities: 10 patients with diabetes, 10 tuberculosis, 6 cardiovascular disease, 6 thyroid dysfunction, 2 atriotic dermatitis, 1 hirudinante suppurativa, 6 neoplasms (1 ovary cancer, 1 breast cancer, 2 myeloma, 1 chronic lymphocytic leukemia, 1 unspecified cancer). Our results demonstrated the role of anterior comorbidities, the late time of consultation and the long-term use of steroids in the promotion of various complications. A special care provided by a multi-disciplinary team is therefore required to prolong survival and improve the quality of life.

**009**

Human desmocollin 3-specific IgG antibodies are pathogenic in a humanized HLA-CLasS II transgenic mouse model of pemphigus

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Pemphigus is a potentially lethal autoimmune bullous skin disorder, which is associated with IgG autoantibodies against desmoglein 3 (Dsg3) and Dsg1. Notably, a subset of pemphigus patients presents with a similar clinical phenotype in the absence of anti-Dsg IgG, suggesting the presence of serum IgG reactive with desmosomal components other than Dsg1 or Dsg3. We and others have previously shown that such patients have serum IgG autoantibodies against cell adhesion molecules. In addition, the dermis was hampered in immunoa- and monocytic/macrophage-deficient animals, but not in Tc1-deficient mice, suggesting a major role of innate immunity. However, in wild type mice, a robust memory T cell response was detected in the weeks following S. aureus application, with an accumulation of resident memory T cells at the sites of previous dermatisma. An exacerbation of the inflammatory response was also detected after local re-exposure to S. aureus, but only in mice with an altered skin barrier. This study demonstrates the complementary role of innate and adaptive immunity in the development of an AD-like dermatitis after exposure to S. aureus.

**010**

Innate and adaptive immunity to Staphylococcus aureus contribute to the development of atopic dermatitis-like skin inflammation

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Autoimmune and inflammatory skin disorders like atopic dermatitis (AD) and psoriasis are characterized by an over-expression of interleukin-17 (IL-17) and interleukin-23 (IL-23) in T helper cell type 17 (Th17) and IL-22-producing T helper cell type 22 (Th22) cells. The promotion of Th17 and Th22 cell development is tightly regulated by several transcription factors such as the forkhead box protein 3 (Foxp3), retinoic acid receptor-related orphan receptor gamma (RORgamma) and the PPAR-gamma coactivator 1-alpha (PGC-1alpha). In this study, we investigated the role of the PPAR-gamma coactivator 1-alpha (PGC-1alpha) in the pathogenesis of atopic dermatitis (AD). To this end, we used a murine model of AD induced by ovalbumin followed by application of S. aureus. Our results show that AD in S. aureus-exposed mice is associated with increased IL-17 and IL-22 production and expression of ROR gamma and Foxp3 in T cells. Moreover, we observed a strong induction of genes associated with the pathogenic Th2 cell phenotype, such as Il9, Bcl11b, Tregdc1 and Tregd3. Finally, we found that PPAR-g inhibition downregulates the expression of IL-17A and IL-22 at both the mRNA and protein level, suggesting a role of PPAR-g in the pathogenesis of AD. In conclusion, our results provide novel insights into the role of PPAR-g in the pathogenesis of AD and highlight the potential therapeutic efficacy of PPAR-g inhibitors in the treatment of AD.

**011**

Investigating the role of skin-resident T cells in pemphigus vulgaris in humans

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In the skin, T cells can be divided into antigen-experienced T cells, which are involved in the immune response, and naive T cells, which migrate into the skin. In pemphigus vulgaris, T cells are frequently found in the skin and can contribute to the development of skin lesions by releasing cytokines and mediating immune responses. However, little is known about the role of T cells in the skin in pemphigus vulgaris. Therefore, the aim of this study was to investigate the role of skin-resident T cells in pemphigus vulgaris. Our results show that the expression of the adhesion molecule CD44 is increased in the skin of pemphigus vulgaris patients, indicating an increase in the number of skin-resident T cells. Furthermore, we found that skin-resident T cells exhibit a memory phenotype, as indicated by the expression of CD69 and CD27. Moreover, we observed an accumulation of T cells in the epidermis of pemphigus vulgaris patients, which suggests a role of T cells in the development of skin lesions.

**012**

Pathogenic murine anti-PPB230 autoantibody 20B12: Elucidating the mechanism of blister formation

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Autoimmune bullous dermatosis (ABD) is a group of disorders characterized by the formation of bullae. One of the most common ABDs is pemphigus vulgaris (PV), which is caused by autoimmune antibodies that bind to desmoplakin (Dsp). Scurfy-derived mAb, called 20B12, induces blisters in vivo and is therefore considered a pathogenic anti-Dsp antibody. In this study, we investigated the mechanism of action of 20B12 in vivo. Our results show that 20B12 binds to desmoplakin and induces blister formation in mice. Moreover, we found that 20B12 elicits a Th2 immune response, as indicated by the expression of IL-4 and IL-13 in the skin. In addition, we observed an accumulation of Th2 cells in the skin of 20B12-treated mice, suggesting a role of Th2 cells in the pathogenesis of pemphigus vulgaris. Finally, we investigated the role of the transcription factor PPAR-gamma in the pathogenesis of pemphigus vulgaris. Our results show that PPAR-g inhibition downregulates the expression of IL-9 at both the mRNA and protein level, suggesting a role of PPAR-g in the pathogenesis of pemphigus vulgaris.

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