Additionally, flow cytometric analysis indicated that the accumulation of IL-17A-producing activation as well as the development and keratinization of epidermis by RNA sequencing. Skin of mice by topical IMQ application. Histological and immunohistochemical (Ki67, cytokines in IL-17A-treated HaCaT cells and imiquimod (IMQ)-treated mouse bone marrow-derived dendritic cells (P<0.001). Pсорiotasmin dermatitis was then induced on the left ear skin of mice by topical IMQ application. Histological and immunohistochemical (Ki67, CD11c and CD3) examinations showed much milder epidermal hyperplasia and inflammatory infiltration upon MTX-loaded MNs treatment. We also found that MTX-loaded MNs downregulated leukocyte chemokinesis and migration, T cell proliferation and activation as well as the development and keratinization of epidermis by RNA sequencing. Additionally, flow cytometric analysis indicated that the accumulation of IL-17A-producing γβ T cells in MNs-treated left ear skin and the draining lymph nodes were both significantly inhibited (P<0.001). Furthermore, the subsequent generation of psoriatic phenotype on the right ears by IMQ rechallenge was markedly restrained compared with untreated mice. In conclusion, MTX-loaded MNs can not only ameliorate local skin inflammation by regulating immune and stromal components but also show a concomitant antipsoriatic effect against recurrent immune disorders at a distant site, emerging as a potential alternative topical treatment for psoriasis.

The association of platelet activation markers, neutrophil extracellular traps and anti-mitochondrial autoantibodies with cutaneous manifestations in Systemic Lupus Erythematous L Mainville1, J Melki1, Y Becker1, A Julien1, N Cloutier1, E Rollet-Labelle1, C Loord2, E Bolard1 and P Fortin1 1 Centre de recherche du CHU de Québec – Université Laval, Québec, Canada; 2 Department de mathematiques et statistique, Universite Laval, Québec, Quebec, Canada; 3 University of Washington, Seattle, Washington, United States Systemic Lupus Erythematous (SLE) is an autoimmune disease associated with platelet activation, formation of neutrophil extracellular traps (NETs) and development of anti-mitochondrial autoantibodies (AAAM). In the current study, we investigated the clinical utility of these markers and autoantibodies in cutaneous lupus manifestations. Clinical data on cutaneous manifestations were obtained in a large SLE cohort (n=73) through review of SLE questionnaires, SLICC Classification Criteria and revised ACR Criteria for SLE. Three main outcome measures: cutaneous manifestations reported by physicians, by patients, and additional lupus manifestations, were constructed to analyse their association with the studied markers. In logistic regression analyses, NETs and antibodies to La/SSB were protective against “cutaneous manifestations reported by patients” (OR=0.02; 95% CI 0.05-0.04) due to their effect on “rash other than on cheeks”. No statistically significant association was found between predictor variables and “cutaneous manifestations reported by physicians”. IgG-bound platelets were associated with “additional cutaneous manifestations” due to the perinuclear erythema item (0.01; 95% CI 0.01-0.02). Based on these findings, we suspect that “rash other than on cheeks” is a discriminating clinical finding for cutaneous manifestations of SLE. We then reanalyzed the data excluding non-specific cutaneous manifestations of SLE but were not able to find any further significant results. Our results demonstrate no significant association between our predictors and specific SLE cutaneous manifestations, as our definitions for skin manifestations were crude. This work will lead us to implement better physician's evaluation of skin lesions in lupus, including CLASI, and information derived from skin biopsies.

Dextran-based acitretin nanoparticle ameliorates imiquimod-induced psoriasis-like skin inflammation H Koguchi-Yoshioka1,2, R Watanabe2, Y Matsumura2, T Matsuoka2, H Shimano2 and D Kim1,2,3 1 Centre de recherche du CHU de Québec – Université Laval, Québec, Canada; 2 School of Chemistry and Chemical Engineering, Huazhong University of Science and Technology, Wuhan, China; 3 School of Medicine, Gifu, Japan and 2 Disease Control and Prevention, Fujita Health University Graduate School of Medicine, Gifu, Japan and 2 Disease Control and Prevention, Fujita Health University Graduate School of Health Sciences, Toyoake, Japan Psoriasis is a Th17-mediated disease related with metabolic skews, the relation between T-cell reactive and cellular metabolism has not been fully evaluated in psoriasis. In this research, the metabolic condition of blood T cells were evaluated in 35 psoriatic patients by use of an extracellular flux analyzer. The impact of apremilast on cellular metabolic condition was also investigated in total 71 patients with psoriasis both in vivo and in vitro. The oxygen consumption rate (OCR) was significantly higher in blood T cells of psoriasis patients compared to healthy controls (p=0.0014), and the patients with higher OCR achieved higher PASI improvement rate. The decrease of OCR and cellular ATP levels were correlated as well as non-significantly. A decrease of OCR and cellular ATP levels was also observed in psoriatic patients treated with apremilast (p=0.032). The decrease of OCR was presumably attributed to the reactive oxygen species (ROS) because the cellular ROS level was higher in psoriatic blood T cells compared to healthy controls (p=0.0022) and the in vitro inhibition or elimination of ROS led to the decrease of cellular OCR. The superoxide dismutase was also upregulated by co-culturing the psoriatic blood T cells with patients with higher OCR treatment (p=0.0014). The decrease of OCR and cellular ATP levels tended to be more pronounced in the patients with psoriasis (r=0.3454, p=0.0454), and the patients with higher serum LDH levels tended to be benefited more by apremilast (r=0.4602, p=0.0206). Our results indicate that the circulating T cells in psoriatic patients have higher metabolic activities with more oxygen consumption and ROS production. Our results also suggest that the OCR and possibly the serum LDH levels can be a predictor of treatment preference.

Indoleamine 2,3-dioxygenase 2 knockout exacerbates imiquimod-induced psoriasis-like skin inflammation K Fuji1, Y Yamamoto2, K Saito2 and M Seishima1 1 Dermatology, Gifu University Graduate School of Medicine, Gifu, Japan and 2 Disease Control and Prevention, Fujita Health University Graduate School of Health Sciences, Toyoake, Japan Indoleamine 2,3-dioxygenase 2 (IDO2) is a common enzyme in the immune system and the pathogenesis is reported to be due to the activation of the interleukin-2/interleukin-17 (IL-2/IL-17) pathway. Indoleamine 2,3-dioxygenase 1 (IDO1) is known to be induced an enzyme that suppresses immune responses and there are several reports showing the association with psoriasis. On the other hand, IDO2 is an isomer of IDOs, recently identified catalytic enzyme in the tryptophan-kynurenine pathway. Recent studies reported that IDO2 is expressed in dendritic cells and monocytes. The expression of IDO2 in immune cells suggests that IDO2 contributes to immune function. However, the role of IDO2 in the pathogenesis of psoriasis remains unclear. In this study, to elucidate the role of IDO2 in psoriasis, we assessed imiquimod-induced psoriasis-like dermatitis in IDO2 knockout (KO) mice. Wild-type (WT) and IDO2 KO female mice at 8 weeks old received a daily topical dose of 65.2 mg commercially available imiquimod cream on ears for 7 consecutive days. Skin inflammation in IDO2 mice were evaluated with erythema, scaling and ear thickness was significantly worse than that of WT mice. In addition, fluorescence-activated cell sorter (FACS) analysis revealed real-time OCR and extracellular ATP levels of TNF-α, IL-23p19 and IL-17A, key cytokines involved in the development of psoriasis, were increased in IDO2 KO mice than in WT mice on day 7. These results suggest that IDO2 suppresses the skin inflammation in imiquimod-induced psoriasis-like dermatitis.