**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 (IFNs), specifically IFN-β, are uniquely elevated in DM, and Stimulator of interferon genes (STING) works as a critical sensor and adaptor in type I 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 used for Western blot. STING-deficient (STING−/−) PBMCs were stimulated by EVs. We found that DM patients’ plasma-derived EVs triggered cytokines release (IFNβ: 30.24 ± 0.65 vs control: 2.63 ± 0.15; TNFα: 1451 ± 98.40 vs control: 16.75 ± 1.40pg/ml; n=6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients’ plasma-derived EVs-triggered cytokines production (IFNβ: 21.58 ± 2.22 vs 28.34 ± 1.73; TNFα: 434 ± 84.90 vs 919 ± 1.13pg/ml; n=6) via suppressing STING and its downstream signal TK1, IRF3, and NFκB phosphorylation. To further explore whether STING phosphorylation and the proinflammatory effects were caused by EVs, we used EVs from patients with systemic lupus erythematosus (SLE) and healthy controls. These EVs did not induce STING phosphorylation and proinflammatory effects in DM patients. We conclude that EVs derived from DM patients’ plasma can 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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A 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 acts as a damage-associated molecular pattern. It has been reported that HMGB-1 expression levels are significantly increased in patients with pustular psoriasis (PV). However, HMGB-1 expression in patients with generalized pustular psoriasis (GPP) was unknown. In this study, we investigated the HMGB-1 levels in the serum and skin in patients with GPP. To analyze the expression levels of HMGB-1, we performed ELISA and immunohistochemistry in the lesional skin samples with GPP. The high levels of HMGB-1 correlated with the disease severity and the effectiveness of treatment in patients with GPP.}

**027 A pilot study of human salivary N- and O-glycan profiles 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). In this study, we aimed to evaluate changes of salivary N- and O-glycan profiles associated with BP. A total of 37 lectins were quantified in BP as compared to healthy donors by performing lectin microarray analysis. Among these quantified lectins, 9 and 13 lectins were up- or down-regulated in BP, respectively. The expression of 9 lectins increased by up to 1.5- to 3.3-fold in BP relative to that of controls, in which AAL, Jacalin and PNA showed significantly increased. Conversely, 13 lectins showed a 0.36- to 0.64-fold decrease in BP patients, in which the PTL-L, PWM, MAL, SNA, PTA and PHA-E showed dramatically decreased NFs. To facilitate the comparison of changes in salivary glycopatterns in BP, these differentially expressed lectins were classified into four categories according to their glycan specificity: (a) mucin-type glycoconjugates recognizing (MALL, SNA, PWM, PTL-L); (b) N-acetyllactosamine motif recognizing lectins (Tαnacalin and PNA); (c) fucose recognizing lectins (AAL) and (d) bi/trisecta antenmy structure recognizing lectins (PHA-E). A decrease in O-glycosylation was observed in BP, on the other hand Tαnacatin 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 proteins in patients with BP vs controls (for AAL) and a corresponding decrease in Insectic N-glyco- sylation was also observed in BP. JAWSI was frequently expressed in BP, and seemed to be associated with disease activity. In conclusion, we associated levels of salvia-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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Circulating 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 A1 Dupont ELISA, R&D systems, Minneapolis, MN, USA). The serum CRP levels were measured with a latex (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 (764.03 ± 146.28 pg/mL, 191.14 ± 208.51 ng/mL vs. 81.85 ± 95.12 ng/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 presented a positive correlation with neutrophil count (r = 0.4, p = 0.04) and disease severity (r = 0.40, P = 0.04). In summary, we described the elevation of circulating SAA levels in patients with GPP, and serum SAA levels may 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.

**029 Transcriptome analysis suggests a role of IL-17-related genes in pemphigus**

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Transcriptome analysis suggests a role of IL-17-related genes in pemphigus vulgaris. In pemphigus vulgaris (PV), IL-17 expression was also reported to be present in pemphigus skin. To better understand the immune signature of pemphigus, we performed transcriptome analysis of pemphigus skin. First, we performed a large scale analysis by whole transcriptome shotgun sequencing (RNA-seq) of six lesional pemphigus vulgaris skin samples. We compared the data of lesional pemphigus skin to data obtained from healthy control skin samples (n=6). By bioinformatics analysis, we identified an unexpected IL-17A-a associated immune signature in pemphigus skin with some similarities to psoriatic skin. We observed a significant increase in IL-17A pathway by RT-PCR in lesional pemphigus vulgaris with a positive feedback effect on functionally different genes varying from skin modelling genes, antimicrobial peptides as well as pro-inflammatory chemokines and cytokines. To confirm the identified pathways, we performed RT-qPCR analysis of IL-17A pathway in lesional and non-lesional skin from 29 patients. In agreement with previous reports, we found some expression of IL-4 and IL-6. Strikingly, we could identify the RNA-seq data and detected high expression of IL-17A and associated mediators. In subsequent analysis, we compared the immune signature of lesional and non-lesional tissue. We found a significant correlation between lesional and non-lesional tissue samples. Together, we found some expression of IL-4 and IL-6, but dominant expression of certain mediators of the IL-17A pathway, strongly suggesting that pemphigus has a unique IL-17A-a associated immune signature that may be important for autoimmunity and skin blistering at focal tissue sites.