025 Extracellular vesicles induce STING-mediated proinflammatory cytokines in Dermatomyositis
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Dermatomyositis (DM) is an acquired immunologic myopathy characterized by chronic skin inflammation. The pathogenesis of DM is still unclear. Extracellular vesicles (EVs) are lipid bilayer membrane vesicles existing in various body fluids and implicated in the pathogenesis of autoimmune diseases. As type I interferons, specifically IFN-λ, 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 subjected for qPCR. STING-deficient PBMCs were stimulated by EVs. We found that DM patients’ plasma derived EVs triggered cytokines release (IFN-λ: 30.24 ± 0.65 vs control (2.63 ± 0.15); TNF-α: 1451 ± 98.40 vs control (16.75 ± 1.40) pg/mL; n = 6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients’ plasma derived EVs-triggered cytokines production (IFN-λ: 21.58 ± 2.22 vs (28.4 ± 1.73); TNF-α: 434.8 ± 9.40 vs (919.1 ± 1.13) pg/mL; n = 6) via suppressing STING and its downstream signal STIK, IRF3, and NFκB phosphorylation. To further explore whether STING phosphorylation and the proinflammatory responses were caused by EVs-captured DNA, we further inhibited the EVs-targeting DNase. We found that EVs-captured DNA, EVs were pretreated with Triton X-100 and DNase to digest DNA. Furthermore, we found that 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 the transcriptional regulation. While outside the cells, it plays as an alarmin or a damage-associated molecular pattern. It has been reported that HMGB-1 expression levels of the serum and skin were increased in patients with psoriasis vulgaris (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 GPP patients. To analyze the expression levels of HMGB-1, we performed ELISA and immunohistochemistry in the lesional skin of patients with GPP. Using a mouse model of systemic lupus erythematosus (SLE) induced by 2,6,10,14-tetramethylpentadecane (TMPD), we recently demonstrated that IRF7-deficient mice developed either glomerulonephritis or the autoantibody production. Furthermore, these genetic knockouts were prompted us to re-examine the role of IFN and proinflammatory cytokines in autoimmune diseases. As type I interferons, specifically IFN-λ, 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 subjected for qPCR. STING-deficient PBMCs were stimulated by EVs. We found that DM patients’ plasma derived EVs triggered cytokines release (IFN-λ: 30.24 ± 0.65 vs control (2.63 ± 0.15); TNF-α: 1451 ± 98.40 vs control (16.75 ± 1.40) pg/mL; n = 6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients’ plasma derived EVs-triggered cytokines production (IFN-λ: 21.58 ± 2.22 vs (28.4 ± 1.73); TNF-α: 434.8 ± 9.40 vs (919.1 ± 1.13) pg/mL; n = 6) via suppressing STING and its downstream signal STIK, IRF3, and NFκB phosphorylation. To further explore whether STING phosphorylation and the proinflammatory responses were caused by EVs-captured DNA, we further inhibited the EVs-targeting DNase. We found that EVs-captured DNA, EVs were pretreated with Triton X-100 and DNase to digest DNA. Furthermore, we found that 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.

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). Herein we aimed to evaluated 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. Among these lectin profiles, lectins defined as up-regulated in BP 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, lacaln 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, MALN, SNA, PWM, PTL-L, BiN, acetylcysteamine motif recognizing lectins T αntigen (lacaln and PNA), (c) fucose recognizing lectins (AAL), and (d) bi/tri/tertha antemery structure recognizing lectins (PHA-E). A decrease in O-glycosylation was observed in BP, on the other hand T antigen was diminished sharply for BP as compared to controls, suggesting biosynthesis of precursor of mucin-type O-glycans was diminished. Aberrant glycosylation is strongly correlated with the pathogenesis of various autoimmune diseases. As type I interferons, specifically IFN-λ, 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 subjected for qPCR. STING-deficient PBMCs were stimulated by EVs. We found that DM patients’ plasma derived EVs triggered cytokines release (IFN-λ: 30.24 ± 0.65 vs control (2.63 ± 0.15); TNF-α: 1451 ± 98.40 vs control (16.75 ± 1.40) pg/mL; n = 6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients’ plasma derived EVs-triggered cytokines production (IFN-λ: 21.58 ± 2.22 vs (28.4 ± 1.73); TNF-α: 434.8 ± 9.40 vs (919.1 ± 1.13) pg/mL; n = 6) via suppressing STING and its downstream signal STIK, IRF3, and NFκB phosphorylation. To further explore whether STING phosphorylation and the proinflammatory responses were caused by EVs-captured DNA, we further inhibited the EVs-targeting DNase. We found that EVs-captured DNA, EVs were pretreated with Triton X-100 and DNase to digest DNA. Furthermore, we found that 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.