Comorbidities and Complications among Pemphigus patients: a retrospective cohort study
E Haji, N. Mezni, K. Senouci, M. Meziane, L. Benzerki and N Ismaili Dermatology, Mohammed V University, Ibn Sina University Hospital, Rabat, Morocco

Pemphigus is a chronic bullous disease with a poor prognosis, especially in case of a mucocutaneous involvement. Due to immune dysregulation, drug reactions, and infections, 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 included: age, history, mean duration of disease before consultation, bedridden duration, clinical phenotype, death. The mean age was 53 years old, 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 complications, these were distributed as follows: 75.4% (50 candidiasis, 36 herpes-simplex, 10 pseudomonas aeruginosa, 1 varicella-zoster, 7 C.vid, 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), oesotrentic 18.2% (20 osteoporosis), endocrine dysfuction in 17.4% (12 diabetes, 10 Cushing syndrome, 3 thyrotoxicosis, 1 hypothyroidism, 1 insulin-dependent diabetes mellitus). This study demonstrates the complementary role of innate and adaptive immunity to S. aureus in pemphigus vulgaris in humans.

Allogeneic hematopoietic cell transplantation in pemphigus vulgaris: Atypical disease course
C. Zimmel, A. Polovkina, D. Didona, H. Unterberger, Z. Zivionek, C. Mols, P. Pitzscher and M. Hettl Department of Dermatology and Allergology, Philips University Marburg, Marburg, Germany; and 2 Department of Gynecology and Obstetrics, Philips University Marburg, Marburg, Germany

Pemphigus is a potentially lethal autoimmune bullous skin disorder, which is associated with IgG autoantibodies against desmogleins (Dsg) 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 Dsc3 in association with HLA-DRB1*04:02. In addition, the dermatis was hampered in immunohistopathology or macrophage-deficient animals, but not in T cell-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 dermatis. An exaggeration 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.

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

To decipher the autocrine function of IL-9 on TH cells, we isolated human TH cells from blister fluid of acute atopic contact dermatitis (aACD), expressing high levels of IL-9. Transcriptional profiling of these cells in presence and absence of recombinant IL-9 showed that approx. 1000 genes are differentially expressed in response to IL-9. Pathway analysis indicated that the upregulated genes are associated with conventional T(H)2 immune response. Surprisingly, we observed a strong induction of genes specifically associated with the pathogenic TH2 phenotype, such as IL9, IL17RB, HPGDS and PDGFB. In summary, we discovered that PPAR-g, a transcription factor closely linked to the pathogenic T(H)2 phenotype - regulates IL-9 expression and that autocrine IL-9 signals promote pathogenic features of TH2 cells. Together, our data provide a functional explanation for the consistently observed overexpression of PPAR-g, IL9, and IL9R in single cell transcriptomic data and suggest that T(H)2 cells might induce their pathogenic phenotype through autocrine IL-9 signaling.

Autocrine IL-9/IL-9R signaling induces a pathogenic phenotype in TH2 cells
N. Bentsch, T. Luther, C. Bazzini, O. Steck and C. Schlagbach Department of Dermatology, Dermatologische Uniere, University of Basel, Switzerland

Pemphigus vulgaris (PV) is a common gamma-chain cytokine, for which a range of pleiotropic functions have been proposed. However, an overarching role in humans remains elusive. IL-9 and its receptor IL-9R are expressed in skin biopsies of PV patients, suggesting an important function of autocrine IL-9 signaling in cutaneous immunity and allergy. Yet, the regulation of IL-9R expression on pTH2 cells and the auto- and paracrine functions of IL-9 remain incompletely understood. Here, we confirmed that IL-9R is strongly enriched in CRTh2+ memory TH2 cells isolated from blood and skin. Since previous data showed that these cells are associated with the expression of the transcription factor PPAR-g, we hypothesized that PPAR-g controls IL-9R expression. Indeed, we found that PPAR-g inhibition downregulated the expression of IL-9R at the RNA as well as the protein level in TH2 clones. To decipher the autocrine function of IL-9 on TH2 cells, we isolated human TH2 cells from blister fluid of acute atopic contact dermatitis (AaCD), expressing high levels of IL-9. Transcriptional profiling of these cells in presence and absence of recombinant IL-9 showed that approx. 1000 genes are differentially expressed in response to IL-9. Pathway analysis indicated that the upregulated genes are associated with conventional T(H)2 immune response. Surprisingly, we observed a strong induction of genes specifically associated with the pathogenic TH2 phenotype, such as IL9, IL17RB, HPGDS and PDGFB. In summary, we discovered that PPAR-g, a transcription factor closely linked to the pathogenic T(H)2 phenotype - regulates IL-9 expression and that autocrine IL-9 signals promote pathogenic features of TH2 cells. Together, our data provide a functional explanation for the consistently observed overexpression of PPAR-g, IL9, and IL9R in single cell transcriptomic data and suggest that T(H)2 cells might induce their pathogenic phenotype through autocrine IL-9 signaling.

Pathogenic murine anti-BP230 autoantibody 20B12: Elucidating the mechanism of blister formation
V. Bolduan, S. Haeberle, E. Viciani, T. Ramcke, A. Enk and F. Hardach

Investigating the role of skin-resident T cells in pemphigus vulgaris in humans
C. Zimmel, A. Polovkina, D. Didona, H. Unterberger, Z. Zivionek, C. Mols, P. Pitzscher and M. Hettl Department of Dermatology and Allergology, Philips University Marburg, Marburg, Germany; and 2 Department of Gynecology and Obstetrics, Philips University Marburg, Marburg, Germany

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

To decipher the autocrine function of IL-9 on TH cells, we isolated human TH cells from blister fluid of acute atopic contact dermatitis (aACD), expressing high levels of IL-9. Transcriptional profiling of these cells in presence and absence of recombinant IL-9 showed that approx. 1000 genes are differentially expressed in response to IL-9. Pathway analysis indicated that the upregulated genes are associated with conventional T(H)2 immune response. Surprisingly, we observed a strong induction of genes specifically associated with the pathogenic TH2 phenotype, such as IL9, IL17RB, HPGDS and PDGFB. In summary, we discovered that PPAR-g, a transcription factor closely linked to the pathogenic T(H)2 phenotype - regulates IL-9 expression and that autocrine IL-9 signals promote pathogenic features of TH2 cells. Together, our data provide a functional explanation for the consistently observed overexpression of PPAR-g, IL9, and IL9R in single cell transcriptomic data and suggest that T(H)2 cells might induce their pathogenic phenotype through autocrine IL-9 signaling.

Pathogenic murine anti-BP230 autoantibody 20B12: Elucidating the mechanism of blister formation
V. Bolduan, S. Haeberle, E. Viciani, T. Ramcke, A. Enk and F. Hardach

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

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

PPAR-g - a transcription factor closely linked to the pathogenic TH2 phenotype - regulates IL-9 expression and that autocrine IL-9 signals promote pathogenic features of TH2 cells. Together, our data provide a functional explanation for the consistently observed overexpression of PPAR-g, IL9, and IL9R in single cell transcriptomic data and suggest that T(H)2 cells might induce their pathogenic phenotype through autocrine IL-9 signaling.