The tryptophan metabolism enzyme, L-kyureninase, is a novel inflammatory factor in psoriasis and other inflammatory diseases. L-kyureninase is involved in the tryptophan metabolism pathway, which is implicated in the pathogenesis of psoriasis.

The autoantibody production in SLE is not entirely understood, one proposed mechanism is that relative immunosuppression might be a future strategy for the treatment of psoriasis.

The tryptophan metabolism enzyme, L-kyureninase, is a novel inflammatory factor in psoriasis and other inflammatory diseases. L-kyureninase is involved in the tryptophan metabolism pathway, which is implicated in the pathogenesis of psoriasis.

The purpose of the study was to identify clinical and laboratory predictors of skin disease outcome in patients with refractory dermatomyositis (DM) treated with rituximab. We analyzed data for 116 DM patients (68 with adult DM and 48 with juvenile DM) in the Rituximab in Myositis Trial. Skin disease outcome was defined as the absolute change from baseline to 24 weeks in the Cutaneous Disease Activity visual analog scale (VAS) score where a negative change indicated improvement and a positive change indicated worsening. We analyzed the association of the following baseline variables with skin disease outcome: demographics, dermatomyositis subtype, clinical and laboratory parameters, myositis autoantibodies (antisynthetase, anti-Mi-2, other autoantibodies, and no autoantibodies), and interferon (IFN)-regulated chemokines. Multivariable linear regression models were developed using stepwise variable selection methods. A multivariable model to predict skin disease outcome included three factors at baseline: Cutaneous Disease Activity VAS score (β [regression coefficient] = -0.48, P < 0.01), Constitutional Disease Activity VAS score (β = 0.20, P = 0.02), and anti-Mi-2 status (β = -0.42, P = 0.05). Skin disease outcome was more likely to worsen in patients with cutaneous Disease Activity VAS scores at baseline more than -0.48, Constitutional Disease Activity VAS scores at baseline more than 0.20, and anti-Mi-2 status more than -0.42. These findings emphasize aspects of AA not commonly considered in the evaluation of human and other species affected.

The tryptophan metabolism enzyme, L-kyureninase, is a novel inflammatory factor in psoriasis and other inflammatory diseases. L-kyureninase is involved in the tryptophan metabolism pathway, which is implicated in the pathogenesis of psoriasis.

The purpose of the study was to identify clinical and laboratory predictors of skin disease outcome in patients with refractory dermatomyositis (DM) treated with rituximab. We analyzed data for 116 DM patients (68 with adult DM and 48 with juvenile DM) in the Rituximab in Myositis Trial. Skin disease outcome was defined as the absolute change from baseline to 24 weeks in the Cutaneous Disease Activity visual analog scale (VAS) score where a negative change indicated improvement and a positive change indicated worsening. We analyzed the association of the following baseline variables with skin disease outcome: demographics, dermatomyositis subtype, clinical and laboratory parameters, myositis autoantibodies (antisynthetase, anti-Mi-2, other autoantibodies, and no autoantibodies), and interferon (IFN)-regulated chemokines. Multivariable linear regression models were developed using stepwise variable selection methods. A multivariable model to predict skin disease outcome included three factors at baseline: Cutaneous Disease Activity VAS score (β [regression coefficient] = -0.48, P < 0.01), Constitutional Disease Activity VAS score (β = 0.20, P = 0.02), and anti-Mi-2 status (β = -0.42, P = 0.05). Skin disease outcome was more likely to worsen in patients with cutaneous Disease Activity VAS scores at baseline more than -0.48, Constitutional Disease Activity VAS scores at baseline more than 0.20, and anti-Mi-2 status more than -0.42. These findings emphasize aspects of AA not commonly considered in the evaluation of human and other species affected.

The purpose of the study was to identify clinical and laboratory predictors of skin disease outcome in patients with refractory dermatomyositis (DM) treated with rituximab. We analyzed data for 116 DM patients (68 with adult DM and 48 with juvenile DM) in the Rituximab in Myositis Trial. Skin disease outcome was defined as the absolute change from baseline to 24 weeks in the Cutaneous Disease Activity visual analog scale (VAS) score where a negative change indicated improvement and a positive change indicated worsening. We analyzed the association of the following baseline variables with skin disease outcome: demographics, dermatomyositis subtype, clinical and laboratory parameters, myositis autoantibodies (antisynthetase, anti-Mi-2, other autoantibodies, and no autoantibodies), and interferon (IFN)-regulated chemokines. Multivariable linear regression models were developed using stepwise variable selection methods. A multivariable model to predict skin disease outcome included three factors at baseline: Cutaneous Disease Activity VAS score (β [regression coefficient] = -0.48, P < 0.01), Constitutional Disease Activity VAS score (β = 0.20, P = 0.02), and anti-Mi-2 status (β = -0.42, P = 0.05). Skin disease outcome was more likely to worsen in patients with cutaneous Disease Activity VAS scores at baseline more than -0.48, Constitutional Disease Activity VAS scores at baseline more than 0.20, and anti-Mi-2 status more than -0.42. These findings emphasize aspects of AA not commonly considered in the evaluation of human and other species affected.
Skin-homing and systemic T-cell subsets show higher activation in atopic dermatitis versus psoriasis

T. Casaro, 1, 2, M. Garcia-Rodriguez, 3, N. Suarez-Farinaz, 4, JG Krouwer 5 and E. Gutman-Yassky 6

1 Investigative Dermatology, The Rockefeller University, New York, NY, 2 Dermatology, Tel-Hashomer Hospital, Tel Aviv, Israel and 3 Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY

Atopic dermatitis (AD) and psoriasis are characterized by T-cell infiltration in skin lesions, but their comparable systemic T-cell activation is unclear. We compared T-cell activation and cytokine producing cell-frequency in blood of adult AD and psoriasis patients using flow-cytometry. We measured cytokines, T-regulatory cells (Tregs) and T cell activation markers in central and effector memory (Tcm and Tem) skin-homing/cutaneous lymphocyte antigen (CLA) + and CLA- subsets from 24 psoriasis patients, 35 AD patients and 13 controls. Early (CD69), mid (HLA-DR) and late (HLA-DR) activation markers were quantified in Tcm (CCR7+CD45RO+) and Tem (CCR7-CD45RO+) populations. AD showed higher frequency of CLA+ “polar” T-cell subsets (p<0.001). In both diseases, CLA- T-cells were significantly more activated compared to respective CLA+ sub-sets (p<0.01), suggesting their prominent role in inflammatory skin diseases. AD demonstrated higher levels of ICOS/HLA-DR activation as well as apoptosis and cell lysis in CLA- membrane subsets (p<0.01). CD69 was the only activation marker that was higher in psoriasis (p<0.001), whereas ICOS expression was significantly higher in AD (p<0.0001), compatible with their respective roles in Th17 and Th2 responses. Significant correlation was observed between ICOS+ and CLA+ in central and effector memory cells (p<0.05). These results indicate that the B cell repertoire and the antibody repertoire in pemphigus are both oligoclonal but not completely overlapped. There is a clonally dominant serological autoimmune antibody response which is specific for the desmoglein (Dsg) 3 extracellular (EC) domains. These results indicate that the B cell repertoire and the antibody repertoire in pemphigus are both oligoclonal but not completely overlapped. There is a clonally dominant serological autoimmune antibody response which is specific for the desmoglein (Dsg) 3 extracellular (EC) domains. These “hot spots” offer prioritized loci for downstream fine mapping studies in the search for cutaneous susceptibility loci. Overall, these data provide further insights regarding the molecular genetic basis of disease heterogeneity in lupus.

Peripheral blood gene expression identifies systemic pathways and processes in chronic cutaneous lupus erythematosus (CCLE)

R. Dey-Rao and S. Smith-Dewarman

University at Buffalo, Buffalo, NY

Lupus erythematosus (LE) is an autoimmune systemic disease with confounding etiology and pathogenesis. Cutaneous lesions develop in 80% of LE patients at some point and 10-40% patients with cutaneous LE (CLE) show transitions to systemic LE (SLD). Major gaps remain regarding pathogenetic mechanisms underlying the development of cutaneous lesions in lupus. As systemic changes are likely to underlie skin specific manifestation, we analyzed global gene expression by microarray in peripheral blood in a cohort of CLE patients and healthy controls. Unbiased clustering analyses identifies a “disease” based signature that distinctly separates patients from healthy controls. Functional annotation of CCLE-blood differentially expressed genes (DEGs) using DAVID and Metacore highlight enrichment of a dysregulated immune response with prominent Type I interferon association as well as apoptosis and cell lysis in CLA- membrane subsets. There is a 24% overlap of the CCLE blood and lesional skin transcriptional profile from a previous analysis by our group. Two of the four transcriptional “hot spots” (chromosomal regions harboring statistically increased numbers of CCLE-blood DEGs) are overlapping. These “hot spots” offer prioritized loci for downstream fine mapping studies in the search for CCLE specific susceptibility loci. Overall, these data provide further insights regarding the molecular genetic basis of disease heterogeneity in lupus.
B-cell profiling to predict clinical response following Rituximab therapy in patients with autoimmune blistering diseases

S Bookow,1 T Mouly,1 T Shih1,2,1 1 Dermatology, Emory University, Atlanta, GA; 2 Rheumatology, Emory University, Atlanta, GA

Autoimmune blistering diseases (AIBD) are an uncommon group of immunologically mediated diseases which can affect both skin and mucous membranes. The importance of B cells in the development and perpetuation of AIBD has been demonstrated by increased numbers of B cells in lesional skin and the ability of B cell depletion therapy with rituximab (Rtx). However many patients will relapse in months to years following therapy with Rtx and the ability to predict clinical response is lacking. We sought to identify unique B cell markers and pathways as a way to develop predictive models of response to therapy. Using multichromatic flow cytometry, we phenotypically characterized patients with pemphigus, bullous pemphigoid, and mucous membrane pemphigoid pretreatment and following therapy with Rtx. At pretreatment, patients with AIBD exhibited a distinct B cell phenotype as compared to healthy controls. We performed in situs analysis and found that higher disease relapse correlates and are preceded by re-expansion of pre-existing memory clones. These data suggest that switched memory B cells may play an important role in contributing to psoriatic populations in active disease and during relapse post Rtx. Ongoing characterization of repopulating B cells in active disease and the functional properties of Treg will further define the role of B cells in disease relapse and provide potential therapeutic targets.

Delineation of ST18 role in the pathogenesis of pemphigus vulgaris

D Wieloch,1 Y Tsuchida,2 N Kanazawa2 and F Funakawa1 1 Dermatology, Wakayama Medical University, Wakayama, Japan; 2 and Dermatology, Anda Municipal Hospital, Wakayama, Japan

ST18 is an intracellular membrane-proximal protein that has been suggested to play a role in desmosomal stability. In this study both functional and expression analyses were performed to understand the role of ST18 in pemphigus vulgaris (PV). To study the functional role of ST18, we supplemented antibodies against ST18 in A13, a PV cell line. Three distinct outcomes were observed: (i) a normal proliferative response, (ii) a decrease in proliferative response, and (iii) apoptosis of the ST18-silenced A13. To understand the mechanism of ST18-mediated apoptosis, we performed transcriptomic analysis that showed significant overlap with keratinocyte death. This study shows that ST18 can play a role in the pathogenesis of PV and suggests that ST18-targeting therapies may be beneficial in this disease.

Activity of interferons beta and gamma in dermatomyositis skin is correlated with characteristic pathologic features

F Furukawa1, T Yoshimasu,2 N Kanazawa1 and Y Inaba1 1 Dermatology, Wakayama Medical University, Wakayama, Japan; 2 Weizmann Institute of Science, Rehovot, Israel

Dermatomyositis (DM) is characterized by skin and muscle inflammation, and is associated with type I and II interferon (IFN) signaling. We performed a gene expression analysis of DM skin from 4 patients using Affymetrix arrays. Comparative pathology analysis uncovered characteristic pathologic features, including dermal mucin deposition and apoptosis, that were associated with increased expression of IFN-β and IFN-γ. These results suggest that interferon signaling plays a role in the pathogenesis of DM and may be a potential therapeutic target.
IL-13 receptor alpha 1 downregulation as a protective mechanism and therapeutic target in pemphigus

K Seiffert-Sinha, E Zhelk, R Dey-Rao and AA Sinha Dermatology, University at Buffalo, Buffalo, NY

Pemphigus vulgaris (PV) is a heterogenous autoimmune blistering skin disease in which an auto-
association between specific HLA class II alleles (DRB1*0402 and DQB1*0602), and increased risk has
been well established. A major unknown is why healthy individuals who express these same HLA
risk alleles (termed HLA-matched controls) do not develop disease. Genome-wide transcriptional
analysis data from our lab recently identified a group of genes that are specifically downregulated in
peripheral blood mononuclear cells (PBMC) of HLA-matched controls, but not in HLA-unmatched
controls, suggesting the novel hypothesis that suppression of critical pathways in genetically sus-
cceptible individuals could function to protect from developing the autoimmune phenotype.

For this presentation, we aimed to identify the expression of IL-13Rα1 on PBMCs from HLA-matched
controls vs. PV patients and HLA-unmatched controls, and also in remitter vs. active PV patients. The IL-13Rα1 gene encodes one component of the common α subunit of the IL-4/13 receptor. Both IL-4 and IL-13 promote differentiation of Th2 cells and are essential for B cell activation and (auto)antibody production. We quantified the expression of IL-13Rα1 on defined PBMC subsets at the protein level by multiparameter flow cytometry in PV patients (active and remitter), HLAmatched controls and HLA-unmatched controls. We find a statistically significant decrease of IL-13Rα1 expression that is localized to the monocyte population of matched controls vs. PV patients and unmatched controls (p<0.01 in both cases). Receptor expression is also downregulated in monocytes of remitter vs. active PV patients, suggesting that the downreg-
ulation of IL-13Rα1 on monocytes is instrumental in the protection against disease development in genetically susceptible, but healthy, individuals, and may also play a role in reverting PV patients into remission. Our findings identify IL-13Rα1 as a possible therapeutic target in PV, and suggest that monocytes are key players in disease pathogenesis.

ABSTRACTS | Auto-Immunity

Atorvastatin attenuates cholesterol loading induced neutrophil extracellular traps

M Liu, M Bahir, J Williams and V Werth 1, 2 1 Dermatology, Philadelphia VAMC, Philadelphia, PA; 2 University of Pennsylvania, Philadelphia, PA; 3 Medicine, Temple University, Philadelphia, PA

Neutrophils (PMNs) are the first line defense, but with underestimated role in autoimmun and
inflammatory diseases. PMNs release granule proteins and chromatin DNA into the extracellular
space to form neutrophil extracellular traps (NETs). NETs are found in atherogenic lesions, and NETs
promote thrombosis. Moreover, pharmacological inhibition of NET formation through pepti-
dyl-arginine deiminase blockade can reduce atherosclerosis and arterial thrombosis in mice. Hyper-
cholesterolemia is one of the central causes of atherothrombosis, and multiple mechanisms are
involved in this setting. In this study, we aimed to investigate whether atorvastatin, a commonly
used medication for lipid lowering, affects the formation of NETs. PMNs were preincubated with
atorvastatin for 24 hours and then reconstituted in culture medium in the presence or absence of
atorvastatin. Neutrophil extracellular traps (NETs) were visualized by green fluorescence microscopy.

We found that atorvastatin significantly reduced the formation of NETs in vitro. Our data suggest that
atorvastatin can attenuate cholesterol-induced NET formation in vitro. Low-dose atorvastatin can attenuate cholesterol-induced NETosis. Our results indicate a potential role of hypercholesterolemia in NET formation and a potential beneficial role for statins.
073 Unmet need for mental health care in cutaneous lupus erythematosus and dermatomyositis

I.C. Achman, J. Okawa, and V. Werth

1 Dermatology, Perelman School of Medicine, Philadelphia, PA and 2 Dermatology, VA Medical Center Philadelphia, PA.

The aim of this study is to characterize unmet need for mental health care in cutaneous lupus erythematosus and dermatomyositis. Patients in the cross sectional study were administered a questionnaire to detect clinical depression and/or anxiety as well as any current treatment for mental illness or barriers to treatment if untreated. Patients with CLE and DM suffer from decreased quality of life compared to the healthy population and patients with other chronic conditions. While psychiatric comorbidities such as depression and anxiety have been thoroughly documented in other chronic, inflammatory, and dermatological conditions, these mental health issues remain less well described in skin-predominant lupus erythematosus and dermatomyositis. To date, the literature does suggest increased rates of mood and anxiety disorders in these diseases in the context of decreased quality of life; however, little is known about access and barriers to unmet need for mental health care in this population. 47 patients with CLE and 37 patients with DM were enrolled in this study. Spearman’s rank correlation coefficient for depression and anxiety were 0.77 and 0.80 (p<0.0001) for CLE and DM respectively. 34.0% (16/47) and 51.4% (19/37) of CLE and DM patients, respectively, met criteria for depression and/or anxiety with need for treatment. Of these patients, 37.5% (6/16) and 31.6% (6/19) of CLE and DM patients, respectively, were untreated for their mental illness. Overall, 12.8% (6/47) and 16.2% (6/37) of CLE and DM patients, respectively, have untreated depression and/or anxiety. Given the significant unmet need for mental health care in these populations and the lack of guidelines for dermatologists treating these autoimmune skin conditions, these findings suggest a need for improvement in awareness, screening, and referral of patients to appropriate psychiatric support services.

074 Epigenetic studies of oral lichen planus as a model for inflammation-mediated cancer development via malignant reprogramming

CG Teppler, Y. Izumiya, H. Murphy, P. Davenport, and N. Fazel

1 Biochemistry and Molecular Medicine, UC Davis, Sacramento, CA and 2 Dermatology, UC Davis, Sacramento, CA.

Oral lichen planus (OLP) is a chronic inflammatory disease that is considered to be a pre-malignant condition. Studies of loss of heterozygosity and microsatellite instability indicate that OLP is molecularly distinct from oral dysplasia and SCC. The operating hypothesis for our studies is that tumors, such as SCC, arise through “malignant reprogramming” driven by a combination of both genetic and epigenetic changes. The primary goal of this pilot study is to identify key sites of aberrant epigenetic regulation in OLP by defining the entire repertoire of differentially-expressed genes and regulatory non-coding in OLP lesions. Towards this goal, we are performing state-of-the-art next-generation sequencing (NGS)-based whole transcriptome profiling (RNA-Seq) analyses of matched pairs of OLP and perilesional normal surrounding tissue samples. The specimens were collected for RNA extraction, chromatin immunoprecipitation, and immunohistological studies. Sequencing libraries prepared from the total RNA samples are currently being sequenced on an Illumina HiSeq 2000 to yield ~10 million reads per sample, which will then be processed with our automated analysis pipeline which incorporates several tools for data pre-processing, read alignment, estimation of transcript abundance, variant analysis, etc. Subsequently, integrative bioinformatics will be applied in order to define an OLP-specific gene expression signature, as well as application of gene set enrichment analysis which incorporates several tools for data pre-processing, read alignment, estimation of transcript abundance, variant analysis, etc. Subsequently, integrative bioinformatics will be applied in order to define an OLP-specific gene expression signature, as well as application of gene set enrichment analysis. These expression changes will be obtained by correlation with the occurrence of somatic mutations (variant analysis) and epigenetic changes, such as histone modifications. We anticipate that characterisation of the latter will lead to the identification of the responsible histone-modifying enzymes, which can then be exploited as novel therapeutic targets.

075 Oxidative stress-induced calreticulin/gC1qR complex production may prevent cells from apoptosis: a new insight into the destruction of melanocytes

L. Li, P. Zhong, Y. Zhang, C. Li and T. Gao

Department of Dermatology, Xijing Hospital, Fourth Military Medical University, Xi’an, China.

Background: Reactive oxygen species (ROS) and autoimmunity interact synergistically, leading to the final destruction of melanocytes in vitiligo. The C1q binding proteins calreticulin (CRT) and gC1qR are highly conserved ubiquitous proteins, which are putative targets for an important role in apoptosis. Objective: We tested the hypothesis that these proteins form a complex prevents in the cytoplasm as a response to oxidative stress and the formation of a cytosolic CRT:gC1qR complex might prevents cell apoptosis by reducing gC1qR translocation into the mitochondria. Methods: To explore CRT:gC1qR complex function in oxidative stress mediated melanocyte damage, we detected the CRT, gC1qR expression patterns in keratinocytes and melanocytes, respectively. Moreover, we observed the localization of the CRT:gC1qR complex by immunofluorescence and confocal using immunoprecipitation in vivo. Results: Total CRT levels increased in a time-dependent manner in human immortalized normal and vitiligo melanocytes exposed to H2O2-induced oxidative stress, while gC1qR expression was unaltered. Similarly, the increased levels of gC1qR were detected later. Furthermore, Western blot analysis using antibodies to CRT or gC1qR in different subcellular fractions showed that gC1qR was also detected in the mitochondrial fraction of the melanocytes. In contrast, we found decreased transcript levels of CRT and gC1qR, and the complex (~97 kDa protein) was present consequently only in the cytoplasm of Hacat cells but was hardly detectable in melanocytes. Conclusion: These data suggest that a CRT:gC1qR complex is induced in the cytoplasm during an early stage of H2O2-induced oxidative stress and this complex prevents apoptosis mainly by reducing gC1qR translocation to the mitochondria.

076 Plumbagin was a potential therapeutic medicine for psoriasis by inhibiting the proliferation and secretion of inflammatory cytokines of keratinocyte

Y. Zhang and G. Wang

Department of Dermatology, Xijing Hospital, Fourth Military Medical University, Xi’an, China.

Plumbagin (PL), a medicinal plant-derived 1,4-naphthoquinone, has been reported to exhibit potential functions for DC-related autoimmune and inflammatory diseases, but less is known about its mechanism of therapy. We present here first time that PL inhibits the inflammatory and proliferation of psoriasis keratinocytes in imiquimod psoriasis mouse model. In this study, we demonstrated that PL inhibits the epidermal secretion inflammatory cytokines IL-6, IL-10, IL-17, IL-22 and IL-23 in a dose-dependent manner. Methods: To explore the effects of PL on the MAPK pathway, and the results indicated significant changes were observed in the levels of phosphorylated ERK1/2, and p38 MAPK, which further confirmed that a decreasing tendency of phosphorylation of MAPK kinases in imiquimod psoriasis mouse model and change in IL-17 and TNF-α-induced hact cell line. These data suggest that PL exerts its anti-inflammatory and inhibit proliferation function by down-regulating the expression of proinflammatory mediators through inhibition of MAPK signal.

077 Defective complement inhibitory function of CD44 predisposes to bullous pemphigoid

C. Zhao and G. Wang

Department of Dermatology, Xijing Hospital, Fourth Military Medical University, Xi’an, China.

Bullous pemphigoid (BP) is a common and intractable autoimmune blistering skin disease. It has been confirmed that binding of the main autoantigen BP180 associated with hemidesmosomes of basal keratinocytes. Innate and adaptive immunity are the two arms of immune response; both are actively involved in BP pathogenesis. However, the role of inflammasome in autoimmune disease is less clear than in autoimmunization, despite the numerous effects IL-16 and IL-18 can have on shaping adaptive immunity. To investigate the activation of inflammasome in bullous pemphigoid, we explored the expression of the different components of the NLRP3 inflammasome as well as other NOD-like receptors (NLRs) in peripheral blood mononuclear cells (PBMCs) obtained from BP patients. Correlations between NLRP3 inflammasome components’ expression and clinical disease progression were investigated. Further, the serum IL-1β and IL-18 levels before and after treatment in the patients with BP were also analyzed and compared. Our data showed that expression of NLRP3 was significantly higher in patients with BP compared with controls. Further, the IL-1β and IL-18 levels were significantly increased in patients with BP compared with controls. These results indicated that the NLRP3 inflammasome is hyperactivated in BP patients. Further research should focus on the mechanism of activate inflammasome in autoimmune disease.
**ABSTRACTS | Auto-Immunity**

**079**

Alopecia areata skin transcriptome correlates with disease severity and response to treatment

A Jabbari1, J E Cersie, 1 Mackay-Wiggan4, M Ducic4, M Hotforsky, 1 VH Price, 1 D Norris, 1 R Clyne2 and A Christiansen1 1 Dermatology, Medical College of Wisconsin, Milwaukee, WI, 2 Dermatology, MD Anderson, Houston, TX, 3 Dermatology, University of Minnesota, Minneapolis, MN, 4 Dermatology, University of California, San Francisco, San Francisco, CA and 5 Dermatology, University of Colorado, Denver, CO

**ABSTRACTS | Auto-Immunity**

**080**

Status of classification criteria for amyopathic dermatomyositis

N Khan1 and V Werth1 1 Dermatology, University of Pennsylvania, Philadelphia, PA, 2 Philadelphia College of Osteopathic Medicine, Philadelphia, PA

Existing classification systems for idiopathic inflammatory myopathies (IM) fail to classify and/or diagnose patients with amyopathic dermatomyositis (ADM). The International Myositis Classification Criteria Project (IMCCP) recently sought to develop classification criteria for IM to help address this problem. Our study examined the clinical presentation of adult patients with dermatomyositis (DM).

We specifically investigated the adequacy of classifying patients with ADM based on the three skin features—Gottron’s sign, Gottron’s papules, and helioporosis—of either the EULAR/ACR criteria or the new IMCCP criteria.

This retrospective study included 115 adult patients with a clinical and histological diagnosis of DM that were enrolled in a database at the Autoimmune Skin Disease Clinic at the University of Pennsylvania. Skin findings were evaluated using the Caturean Dermatomyositis Disease Area and Severity Index (CADASI). A web-calculator created by the IMCCP based on the EULAR/ACR criteria was used to determine if patients with ADM met the suggested 55% minimum probability cutoff for classification. Within our database, 64.3% of patients with ADM (n=56) would be classified with an IM based on the three skin variables included in the new EULAR/ACR criteria. These patients were able to meet the minimum probability cutoff for classification by presenting with at least two of the three skin variables. The remaining 35.7% of patients with ADM did not have the skin features necessary to meet the cutoff for classification. Therefore, the three skin variables included in the EULAR/ACR classification criteria for IM—Gottron’s sign, Gottron’s papules, and helioporosis—are not adequate for classifying patients with ADM. It is important to consider the inclusion of additional variables such as skin biopsy or other IM skin findings to provide criteria for ADM within any new classification criteria for IM and avoid the inclusion of mimicking skin diseases.

**081**

Eruptive papules in a patient with connective tissue disease

N Dolly, and S Ramachandran Dermatology, New York University, New York, NY

Eruptive collagenomas are rare connective tissue nevi (hamartomas) consisting of collagen. They were first reported by Colomb in 1955. They are classified as eruptive, acquired or familial. Here we present a case of a patient with eruptive collagenomas. Case Description: A 66 year old woman presented with a history of lesions first noticed three to four years prior to presentation. These lesions were first noted on the central chest then on the upper abdomen, breasts, arms, neck and upper back. There was no associated pruritus, erythema, or discharge. Physical history was significant for Systemic Lupus erythematosus well controlled on oral medications. Physical examination revealed hundreds of tan to pink 1-2 mm firm papules of the abdomen, back, abdomen and upper extremities. Darrow’s sign, pseudo Darrow’s sign, pustules or colarettes were not present. Histological examination of punch biopsies, on two separate office visits, showed an unremarkable epidermis and the reticular dermis was expanded by randomly arranged coarse collagen bundles of various sizes. EVG stain showed decreased elastic tissue. Based on the histological appearance, a diagnosis of collagenoma was made. No specific treatment has been shown to be efficacious. Conclusion: Eruptive collagenomas rarely occur in patients with Multiple Endocrine Neoplasia. This is the first report of such occurring in patients with Multiple Endocrine Neoplasia. This is the first report of eruptive collagenomas.

**082**

Expanded αβ T cell clones are present in the healed lesions of psoriasis and likely represent the autoaggressive T cells of origin

B Böhm1, R Bindl2, J Teague3, E Lowey1, H Robbins1, T Skupper4, JG Kneuger5 and R Clark6 1 Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, 2 Adaptive Biotechnologies, Seattle, WA and 3 Rockefeller University, New York, NY

We present a case of a patient with eruptive collagenomas. Case Description: A 66 year old woman presented with a history of lesions first noticed three to four years prior to presentation. These lesions were first noted on the central chest then on the upper abdomen, breasts, arms, neck and upper back. There was no associated pruritus, erythema, or discharge. Physical history was significant for Systemic Lupus erythematosus well controlled on oral medications. Physical examination revealed hundreds of tan to pink 1-2 mm firm papules of the abdomen, back, abdomen and upper extremities. Darrow’s sign, pseudo Darrow’s sign, pustules or colarettes were not present. Histological examination of punch biopsies, on two separate office visits, showed an unremarkable epidermis and the reticular dermis was expanded by randomly arranged coarse collagen bundles of various sizes. EVG stain showed decreased elastic tissue. Based on the histological appearance, a diagnosis of collagenoma was made. No specific treatment has been shown to be efficacious. Conclusion: Eruptive collagenomas rarely occur in patients with Multiple Endocrine Neoplasia. This is the first report of such occurring in patients with Multiple Endocrine Neoplasia. This is the first report of eruptive collagenomas.

**083**

Bullous pemphigoid autoantibodies and complement are required for eosinophil localization to the dermo-epidermal junction

JW Wang, HM Holohan, SR Srikantna, S Aust, K Messingham and JA Fairley 1 Dermatology, University of Iowa, Iowa City, IA and 2 VA Medical Center, Iowa City, IA

Bullous pemphigoid (BP) is an autoimmune disease characterized by sub-epidermal blistering and antibodies (IgG and IgE) targeting adhesion proteins located at the dermal epidermal junction (DEJ). Histologic examination of lesions reveals the presence of inflammatory cells, including neutrophils and eosinophils, and evidence of their degranulation. Using a human skin cryosection model, others have shown that IgG autoantibodies are critical for neutrophil localization and degranulation at the DEJ and subsequent formation of a subepidermal blister. However, the role of eosinophils in BP is not well understood. Herein, we utilized a human cryosection model to investigate the role of αβ T cells and complement in eosinophil recruitment and activation at the DEJ. TCR sequencing demonstrated the human eosinophilic cell line, 15HL-60, confirmed expression of receptors for IgG, IgE, complement and expression of eosinophil granule proteins (eosinophil derived neurotoxin (EDN) and eosinophil peroxidase (EPX)). IgG (primarily IgG2 and IgG4) and IgE were purified from well characterized αβ T cell clones stimulated with either control, separation at the DEJ was observed when human leukocytes were incubated with BP serum and human complement. Interestingly, BP serum and complement were both required for localization of 15HL-60 cells to the DEJ; separation of CD4 and CD8 T cells from the αβ T cell population respectively. By matching TCR α and β sequences of initiating clones based on the three skin variables included in the new EULAR/ACR criteria for IM—Gottron’s sign, Gottron’s papules, and helioporosis—are not adequate for classifying patients with ADM. It is important to consider the inclusion of additional variables such as skin biopsy or other IM skin findings to provide criteria for ADM within any new classification criteria for IM and avoid the inclusion of mimicking skin diseases.

**084**

Collagen XVII autoantibodies are present in Parkinson’s Disease patients and co-localize with human hyaluronyslase in the substantia nigra

K Messingham, N Narayanan, S Aust, H Helfenberger, M Cassell, S Alperico and A Fairley 1 Dermatology, University of Iowa, Iowa City, IA, 2 Neurology, University of Iowa, Iowa City, IA, 3 Anatomy and Cell Biology, University of Iowa, Iowa City, IA and 4 VA Medical Center, Iowa City, IA

Recent data indicates a strong epidemiologic link between Parkinson’s disease (PD) and dementia with the autoimmune blistering disease, bullous pemphigoid (BP). Here we tested the hypothesis that patients with Parkinson’s disease (PD), or dementia but without BP, would have increased human hyaluronyslase (HY) and at least one IgG against Collagen XVII (Col XVII) in their sera. We tested for the presence of HY and both IgG against Collagen XVII in the sera of 25 PD patients and 25 patients with non-Parkinsonian dementia, and 25 age-matched controls. Levels of serum autoantibodies to the pathogenic region of Col XVII (NC16A) were determined by ELISA; reactivity to the extracellular or intracellular domains via immuno blot. Overall, 14/50 (28%) patients with either PD or dementia had collagen XVII autoantibodies in their sera. Of these, 1/25 dementia sera and none of the PD sera had autoantibodies against NC16A. Immunoblot against the recombinant extracellular domain of collagen XVII revealed that 7/25 PD sera (p<0.05) and 1/25 dementia sera exhibited autoantibody reactivity above the 95% CI established with control sera (n = 23). Immunoblot against the recombinant intracellular domain of collagen XVII revealed that 5/25 dementia sera and 2/25 PD sera displayed antibody levels above the 95% CI. Autoantibody binding to the substantia nigra of rat and human brain was tested by indirect immunofluorescence utilizing antibodies to tyrosine hydroxylase in the substantia nigra. The substantia nigra of rat and human brain was tested by indirect immunofluorescence utilizing antibodies to tyrosine hydroxylase in the substantia nigra.
**085**
The Asian atopic dermatitis phenotype combines features of atopic dermatitis and psoriasis with increased Th17 polarization

S. Noda 1, 2, M. Suwa 1, 2, K. Hanabusa 1, 2, K. H. Lee 1, K. Kakuhashi 1, J. G. Knuepfer 3 and E. Gutmans-Yassky 1

1 Laboratory of Investigative Dermatology, The Rockefeller University, New York, NY, 2 Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, NY, 3 Department of Dermatology, Yonsei University College of Medicine, Seoul, Korea (the Democratic People’s Republic of) and 4 Department of Dermatology, Kyoto University Graduate School of Medicine, Kyoto, Japan

Atopic dermatitis (AD) has a very high prevalence (7-10% of adults) in Asia, with a large unmet need for effective therapies. Earlier studies suggest that different AD phenotypes in different ethnicities and regions are associated with distinct genetic backgrounds and clinical manifestations. In this study, we investigated the skin biopsy samples from patients with AD in Japan and Korea, focusing on the expression patterns of pro-inflammatory cytokines and their receptors. Our findings indicate that Japanese AD patients exhibit a distinct cytokine profile compared to Korean AD patients, suggesting the potential for region-specific therapeutic approaches based on these differences. Further studies are needed to validate these findings and explore the implications for treatment strategies.
ABSTRACTS | Auto-Immunity

091
Anti-BP180 IgG4 autoantibodies are inhibitory in BP in BP180 humanized mouse model
Y Zhao, J Evangelista, A Guillabert, N Li, LA Diaz 1 University of North Carolina, Chapel Hill, NC and 2 Hospital General de Granollers, Barcelona, Spain

Bullous pemphigoid (BP) is an autoimmune inflammatory subepidermal blistering disease associated with autoantibodies against two hemidesmosomal components of the basement membrane zone (BMZ), the BP180 and BP230. BP IgG autoantibodies mainly target the NC16A domain of BP180 and NC16A-specific IgG4 induce BP-like skin lesions in BP-180 humanized mice. Subepidermal blistering induced by anti-NC16A IgG depends on complement, mast cells, and neutrophils. In BP patients, NC16A-specific IgG predominantly belong to IgG1, IgG3 and IgG4 subclasses. Since IgG4 do not activate complement, the exact role of NC16A-specific IgG4 in BP remains to be defined. In this study, we determined the role of NC16A-specific IgG4 in BP using NC16A humanized (NC16A) mice and highly purified anti-NC16A IgG4 from BP patients. In vitro, NC16A-specific IgG1, IgG3 bound and activated complement at the BMZ of the NC16A mouse skin, whereas NC16A-specific IgG4 bound to the BMZ but did not activate complement. Preincubation with NC16A-specific IgG4 reduced the BMZ binding of NC16A-specific IgG1 and IgG3. In IgG passive transfer model, NC16A-specific IgG1 and IgG3 but not NC16A-induced BP associated with C3 deposition at the BMZ and elevations of 5 kDA levels in the blister cavity. Furthermore, NC16A mice, when pretreated with NC16A-specific IgG4, became resistant to BP induced by NC16A-specific IgG1 and IgG3. This in vivo inhibitory activity of NC16A-specific IgG4 was associated with reduced IgG1 and IgG3 generated T-bet CD11c+ double knockout mice, which lacked iNKT cells. In contrast to the protection in T-bet/-/- mice, T-bet+/+KO mice had severe IMQ-induced dermatitis compared to WT mice. Our data suggest that NC16A-specific IgG1 and IgG3 promote BP, whereas NC16A-specific IgG4 inhibit BP by competing for the elicitor binding site(s) in the NC16A mouse model. Our findings suggest that different BP180NC16A-specific IgG subclasses have different roles in BP pathogenesis and paves the way for NC16A-specific IgG4-centered therapies in BP.

093
T-bet-deficient mice are protected from imiquimod-induced psoriasis-like dermatitis due to the protective IL-4 producing NK T cells
D Wu, Z Li, H Han, N Zhou, C Lu and Q Mi 1 Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, China and 2 Dermatology, Henry Ford Health System, Detroit, MI

The transcription factor T-bet is critical for Th1 polarization of CD4 T cells. It was reported that the expression of T-bet in the PBMCs and lesional skin were upregulated in psoriatic patients. However, the function of T-bet in psoriasis development is still unclear. In this study, to investigate the in vivo roles of T-bet in the pathogenesis of psoriasis, we induced psoriasis-like skin inflammation with topical application of imiquimod (IMQ) in T-bet/-/- and wild type (WT) mice. We found that mice lacking functional T-bet were largely protected from IMQ-induced psoriasis-like dermatitis. IfNγ, IL-17- and IL-22-producing T cells, including gamma/delta T cells, were dramatically reduced in the skin lesions from T-bet-/- mice, but not in the skin lesions from WT mice. In contrast, the expression of IFNγ, IL-17- and IL-22-producing T cells was significantly reduced in spleen and lymph node, while IL-4 producing CD4 T cells and iNKT cells were significantly increased in T-bet/-/- mice. To further investigate the role of iNKT cells in psoriasis, we generated T-bet CD11c+ double knockout mice, which lacked iNKT cells. In contrast to the protection in T-bet/-/- mice, T-bet+/+KO mice had severe IMQ-induced dermatitis compared to WT mice. IL-17 and IL-22-producing T cells and gamma/delta T cells were significantly increased in lymph nodes from T-bet+/+KO mice. In conclusion, our data suggest that T-bet plays critical roles in psoriasis development and IL-4 producing iNKT cells contribute to T-bet deficiency-mediated protection from IMQ-induced psoriasis-like skin inflammation.

095
Immunologic signatures in Treggs and Tefells in psoriasis
G Najafi, M Singer, M Baelum, M Loven, K Tawata, W Liao and MD Rosenblum 1 University of California, San Francisco School of Medicine, San Francisco, CA and 2 University of California, Irvine School of Medicine, Irvine, CA

Psoriasis is a chronic inflammatory skin disease characterized by infiltration of effector CD4 T cells and CD8 T cells. Efferent T cells (Teffs) are well-known to be a major factor in the pathogenesis of psoriasis, producing cytokines that induce inflammation. However, it has recently been shown that regulatory T cell (Tregs) also play a role, as Tregs in psoriatic lesions were shown to be highly proliferative and to produce IL17, compared to their relatively unresponsive state in normal skin. The objective of our study is to identify differences in the transcriptional profile of Treggs found in psoriatic skin lesions compared to those of normal skin. To do so, an optimal protocol to sort Treggs from psoriasis biopsy samples was developed. We have previously shown that CD25 and CD27 co-expression identifies skin-resident Tregs and differentiates them from Teffs to a high degree of purity (>90%). Cells from the skin of healthy human donors or psoriatic lesion biopsies were stained and sorted into Tregs (CD25+CD27+) or Teffs, with gating verified by an internal FOXP3 stained control. Once an appropriate number of Tregs and Teffs were obtained from the skin sample, analysis of RNA was completed via RNAseq. Preliminary results demonstrate that sorting Treg and Teff cells from human skin is relatively easy and recoverable for samples. The maximal number of Tregs and Teffs needed to obtain high quality RNA from healthy and diseased human skin samples was determined. RNA of sufficient integrity (RIN=7) for downstream RNAseq analyses was obtained from as few as 3000 Tregs sorted from healthy human skin sample. By characterizing the Tregs in psoriasis skin lesions with transcriptional differences to those found in normal skin, we can better understand disease pathogenesis.