**Adaptive and Auto-Immunity | ABSTRACTS**

**025** Extracellular vesicles induce STING-mediated proinflammatory cytokines in Dermatomyositis

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Dermatomyositis (DM) is an acquired inflammatory myopathy characterized by chronic skin inflammation. The pathogenesis of DM is still unclear. Extracellular vesicles (EVs) are lipid bilayer membrane vesicles existing in various bodily fluids and implicated in the pathogenesis of autoimmune diseases. As type I interferons, specifically IFNβ, are uniquely elevated in DM, and Stimulator of interferon genes (STING) works as a critical sensor and adaptor in type 1 IFN signaling, we hypothesized that EVs derived from DM patients' plasma might trigger STING-mediated proinflammatory effects. DM patients were recruited in the dermatology clinic at U Penn. Peripheral blood mononuclear cells (PBMCs) were isolated by Ficoll gradient. EVs derived from plasma were isolated via ultracentrifugation. The supernatant was harvested for ELISA and the lysed cells were subjected to Western blot (WB). PBMCs were stimulated by EVs. We found that DM patients’ plasma-derived EVs triggered cytokines release (IFNβ: 30.24±0.65 vs control (2.68±0.35); TNFα: 1451±98.40 vs control (16.75±1.407)pg/mL; n=6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients’ plasma derived EVs-triggered cytokines production (IFNβ: (21.58±2.25 vs (28.34±1.73); TNFα: (434.8±94.50 vs (919.1±1.33).Phosphorylation. To further explore whether STING phosphorylation and the proinflammatory effects were dependent on EVs-captured DNA, EVs were pretreated with DNase I and Triton X-100 and DNase to digest DNA. TNFα-100 and DNase pretreatment decreased EVs-triggered cytokines release (IFNβ: (4.7±13±2.80 vs (28.94±5.47); TNFα: (920.3±137.03 vs (136±329.3 pg/mL; n=4) and STING activation. Thus we found EVs derived from plasma could trigger STING-mediated proinflammatory effects in DM. The STING phosphorylation during EVs triggering of proinflammatory effects was at least partially mediated by DNA captured by EVs. Targeting STING might provide insight into a potential therapeutic approach for DM.

**026** Increased levels of high mobility group box 1 in the serum and skin in patients with generalized pustular psoriasis

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High-mobility group box-1 (HMGB-1) is a highly abundant pro-inflammatory protein which is associated with the pathogenesis of inflammatory and autoimmune diseases, such as drug eruption, sepsis, and rheumatoid arthritis. HMGB-1 has a dual function: inside the cells, it plays a role in transcriptional regulation. While outside the cells, it plays an alarm function or damage-associated molecular pattern. It has been reported that HMGB-1 expression levels in the serum and skin were increased in patients with psoriasis vulgaris (PV). However, HMGB-1 expression in patient with generalized pustular psoriasis (GPP) was unknown. In this study, we investigated the HMGB-1 levels in the serum and skin in patient. To analyze the expression levels of HMGB-1, we performed ELISA and immunohistochemistry in the lesional skin. GPP patients with CD, glomerulonephritis (GN), and healthy controls (HC). Immunohistochemistry analysis revealed that HMGB-1 expression levels in epidermis were significantly increased in patients with GPP compared to that in patients with PV, AD and HC. In addition, GPP patients had elevated serum HMGB-1 levels compared to AD patients and HC. Furthermore, serum levels of HMGB-1 were significantly decreased after the systemic treatment compared to baseline levels. In the correlation analysis, a high positive correlation was detected between serum HMGB-1 levels and Japanese severity criteria for GPP in patients with GPP. In conclusion, our findings show that HMGB-1 might be involved in the pathogenesis of GPP and is a simple and attractive marker for the analysis of disease severity and the effectiveness of treatment in patients with GPP.

**027** A pilot study of human salivary N- and O-glycans in Bullous pemphigoid

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Aberrant glycosylation is strongly correlated with the pathogenesis of various autoimmune diseases. However, the precise alterations of glycosylation remain largely unknown in Bullous pemphigoid (BP). Herein we aimed to evaluate changes of salivary N- and O-glycan profiles associated with BP. A total of 37 lesions were quantified in BP as compared to healthy donors. Among these quantified lesions, 9 and 13 lesions were up- or down-regulated in BP, respectively. The expression of 9 lesions increased by up to 1.5- to 3.3-fold in BP relative to that of controls, in which AAL, LACal and PNA showed significantly increased. Conversely, 13 lesions showed a 0.36- to 0.64-fold decrease in BP patients, in which the PTL-L, PWMM, MALN, SNA, PWN and PTL-L showed dramatically decreased levels. The comparison of changes in salivary glycopatterns in BP, these differentially expressed lesions were classified into four categories according to their glycan specificity: (a) mucin type O-glycans, (b) GalNAc 认识 motif recognizing lectins T antigens (LCA and M1C), (c) fucose recognizing lectins (LAA) and (d) III/tri/tertia antenary structure recognizing lectins (PHA-E). A decrease in O-glycans was observed in BP, on the other hand T antigens was diminished sharply for BP as compared to controls, suggesting biosynthesis of precursor of mucin-type O- glycan was activated in BP. Furthermore, we observed an increase in fucosylated salivary in patients with BP vs controls (for AAL) and a corresponding decrease of inverting N-glyco- sylation (MAL-I) associated to be associated with disease severity. In conclusion, we associated levels of saliva-glycosylation with BP compared to controls. These findings could increase our understanding mechanisms of BP pathogenesis and be used to develop diagnostics or guide treatment.

**028** Circulating serum amyloid A levels correlate with the severity of generalized pustular psoriasis

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Generalized pustular psoriasis (GPP) is a severe and rare variant of psoriasis, which presents with skin blisters at local tissue sites. The pathogenesis is not fully understood. Some data suggest an association with certain mediators of the IL-17A pathway, strongly suggesting that pemphigus has a unique proinflammatory profile. In the present study, we report on the levels of circulating serum amyloid A (SAA) in patients with GPP and psoriasis vulgaris (PV) as well as healthy controls, and assessed its correlations with inflammatory markers like blood neutrophil count and CRP levels. Serum amyloid A (SAA) is one of the most prominent positive acute phase proteins, which is highly elevated in serum due to systemic inflammation. Here, we measured the levels of circulating SAA in patients with GPP and psoriasis vulgaris (PV) as well as healthy controls, and assessed its correlations with inflammatory markers like blood neutrophil count and CRP levels. Sera were obtained from 25 patients with GPP (17 males and 8 females) ranging from 16 to 69 years old (mean = 45.9), 40 patients with PV (28 males and 12 females, mean = 51.2, PASS score < 10), and 38 healthy controls (22 males and 16 females, mean = 48.8). Serum SAA levels were evaluated by ELISA (Human Serum Amyloid A1Dustell ELISA, R&D systems, Minneapolis, MN, USA). The serum CRP levels were measured by latex High-Sensitivity, Roche Diagnostics, Shanghai, China. The mean levels of serum SAA in GPP and PV patients were significantly higher than healthy control subjects (76.0±3.14±28.8 mg/mL; 191.1±2.3±208.51 mg/mL vs. 81.8±9.5±12 mg/mL, while the difference between GPP and PV groups was also significant. As for the correlation between SAA levels and markers for disease severity in patients with GPP, we observed that SAA levels positively correlated with neutrophil count (r = 0.40, P = 0.04). In summary, we described the elevation of circulating SAA levels in patients with GPP, and serum SAA levels might reflect the clinical severity of GPP, though the findings of this study should be confirmed in a prospective study of a larger number of patients.