## Oral Abstract Session 1

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>3:45 p.m.  –  3:55 p.m.</td>
<td>Immunohistochemical Analysis of P40 and Androgen Receptor in the Spectrum of Sebaceous Tumors and its Utility in Distinguishing Sebaceous Carcinoma from Basal Cell Carcinoma</td>
<td>Smita C. Patel, MD</td>
</tr>
<tr>
<td>3:55 p.m.  –  4:05 p.m.</td>
<td>S-Hydroxymethylxotosine in Histologically Ambiguous, Heavily Pigmented Melanocytic Lesions: A Comparative, Immunohistochemical, Retrospective Cohort Study</td>
<td>Jonathan J. Lee, MD</td>
</tr>
<tr>
<td>4:05 p.m.  –  4:15 p.m.</td>
<td>Tumor-Normal Whole Exome Sequencing of Subcutaneous Panniculitis-like T-cell Lymphoma, Lupus Panniculitis, and Systemic Peripheral T-cell Lymphoma</td>
<td>Sebastian Fernandez-Pol, MD, PhD</td>
</tr>
<tr>
<td>4:15 p.m.  –  4:25 p.m.</td>
<td>Differentiation of Benign Melanocytic Nevi from Malignant Melanomas Solely by Nuclear Features</td>
<td>Nemanja Rodic, MD, PhD</td>
</tr>
<tr>
<td>4:25 p.m.  –  4:35 p.m.</td>
<td>Expression of SPARC Immunohistochemistry in Cutaneous Angiosarcoma and Selected Mimickers</td>
<td>Shakuntala H. Mauzo, MD</td>
</tr>
<tr>
<td>4:35 p.m.  –  4:45 p.m.</td>
<td>p15, a Potential Biomarker of Spitzoid Melanocytic Lesions</td>
<td>Sophia A. Ma, MD</td>
</tr>
<tr>
<td>4:45 p.m.  –  4:55 p.m.</td>
<td>Analysis of Immune Signatures in Longitudinal Tumor samples yields insight into Biomarkers of Response and Mechanisms of Resistance to Immune Checkpoint Blockade</td>
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</tr>
<tr>
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<td>High-throughput Sequencing of TCRB and TCRG in Multiple Biopsies from Patients with Atypical Lymphoid Infiltrates to Evaluate for Mycosis Fungoides and Sézary Syndrome</td>
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</tr>
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<td>5:05 p.m.  –  5:15 p.m.</td>
<td>Genetic Signature Testing in Cutaneous Melanoma Correlates Well with Current Histopathologic and Surgical Staging Parameters</td>
<td>Alae Abod Yaseen, MD</td>
</tr>
</tbody>
</table>
Oral Abstract Session 1

Immunohistochemical Analysis of P40 and Androgen Receptor in the Spectrum of Sebaceous Tumors and its Utility in Distinguishing Sebaceous Carcinoma from Basal Cell Carcinoma

Smita C. Patel, MD
Smita C. Patel, MD1; Allen Gown, MD2; Paolo Gattuso, MD1; Pincus Bitterman, MD1; Vijaya Reddy, MD1
1Rush University Medical Center, Chicago, Illinois, USA
2Phenopath Laboratories, Seattle, Washington, USA

Background: The histological distinction amongst the spectrum of sebaceous tumors (ST) can pose diagnostic problems, particularly in small biopsies. Sebaceous carcinoma (SBC) is highly aggressive and must be distinguished from its histologic mimic, basal cell carcinoma (BCC), especially if they are poorly differentiated. P40 (ΔNp63) is a truncated, nontransactivating p63 isoform and highly specific for squamous cells, while its applicability in ST has not been previously addressed. The aim of this study was to evaluate p40 and androgen receptor (AR) expression in the spectrum of ST and investigate the utility of this panel to differentiate SBC from BCC. Design: Immunohistochemistry for p40 and AR was performed in 53 tumors and evaluated for nuclear expression by 2 independent pathologists. A semi-quantitative scoring method was used to determine the percent of positive tumor cells and staining intensity as 0 (none), 1+ (1-24%), 2+ (25-49%), 3+ (50-100%). The location of positive staining was recorded in the more differentiated ST. Results: The cases included 14 sebaceous hyperplasia (SH), 9 sebaceoma (SB), 5 well-differentiated SBC (WDSBC), 11 poorly-differentiated SBC (PDSBC), and 14 BCC. 93% SH showed less (1+-2+) and weak p40 expression while 77.8% SB, 100% WDSBC and 81.8% PDSBC showed high (3+) but weak p40 expression, p <0.001. AR expression was strong and high (3+) in 93% SH, 88.9% SB and 80% WDSBC while less (1+) in 81.9% PDSBC, p <0.001. All BCC showed strong and high (3+) p40 expression while were completely negative (57%), or showed only 1+ expression (43%) for AR, p <0.001. P40 was localized in basal cells diffusely while focally in peripheral and mature sebocytes. AR was localized in peripheral sebocytes diffusely while focally in mature sebocytes and basal cells. Conclusion: To the best of our knowledge, this is the first study addressing the expression of p40 and AR in various ST and its utility to distinguish SBC from BCC. Intensification of p40 and reduction but still focally retained AR expression was observed across the spectrum from SH to PDSBC. While assessment of typical histological features remains the cornerstone of diagnosis, for cases with equivocal histology and in small biopsies, this study supports the use of p40 and AR as reliable means of separating SBC (P40weak+/AR+) from BCC (p40strong+/AR-).
5-Hydroxymethylcytosine in Histologically Ambiguous, Heavily Pigmented Melanocytic Lesions: A Comparative, Immunohistochemical, Retrospective Cohort Study

Jonathon J. Lee, MD
Jonathon J. Lee, MD1; Ricardo E. Vilain, MD2; Scott R. Granter, MD1; Nina Hu, PhD1; Scott Bresler, MD, PhD1; Shuyun Xu, MD, PhD1; Alexander H. Frank1; Martin C. Mihm, Jr., MD1; Christopher D.M. Fletcher, MD1; Richard A. Scolyer, MBBS3; George F. Murphy, MD1; Christine G. Lian, MD1
1Brigham and Women’s Hospital/Harvard Medical School, Boston, Massachusetts, USA
2Faculty of Health, University of Newcastle, Callaghan, Australia
3Sydney Medical School, University of Sydney, Sydney, Australia

Background: Heavily pigmented melanocytic lesions can be diagnostically challenging and difficult to classify biologically, and a subset carries an undefined malignant potential. ‘Loss of 5-hydroxymethylcytosine’ (5-hmC) is an epigenetic hallmark shown to correlate with worse prognosis in melanoma while its presence supports a melanocytic tumor’s benignity and well-differentiated biological state. We sought to explore 5-hmC immunoreactivity and its pathobiological implications in histologically ambiguous, heavily pigmented melanocytic tumors to help define their natural history. METHODS: Seven deep penetrating nevi with moderate to severe atypia (atypical DPN), 10 heavily pigmented melanocytic tumors of uncertain malignant potential (MELTUMP), and 8 lesions qualifying histologically for the designation of pigmented epithelioid melanocytoma (PEM) were evaluated by immunohistochemistry for 5-hmC using a red chromogen. Controls consisted of a) pigmented melanocytic lesions without atypia (5 blue nevi with epithelioid change (BNE), 5 non-atypical DPNs, and 12 combined nevi (CN), which showed features of either DPN or blue nevus in addition to ordinary nevocellular nevus, and b) 8 cases of malignant blue nevus (MBN, 6 of which arose adjacent to a benign blue nevus). Semi-quantitative analysis of 5-hmC immunoreactivity was assessed as the product of intensity (0-3 scale) and % positive melanocytic cells over 5 random high power fields. Significance was determined via one-way ANOVA analysis. RESULTS: Benign melanocytic lesions (5/5 BNE; 12/12 CN; 5/5 DPN) showed strong nuclear 5-hmC reactivity. In contrast, 8 of 8 MBN and 7 of 8 PEMs showed significant 5-hmC loss. In addition, 5 of 7 atypical DPNs and 8 of 10 MELTUMP cases demonstrated low to intermediate 5-hmC immunoreactivity. CONCLUSION: Loss or low to intermediate immunoreactivity for 5-hmC in atypical, heavily pigmented melanocytic tumors (PEM and pigmented MELTUMPs) supports the potentially aggressive nature of these diagnostically challenging and biologically borderline heavily pigmented lesions. Our findings further support the utility of loss of 5-hmC for defining melanocytic lesions that require close patient follow-up after excision.
Tumor-Normal Whole Exome Sequencing of Subcutaneous Panniculitis-like T-cell Lymphoma, Lupus Panniculitis, and Systemic Peripheral T-cell Lymphoma

Sebastian Fernandez-Pol, MD, PhD
Sebastian Fernandez, MD, PhD1; Costa Helio, PhD1; David Steiner, MD, PhD1; Youn Kim, MD2; Jinah Kim, MD, PhD2

1Stanford University, Stanford, California, USA
2Stanford University School of Medicine, Palo Alto, California, USA

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a malignant primary cutaneous T-cell lymphoma that is challenging to distinguish from lupus erythematosus panniculitis (LEP) due to significant clinical, histopathologic, and immunophenotypic overlap. To identify molecular changes unique to SPTCL for diagnostic purposes or to predict response to therapy, we performed tumor-normal paired whole exome sequencing on biopsies from four cases of SPTCL, two cases of lupus panniculitis, and one case of peripheral T-cell lymphoma. The mean and median number of variants identified in lesional tissue compared with normal tissue was 532 (median = 479, range = 343-980). Mean read depth for variants was 70X (median = 61, range = 39-161). We found that the cases had an average of 46 variants that were predicted to result in changes to protein sequence (i.e., nonsynonymous mutations, frameshift mutations, and mutations of canonical splice sites). The four SPTCL cases had a mean of 48 nonsynonymous variants compared with 40 in the two LP cases and 49 in the PTCL case. The average variant allele frequency for the nonsynonymous variants was not markedly different between SPTCL cases (mean 0.15) compared with the LEP cases (0.2) or the PTCL case (0.23). In this small sample number, we were not able to find recurrent mutations that were specific to SPTCL cases; however variants predicted to affect genes involved in drug-targetable pathways, including RAF1, DNMT1, FLT4, FGFR1, BCL2, and MAP2K1, were identified in three of the four SPTCL cases. Of these variants, the only coding region variant found was in FGFR1. Our work provides a framework to improve knowledge of the molecular aspects of this rare type of cutaneous lymphoma and open possibilities for therapy.

Differentiation of Benign Melanocytic Nevi from Malignant Melanomas Solely by Nuclear Features

Nemanja Rodic, MD, PhD
Nemanja Rodic, MD, PhD1; Jamaal Rehman, MD1; Ying-Chun Lo, MD, PhD1; Alexander S. Baras, MD, PhD2; Robert W. Veltri, PhD2

1Yale School of Medicine, New Haven, Connecticut, USA
2Johns Hopkins Hospital, Columbia, Maryland, USA

On occasion, it may be a challenge for dermatopathologists to best classify small collections of melanocytic cells as either malignant or benign. To learn more about nuclear feature in melanocytic lesions we studied Feulgen (quantitative DNA dye) stained sections of tissue microarray that contained benign melanocytic nevi (n = 32), primary malignant melanomas (n = 32), and metastatic malignant melanomas (n = 64). We started by capturing digital images of Feulgen stained sections using the AutoCyte imaging system. Sixty one nuclear morphometric descriptors (NMDs) were calculated for each lesional nucleus. Using logistical regression analysis we determined that variance of seven NMDs were
informative to distinguish benign melanocytic nuclei from melanoma nuclei. Specifically, informative NMDs were measures of nuclear size (feret X&Y), nuclear texture (diagonal moment, transmission), DNA content (gray value mean & median, optical density median). Based on AutoCyte analysis we describe four novel melanoma nuclear features (nuclear membrane prominence, nuclear membrane irregularity, micronuclei/apoptotic bodies, and chromatin microvesiculation).

Expression of SPARC Immunohistochemistry in Cutaneous Angiosarcoma and Selected Mimickers

Shakuntala H. Mauzo, MD
Shakuntala H. Mauzo, MD1; Victor Prieto, MD, PhD2; Carlos Torres-Cabala, MD2; Wei-Lien Want, MD2; Michael Tetzlaff, MD, PhD2; Nitin Chakravarti, PhD2; Denai Milton, MS2; Robert E. Brown, MD1; Phyu P. Aung, MD, PhD2

1University of Texas Health Science Center, Houston, Houston, Texas, USA
2MD Anderson Cancer Center, Houston, Texas, USA

Background: Serum protein acidic and rich in cysteine (SPARC) is a matricellular glycoprotein, which regulates cell proliferation and facilitates intracellular transport of albumin bound particles including chemotherapeutic agents; Nab-paclitaxel/ABI-007. This can be beneficial in achieving higher intratumoral drug concentration with lower dosage and thus reducing systemic side-effects. Multiple ongoing and completed trials of ABI-007, in malignant melanoma (Mel), show promising clinical activity.

Design: Fifty four cases of dermal based pleomorphic neoplasms were retrieved including 24 angiosarcoma (AS), 10 hemangioma, 9 nodular Mel, 4 Kaposi sarcoma (KS), 3 leiomyosarcoma (LMS), 3 atypical fibroxanthoma (AFX) and 1 spindle cell squamous cell carcinoma (SSCC). SPARC immunohistochemistry was performed with mouse monoclonal antibody (MAB941). The tumor cells were assessed for intensity and graded as: 0-1+ (negative) and 2-3+ (positive). Demographics and; relevant clinical and pathologic measures were collected. Variables were summarized by descriptive statistics and assessed using standard statistical analysis methods.

Results: SPARC expression was detected in majority of AS (17/24), Mel (8/9), AFX (3/3) and KS (4/4) with some expression in hemangioma (3/10), while being negative in SCC (0/1); and was significantly associated with tumor group (p<0.001). LMS (3/3) showed patchy positivity from 0-2+. Conclusion: Although SPARC expression in Mel and AS has been described in literature, its positivity in KS and AFX is a new finding. Paclitaxel has been seen to be effective in AS, Mel and KS and hence ABI-007 could be beneficial in treatment of these patients. To our knowledge, investigation of SPARC expression in dermal based neoplasms has not been previously reported.
p15, a Potential Biomarker of Spitzoid Melanocytic Lesions
Sophia A. Ma, MD
Sophia A. Ma, MD1; Conor P. O’Day, MS2; Tzvete Dentchev, MS2; John T. Seykora, MD, PhD1; Emily Y. Chu, MD, PhD1
1Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA
2University of Pennsylvania, Philadelphia, Pennsylvania, USA

Introduction: Classification and prognostication of Spitzoid melanocytic lesions are notoriously difficult due to the overlapping clinical and histological patterns. The loss of p16 immunoeexpression corresponds with the loss of the CDKN2A gene, an inhibitor of cell cycle proliferation, and p16 immunohistochemistry (IHC) has used as an adjunct to help distinguish benign and malignant Spitzoid lesions, although its expression can be variable. p15 is a protein encoded by the neighboring CDKN2B gene, deletions of which have been shown to directly promote transition from benign nevus to melanoma. We hypothesized that p15 immunohistochemistry could prove useful to distinguish Spitz nevi from Spitzoid melanomas. Methods: We randomly selected 74 formalin fixed paraffin embedded tissues from patients diagnosed with classic Spitz nevi (n=19), dysplastic Spitz nevi (n=15), atypical Spitzoid tumors (ASTs) (n=26), and Spitzoid melanomas (n=14). IHC staining for p15 and p16 expression was performed using a peroxidase/diaminobenzidine-complex method. Immunoeexpression for p15 and p16 were categorized by intensity: 1+ (weak), 2+ (moderate), 3+ (high). Lesional mitotic figures were identified in mm2 and compared to the staining intensity. Results: For p15, 95% of classic Spitz nevi showed at least 2+ immunoreactivity, while 70% of the nevi had 3+ immunoreactivity. By comparison, for p16, 90% of nevi expressed at least 2+ and only 50% showed 3+ intensity. Spitzoid melanomas showed a significant loss of p15 staining intensity compared to that seen in classic Spitz nevi (p<0.001); however, p16 showed a more variable staining pattern in both nevi and melanomas. Interestingly, absent/weak p15 expression in ASTs is associated with increased mitotic counts (mean mitotic count=2.8/mm2, correlation coefficient, r=-0.6), whereas p16 expression in these lesions did not. Conclusion: These data illustrate diminished p15 expression in Spitzoid melanomas when compared with Spitz nevi. p15 may therefore be a useful biomarker to help in distinguishing Spitzoid lesions.

Analysis of Immune Signatures in Longitudinal Tumor Samples Yields Insight into Biomarkers of Response and Mechanisms of Resistance to Immune Checkpoint Blockade
Pei-Ling Chen, MD, PhD
Pei-Ling Chen, MD, PhD1; Whijae Roh, MS1; Alexandre Reuben, PhD1; Zachary A. Cooper, PhD1; Christine N. Spencer, BS, MPH1; Peter Prieto, MD1; John P. Miller, PhD1; Roland Bassett, PhD1; Vancheswaran Gopalakrishnan, DDS1; Khalida Wani, PhD1; Mariana Petaccia De Macedo, MD1; Jacob L. Austin-Breneman, BS1; Hong Jiang, PhD1; Wei-Shen Chen, MD, PhD1; Sangeetha Reddy, MD1; Wencai Ma, BS1; R. Eric Davis, MD1; Michael T. Tetzlaff, MD PhD1; Russell J. Broadus, MD, PhD1; Alexander J. Lazar, MD, PhD1; Victor G. Prieto, MD, PhD1; Hu Jianhua, PhD1; Jorge Blando, DVM1; P. Andrew Futreal, PhD1; Padmanee Sharma, MD, PhD1; James P. Allison, PhD1; Lynda Chin, MD2; Jennifer A. Wargo, MD, MMSc1
1University of Texas MD Anderson Cancer Center, Houston, Texas, USA
3The University of Texas System, Houston, Texas, USA
Immune checkpoint blockade represents a major breakthrough in cancer therapy, however responses are not universal. Genomic and immune features in pre-treatment tumor biopsies have been reported to correlate with response in patients with melanoma and other cancers, but robust biomarkers have not been identified. We studied a cohort of metastatic melanoma patients initially treated with cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) blockade (n=53) followed by programmed death-1 (PD-1) blockade at progression (n=46), and analyzed genomic and immune signatures in longitudinal tissue samples collected at multiple time points during therapy. Here we demonstrate via immunohistochemical studies, targeted gene expression analysis, and high throughput TCR sequencing that while immune profiling and targeted gene expression analysis in pre-treatment samples largely fail to predict clinical response, adaptive immune signatures and TCR clonality in early on-treatment tumor biopsies are highly predictive. These observations are highly relevant to the field of cancer immunotherapy, as many clinical trials of immune checkpoint inhibitors currently mandate assessment of immune markers only in pre-treatment tumor tissue. However, our findings suggest that we should reconsider this approach and assess adaptive immune signatures in on-treatment biopsies on checkpoint blockade therapies. Furthermore, these studies also demonstrate differential effects on the tumor microenvironment induced by CTLA-4 and PD-1 blockade, highlighting mechanistic differences of CTLA-4 and PD-1 blockade. Lastly, these studies yield insight into mechanisms of therapeutic resistance to immune checkpoint blockade that are potentially actionable, including down-regulation of VEGF and defects in IFN signaling as well as HLA expression. These concepts have important clinical implications in this age of precision medicine, and should be explored in the setting of treatment with immune checkpoint blockade across different cancer types.

High-throughput Sequencing of TCRB and TCRG in Multiple Biopsies from Patients with Atypical Lymphoid Infiltrates to Evaluate for Mycosis Fungoides and Sézary Syndrome
Ryanne A. Brown, MD, MBA
Ryanne A. Brown, MD, MBA; Youn H. Kim, MD; Jinah Kim, MD, PhD
1Stanford University School of Medicine, Stanford, California, USA

Recently, High-Throughput Sequencing of TCRB and TCRG (HTS-TCR) has demonstrated utility in the diagnosis of cutaneous T-cell lymphoma (CTCL) in single biopsies. Here, we describe the results of comparing T cell repertoire to dominant sequences identified via HTS-TCR of multiple skin biopsies from patients with atypical lymphoid infiltrates and clinical concern for mycosis fungoides (MF)/Sézary syndrome (SS). In 12 patients (8 males, 4 females) ages 39-85, multiple skin biopsies were evaluated using HTS-TCR. Our results demonstrated that the identification of identical dominant sequences in multiple skin biopsies increased our ability to resolve indeterminate clinical and histopathologic findings in the following clinical settings: 1) initial diagnosis of MF/SS and distinction from inflammatory dermatosis (n=7), 2) diagnosis of minimal residual disease (MRD) in the post-transplant setting (n=2), and 3) distinction of MF/SS from lymphomatoid drug reaction in clinical trials of experimental therapies (n=3). In 2 patients with suspected atopic dermatitis and positive results by standard PCR, HTS-TCR results failed to identify a shared dominant sequence in multiple biopsies, supporting our suspicion of an
inflammatory process. In 5 patients with suspected MF, HTS-TCR confirmed the clinicopathologic impression of CTCL by identifying shared clones in multiple biopsies from each patient. We identified residual/recurrent SS in 2 post-transplant patients. One patient demonstrated identical dominant TCRB sequences and 2 identical dominant TCRG sequences in multiple biopsies. Another patient showed 2 identical dominant TCRB sequences in concurrent biopsies. In 3 patients receiving experimental therapies, 2 dominant TCRB and TCRG sequences were identified in samples taken both concurrently and over time. The ability of HTS-TCR to monitor the molecular signature of clonal T-cell populations has proved to be exceptionally helpful in the diagnosis of MRD post-transplant, as well as initial diagnosis of MF/SS and distinction from lymphomatoid drug reaction in patients in experimental drug trials. This cohort illustrates the variety of clinical settings in which increased accuracy for MF/SS diagnosis can be achieved via HTS-TCR identification of shared TCRB and TCRG sequences in multiple biopsies.

Genetic Signature Testing in Cutaneous Melanoma Correlates Well with Current Histopathologic and Surgical Staging Parameters
Alae Abod Yaseen, MD
Alae Abod Yaseen, MD1; Janine C. Malone, MD2
1University of Louisville, Louisville, Kentucky, USA
2University of Louisville School of Medicine, Louisville, Kentucky, USA

Melanoma Genetics/Genomics have great prognostic potential but few genome-based assays are currently validated for clinical use. In this independent study we assessed our institution’s experience utilizing a new gene-expression array (DecisionDx-Melanoma®) in the management of patients with melanoma. Retrospective analysis of our institution’s database between August 2012 and April 2016 disclosed 424 invasive melanomas, 43 (10%) of which underwent DecisionDx-Melanoma® testing. We assessed the prognostic significance of the reported Probability Value (PV) and Melanoma Class (Class 1=low risk; Class 2=high risk) by correlating these results with current clinical and pathologic staging parameters for cutaneous melanoma. Patients in our cohort had a mean age of 60 years at presentation, and there was an equal gender ratio. Histologically, 30 cases (69.8%) were superficial-spreading while 12 (29%) were of nodular type. Lesions had a mean mitotic rate of 4.0/mm2 and tumor-thickness of 4.44 mm; and eleven lesions (26%) demonstrated ulceration. The mean reported test PV was 0.40. Higher PV correlated with nodular histologic subtype, ulceration, increased tumor thickness, and higher mitotic index (p<0.0001). Also, thicker and nodular lesions with high mitotic-rate were more likely to be Class 2. Furthermore, clinical/pathological stage-I and II patients have significantly lower PV compared to stage-III and IV patients. Our data confirm that this gene-based testing correlates significantly with current clinical and pathologic parameters and may provide additional prognostic information in patients with melanoma who cannot be adequately staged. Molecular testing combined with pathologic and clinical staging may collectively provide better prognostic accuracy for patients with cutaneous melanoma.
<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
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<tbody>
<tr>
<td>5:15 p.m. - 5:20 p.m.</td>
<td>Multifocal but Non-Disseminated Phaeohyphomycosis in a Healthy Man Via a Unique Mechanism: Ejection from MVA into a Vegetable Field Resulting in Contaminated Skin Wounds</td>
<td>Ryan Campbell, MD</td>
</tr>
<tr>
<td>5:20 p.m. - 5:25 p.m.</td>
<td>Cutaneous Granular Cell Angiosarcoma: A Rare Histologic Variant Closely Mimicking Benign Granular Cell Tumor</td>
<td>Daniel C. Skipper, DO</td>
</tr>
<tr>
<td>5:25 p.m. - 5:30 p.m.</td>
<td>Deficiency of Adenosine Deaminase 2 in a 13-Year-Old Female with Recurrent Ischemic Strokes, Vasculitis, and Livedo Racemosa</td>
<td>Mustafa M. Mohammad, MD</td>
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<tr>
<td>5:30 p.m. - 5:35 p.m.</td>
<td>Unique Pattern of Response to BRAF Inhibition in a Case of Advanced Melanoma</td>
<td>Diana Braswell, MD</td>
</tr>
<tr>
<td>5:35 p.m. - 5:40 p.m.</td>
<td>Syphilitic Proctocolitis in HIV-negative Female Diagnosed Retrospectively After Skin Biopsy</td>
<td>Elisheva Shanes, MD</td>
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<tr>
<td>5:40 p.m. - 5:45 p.m.</td>
<td>Eccrine Syringofibroadenoma in Association with Acquired Epidermodysplasia Verruciformis</td>
<td>Timothy Tan, DO</td>
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<tr>
<td>5:45 p.m. - 5:50 p.m.</td>
<td>Two Faces of Melanoma: A Case of Melanoma with Transformation from Spindle Cell to Basaloid Histomorphology</td>
<td>Natasha K. Klimas, MD</td>
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<td>5:50 p.m. - 5:55 p.m.</td>
<td>Galli-Galli Disease: A Rare Acantholytic Variant of Dowling-Degos Disease</td>
<td>Audrey Green, MD</td>
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<tr>
<td>5:55 p.m. - 6:00 p.m.</td>
<td>Is There a Clinically Distinct Subset of Marginal Zone B-cell Lymphomas with Epidermotropism? A Case Report and Review of the Literature</td>
<td>Amin A. Hedayat, MD</td>
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<tr>
<td>6:00 p.m. - 6:05 p.m.</td>
<td>Molecular and Histologic Assessment of a Congenital Melanoma and Proliferative Nodules Arising in Medium Sized Congenital Nevus in a New Born</td>
<td>Maria C. Isales, MD, MPH</td>
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<tr>
<td>6:05 p.m. - 6:10 p.m.</td>
<td>A Question of Origin: A Case of Cellular Neurothekeoma Merging with an Intradermal Nevus</td>
<td>Brianne Dickey, MD</td>
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<td>6:10 p.m. - 6:15 p.m.</td>
<td>A Rare Case of Cutaneous Blastoid Mantle Cell Lymphoma</td>
<td>Ata Moshiri, MD, MPH</td>
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<td>AGEP Secondary to Stribild in an AIDS Patient</td>
<td>Aimee Coscarart, MD</td>
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<td>6:20 p.m. - 6:25 p.m.</td>
<td>Hypertensive Leg Ulcers (Martonell's ulcer), a Forgotten Entity</td>
<td>Georgina Uberti, MD</td>
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<td>Presenter</td>
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<td>6:25 p.m. - 6:30 p.m.</td>
<td>Primary Cutaneous Low-grade Neuroendocrine Tumor: An Exceedingly Rare Entity</td>
<td>Tiffany Chen, MD</td>
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<tr>
<td>6:30 p.m. - 6:35 p.m.</td>
<td>Amyloidosis of AL Type Presenting with Large Cutaneous Plaques and a Breast Mass in a Patient with Scleroderma in the Absence of Plasma Cell Dyscrasia</td>
<td>Nariman A. Nawar, MD</td>
</tr>
<tr>
<td>6:35 p.m. - 6:40 p.m.</td>
<td>Compound Melanocytic Nevus Arising Within an Organoid Nevus: A Rarely Reported Clinical and Histopathologic Finding in a Girl with Phakomatosis Pigmentokeratotica</td>
<td>Amber Fresco, MD</td>
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<tr>
<td>6:40 p.m. - 6:45 p.m.</td>
<td>Pembrolizumab-Induced Widespread Ulcerations in a Patient with Metastatic Melanoma and Squamous Cell Carcinoma</td>
<td>Dinesh Pradhan, MD</td>
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Multifocal but Non-Disseminated Phaeohyphomycosis in a Healthy Man via a Unique Mechanism: Ejection from MVA into a Vegetable Field Resulting in Contaminated Skin Wounds

Ryan Campbell, MD
Ryan Campbell, MD¹; Omar Malikzai, MD²; Janat Gul Sahak, MD²; Mirwais Abbas, MD²; Jerad M. Gardner, MD¹

¹University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA
²CURE International Hospital of Kabul, Kabul, Arkansas, USA

Phaeohyphomycosis is a fungal infection caused by various species of soil dwelling saprophytic dematiaceous (pigmented) fungi, which are seen as pigmented hyphae in the dermis. The typical presentation is an inflamed nodule in the lower extremity secondary to penetrating injury with soil contamination. Multifocal lesions may indicate disseminated systemic fungal infection; this occurs in immunosuppressed patients and has a significant risk of mortality. We report a 20 yo male with multiple subcutaneous nodules on the head, neck, chest and oral cavity. FNA and biopsy of several of these masses all showed pigmented fungal hyphae diagnostic of multifocal phaeohyphomycosis. The presentation initially raised concern for disseminated disease and occult immunosuppression. However, the patient appeared to be immunocompetent and was otherwise healthy aside from these nodules. Further inquiry revealed a surprising history: several years prior to development of these lesions, the patient was involved in a motor vehicle accident where he was ejected into a vegetable field resulting in multiple skin wounds and other injuries. The patient is currently undergoing a 12-month course of oral itraconazole 200mg twice daily; most of the lesions are regressing with this regimen. Any residual lesions remaining after completion of pharmacologic therapy will be excised. Multifocal phaeohyphomycosis is usually a sign of disseminated systemic disease due to immunosuppression and carries a grave prognosis. In our case, the unique clinical scenario of multiple skin wounds sustained during a motor vehicle accident, all of which were likely contaminated by soil from the field into which the patient was ejected, explained the development of multifocal phaeohyphomycosis in the absence of immunosuppression or systemic dissemination. The old adage may be tired but it is still true: “Clinical correlation is essential.”
Cutaneous Granular Cell Angiosarcoma: A Rare Histologic Variant Closely Mimicking Benign Granular Cell Tumor

Daniel C. Skipper, DO
Daniel C. Skipper, DO¹; Cesar A. Alvarenga, MD, PhD²; Jorge Mali Jr., MD, PhD³; Jerad M. Gardner, MD⁴;
¹Medical University of South Carolina, Charleston, South Carolina, USA
²Instituto de Patologia de Campinas and São Leopoldo Mandic, São Paulo, Brazil
³Londrina Cancer Hospital, Paraná, Brazil
⁴University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

Angiosarcoma (AS) is a rare malignant neoplasm of endothelial cells. The wide histologic variation in AS can be daunting: well-differentiated examples can simulate vascular malformation or hemangioma, whereas poorly differentiated epithelioid or spindled examples can histologically mimic carcinoma, melanoma, or other types of sarcoma. In 1985, McWilliam and Harris described a rare variant of AS with histologic and ultrastructural features similar to granular cell tumor. Very few cases of granular cell AS have been described in the literature to date. We report an additional case in the scalp of a 74-year-old Brazilian female. She presented with a small red lesion on the scalp that developed over 9 months into a 15 cm mottled erythematous plaque. Histologically, a solid sheet of epithelioid cells with abundant granular eosinophilic cytoplasm filled the dermis. In the deep aspect, these granular cells were arranged into irregular, anastomosing vascular channels that dissected through subcutaneous fat and into skeletal muscle. Nuclear atypia was seen, but some areas had relatively bland and uniform nuclei. Immunohistochemically, tumor cells expressed CD34, CD31, ERG, CD68, and D2-40; Ki-67 showed a high proliferative index. S100 protein, AE1/AE3, CD10, desmin and EMA were negative. She underwent wide local excision with negative margins followed by 20 sessions of radiation. She is alive with no evidence of disease at 12 months after diagnosis. The histologic similarity between granular cell AS and benign granular cell tumor is striking and poses a dangerous diagnostic pitfall: AS is an aggressive malignancy, whereas granular cell tumor is benign. Immunohistochemistry can easily distinguish between these entities, provided the pathologist is aware of this rare variant.

Deficiency of Adenosine Deaminase 2 in a 13-Year-Old Female with Recurrent Ischemic Strokes, Vasculitis, and Livedo Racemosa

Mustafa M. Mohammad, MD
Mustafa M. Mohammad, MD¹; Jeremy M. Hugh, MD¹; Joseph C. Pierson, MD¹; Laura A. Greene, MD¹
¹The University of Vermont Medical Center, Burlington, Vermont, USA

We present a 13 year old female with a history of livedo racemosa, recurrent ischemic strokes, and recurrent subclinical strokes on imaging with no evidence of a hypercoagulable disorder who presented with firm subcutaneous nodules on her legs. Clinically, the patient was suspected to have Sneddon’s disease and a punch biopsy of a nodule was performed. The biopsy demonstrated a vasculitis of medium-sized subcutaneous blood vessels with associated neutrophils, lymphocytes, and cellular debris within the vessel wall. Nodular aggregates of histiocytes surrounded the vessel and were admixed with eosinophils and lymphocytes. The typical arteriolar thrombosis seen in the context of Sneddon’s disease
was not noted with the biopsy instead showing a primary vasculitic process. Serologies, including ANCA, were unremarkable. The patient was placed on Rituximab and high dose prednisone for the vasculitis with continued surveillance. Further investigation prompted testing for the CECR1 gene mutation which is seen in the context of Deficiency of Adenosine Deaminase 2 (DADA2). The patient was found to harbor this mutation. DADA2 was first described in 2014 and is seen in patients with early onset stroke. Additional findings include livedoid racemosa, polyarteritis nodosa-like vasculitis, fever, joint pain, anemia, and fatigue. While the pathogenesis is unknown, ADA2 has been shown to be vital to the differentiation of monocytes to macrophages and blood vessel development. The patient was placed on a trial of a TNF inhibitor. To date, patients have had no further strokes once on this medication, including our patient. This case broadens the differential of medium vessel vasculitides, especially in the setting of neurologic complications in the pediatric population.

**Unique Pattern of Response to BRAF Inhibition in a Case of Advanced Melanoma**

Diana Braswell, MD

Diana Braswell, MD1; Zeynep Eroglu, MD2; Vernon K. Sondak, MD2; Jane L. Messina, MD2

1University of South Florida Morsani College of Medicine, Tampa, Florida, USA
2Moffitt Cancer Center, Tampa, Florida, USA

Neoadjuvant BRAF/MEK inhibition of melanoma typically results in partial to complete pathologic response upon surgical resection. We present a unique case of cellular maturation of melanoma after neoadjuvant BRAF/MEK inhibition. A 49 year-old male presented with a 6-month history of a rapidly growing multinodular right lower back cutaneous plaque measuring 3x2.8 cm surrounded by numerous satellite lesions encompassing an area 15x12 cm, diagnosed as BRAFV600E-mutated locally advanced primary melanoma, 3.2 mm in depth. Although initially deemed unresectable, it shrank dramatically following 10 months of dabrafenib/trametinib therapy and was excised, revealing residual recurrent/in-transit melanoma, 8.5x5 cm, with treatment effect: tumor nodules throughout the dermis and subcutaneous fat showed variation in cellularity with expansile sheet-like nodules, looser aggregates and single file arrays. The melanocytes showed striking uniformity, lack of pleomorphism, low nuclear cytoplasmic ratio, small nuclei with homogeneous chromatin and no mitotic activity. Pre-treatment Ki-67 index was 30% compared to 1% post-treatment, and BRAF VE1 expression was homogenous after treatment compared to heterogeneous pre-treatment. No changes in expression of p16 (negative) or Melan-A/HMB-45 (positive) were seen with treatment. This morphologic change resembling maturation secondary to treatment has not been previously reported in the literature. We hypothesize that BRAF/MEK inhibition selected for a tumor clone that was BRAF-mutated but had suppressed proliferation, similar to the senescence that occurs in BRAF-mutated nevi. While intact p16 can suppress melanocyte proliferation in BRAF-mutant nevi, this mechanism is ruled out in this case. Recognition of this pattern of response to therapy is important; further studies will be needed to determine whether this pattern is associated with different outcome compared to the typical patterns of response to BRAF/MEK inhibition.
Syphilitic Proctocolitis in HIV-negative Female Diagnosed Retrospectively after Skin Biopsy
Elisheva Shanes, MD
Elisheva Shanes, MD1; Thomas Cibull, MD1
1University of Chicago (NorthShore University HealthSystem), Evanston, Illinois, USA

A 32-year old female presented to her dermatologist with a maculopapular rash clinically thought to be a drug eruption. 3 weeks prior she had presented with abdominal pain, nausea, fecal urgency, hematochezia, and low grade fevers. At that time CT scan showed circumferential rectal wall thickening with pelvic and abdominal lymphadenopathy. A flexible sigmoidoscopy revealed normal mucosa, and random colon biopsies were taken. Though most biopsy fragments were unremarkable, one fragment demonstrated chronic inflammation expanding the lamina propria without significant active colitis. The initial diagnosis rendered was nonspecific chronic inflammation; the patient was given the clinical diagnosis of irritable bowel syndrome and was medicated. Punch biopsy of the rash demonstrated lichenoid psoriasiform dermatitis with plasma cells. IHC for T. pallidum showed spirochetes at the dermal-epidermal junction consistent with secondary syphilis. In light of this finding, IHC for T. pallidum was performed on the colon biopsy revealing spirochetes within the lamina propria and crypt epithelium consistent with syphilitic colitis. Further work-up of the patient revealed she was HIV-negative. Syphilitic proctocolitis is an entity almost entirely associated with HIV-positive men who have sex with men. While often treated empirically, biopsy demonstrates relatively non-specific findings including a submucosal plasma cell infiltrate and lamina propria expansion by chronic inflammation, without significant crypt damage or abundant eosinophils. This case is significant in that there are no previously reported cases of syphilitic colitis in healthy female patients. Additionally, this case highlights the role a dermatopathologist can play in uncovering underling systemic illness by evaluating skin biopsy.

Eccrine Syringofibroadenoma in Association with Acquired Epidermodysplasia Verruciformis
Timothy Tan, DO
Timothy Tan, DO1; Joan Guitart, MD1; Luzheng Lisa Liu, MD, PhD1; Joaquin Brieva, MD1; Sapna Amin, MD1; Monica Rani, MD1; Pedram Gerami, MD1; Pedram Yazdan, MD1
1Northwestern University Feinberg School of Medicine, Chicago, IL, USA

A 75-year-old man with human immunodeficiency virus (HIV) infection and numerous biopsy-proven warts for 10 years refractory to cryosurgery, oral cimetidine and topical imiquimod, presented with numerous pink to hypopigmented verrucous papules and plaques involving the face, trunk, buttocks, and groin. Laboratory evaluation revealed an absolute CD4 T-cell count of 62/µL and a HIV viral load of <117 copies/mL. Shave biopsy of a large plaque groin lesion was performed. Histopathology revealed vertically oriented anastomosing strands of basaloid epithelium arising from multiple points along the epidermis in a background fibrovascular stroma. Focal ductal differentiation was identified. Areas of epidermis also showed compact orthokeratosis, coarse hypergranulosis, and keratinocytes with abundant steel-blue gray cytoplasm, indicative of viral cytopathic changes. Cytologic atypia was not identified. Human papilloma virus (HPV) genotyping of this lesion was positive for types 5 and 14. Overall, the findings were consistent with epidermodysplasia verruciformis (EV) in association with
eccrine syringofibroadenoma (ESFA). The patient was subsequently treated with acitretin and showed clinical improvement. EV is a rare autosomal recessive genodermatosis characterized by wart-like eruptions caused by HPV infection and predisposes patients to development of squamous cell carcinoma. “Acquired” EV can occur in patients with impaired cell-mediated immunity. While ESFA and its association with HPV has been reported in Clouston syndrome, a potential association in the setting of acquired EV has not been described. The changes in this case may possibly be the result of HPV inducing transformative changes causing development of ESFA.

Two Faces of Melanoma: A Case of Melanoma with Transformation from Spindle Cell to Basaloid Histomorphology

Natasha K. Klimas, MD
Natasha K. Klimas, MD¹; Ramya Kollopara, MD¹; Michelle B. Tarbox, MD¹
¹Texas Tech Health Sciences Center, Lubbock, Texas, USA

The histologic heterogeneity of melanoma is profound, as over 20 pathologic variants have been described. Variation in overall architecture, cytology, and stromal array is characteristic for melanoma. Moreover, melanoma is widely-recognized as a formidable histologic mimic of myriad other benign and malignant tumors, including but not limited to the giant cell variant of glioblastoma multiforme, acantholytic squamous cell carcinoma, and even the common wart. Procedural interventions, chemotherapy, and immunotherapy may further alter the histologic milieu of melanoma, which may present considerable challenges for the dermatopathologist. Here we present a case of melanoma of the scalp, initially surgically resected and subsequently managed with pembrolizumab. Longitudinal histopathological assessment of our patient revealed distinct in-transit metastases demonstrating spindle cell morphology with evolution to assume features resembling those of basal cell carcinoma following initiation of immunotherapy. To our knowledge, this is the first report of melanoma treated with pembrolizumab characterized by dramatic transformation from spindle cell to basaloid tumor histomorphology. This case underscores the aggressive and recurrent nature of melanoma of the scalp, as well as the importance of frequent surveillance among this patient population. Moreover, our case highlights the extraordinary microscopic mutability of melanoma, and highlights histologic changes incurred during immunotherapy.

Galli-Galli Disease: A Rare Acantholytic Variant of Dowling-Degos Disease

Audrey Green, MD
Audrey Green, MD¹; Tammie Ferringer, MD¹; George Lin, MD¹; Christen Mowad, MD¹
¹Geisinger Medical Center, Danville, Pennsylvania, USA

Galli-Galli disease (GGD) is a rare, autosomal dominant, variant of Dowling-Degos disease (DDD). GGD is one of the reticulated pigment disorders that also include reticulated acropigmentation of Kitamura, symmetrical acropigmentation of Dohi, and Haber’s syndrome. Clinical manifestations of such entities are often quite similar, but may be distinguished by the age of onset and other associated cutaneous
findings. While these disorders also resemble one another histologically, the acantholysis of GGD is a unique distinguishing feature. A 38 year old female with a history of melanoma and dysplastic nevi first presented to our dermatology clinic in 2006 with a several year history of a pruritic rash involving the arms, legs, chest, back and neck. It flared several times a year without full resolution. Multiple biopsies were performed over a 10 year period with the original clinical suspicion of lichenoid dermatitis. The initial biopsies revealed a lentigo-like epidermal pattern with little to no inflammatory component. In 2008, the biopsies also began to show acantholysis and dyskeratosis suggesting the possibility of Grover’s disease or Darier disease. The elongate and somewhat bulbous interconnecting rete become more prominent in subsequent biopsies and the clinical differential also included confluent and reticulated papillomatosis. Collective review of the prior biopsies and clinical images showing diffuse red-brown macules and keratotic papules coalescing in a lacy, reticulate pattern also involving the axillae and inframammary folds, suggested GGD. Genetic testing showed a keratin 5 (KRT5) mutation confirming the diagnosis. Although she denied a prior family history of GGD, she described a similar eruption in her 29 year old son. As with our patient, multiple biopsies are often necessary to confirm the diagnosis. Elongate, pigmented rete, similar to DDD, with acantholysis should suggest GGD.

Is There a Clinically Distinct Subset of Marginal Zone B-cell Lymphomas with Epidermotropism? A Case Report and Review of the Literature
Amin A. Hedayat, MD
Amin A. Hedayat, MD; Joi B. Carter, MD; Robert E. LeBlanc, MD

Dartmouth Hitchcock Medical Center and Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA

We report an exceedingly rare case of epidermotropic B-cell lymphoma with an extranodal marginal zone phenotype that behaved indolently for 11 years with intermittent cutaneous manifestations responding to narrowband ultraviolet B phototherapy. A 66-year-old woman presented with an asymptomatic papular rash that improved each spring and worsened in winter. It gradually spread to involve her back, buttocks, and thighs; however, she was otherwise healthy. Her biopsy revealed a band-like dermal lymphoid infiltrate including enlarged monocytoid forms that extended to the dermoepidermal junction and epidermis without classic Pautrier-type microabscess formations of mycosis fungoides. The cells expressed CD20, CD79a, CD19, Bcl-2, CD43, and IgG; and were negative for CD3, CD4, CD8, Cyclin D1, CD5, CD23, CD138, CD10, Bcl-6, IgM, and IgD. An IGH clone was detected in the skin by PCR. Accompanying T-cells were polyclonal. Flow cytometry performed on peripheral blood and marrow aspirate samples revealed low-level involvement by the monoclonal kappa-restricted B-cell population. There are rare prior reports of epidermotropic B-cell lymphomas with a marginal zone phenotype. Previously described patients were predominantly older men presenting with disseminated papular rashes. Some had involvement of their marrow, peripheral blood, and spleen. PET imaging of our patient has also revealed presumptive splenic involvement. None of the reported patients died of their disease and some showed dramatic responses of skin lesions to phototherapy. These cases may represent a rare subset of marginal zone lymphoma with distinct clinical features, a tendency toward indolent behavior, and an epidermotropic appearance that mimics cutaneous T-cell lymphoma.
Molecular and Histologic Assessment of a Congenital Melanoma and Proliferative Nodules Arising in Medium Sized Congenital Nevus in a New Born
Maria C. Isales, MD, MPH
Maria C. Isales, MD, MPH1; Pedram Gerami, MD1
1Northwestern Memorial Hospital, Chicago, Illinois, USA

Differentiating between malignant melanoma and proliferative nodules arising in congenital nevi in the newborn population is both challenging and critical given that over 40% of patients diagnosed with infantile melanoma die within 18 months of diagnosis. A comprehensive review of the literature revealed twenty-seven cases of infantile or congenital melanoma reported since 1925. Three types of congenital melanoma exist: those associated with a congenital melanocytic nevus, de novo congenital melanoma, and transplacental metastases. Array comparative genomic hybridization (CGH) and FISH have been utilized as an adjunctive tool in melanoma and more recently in de novo congenital melanoma. Amplifications in regions with known oncogenes, including BRAF, NRAS, MITF, and MDM2 have been seen in congenital melanomas. We present a case of an African American female noted to have a 5.0 cm exophytic nodule as well as several other smaller nodules within a congenital nevus at birth. There was no family history of melanoma or other cancers. Given the rapid growth of the lesions over the following two months, several biopsies were performed. Histopathologic review of the largest nodule showed a nodular dermal proliferation with sheets of intermediate round cells with coarse chromatin and high grade nuclear atypia. The lesion was diagnosed as malignant melanoma with Breslow depth 2.75 mm with prominent mitotic activity. Fluorescence in situ hybridization (FISH) evaluation of the tumor showed segmental gains in 6p25 corroborating the diagnosis of melanoma. Adjacent smaller nodules showed morphologic changes of proliferative nodules and showed whole chromosomal copy number changes by FISH. The current report demonstrates the importance of correlating molecular and histopathologic interpretation in coming to a correct diagnosis. Molecular assessment limited to the proliferative nodular area may have resulted in an incorrect diagnosis. A sentinel lymph node biopsy also revealed metastatic melanoma involving the lymph nodes.

A Question of Origin: A Case of Cellular Neurothekeoma Merging with an Intradermal Nevus
Brianne Dickey, MD
Brianne Dickey, MD1; Scott Kelley, MD2
1Medical College of Wisconsin, Milwaukee, Wisconsin, USA
2Dermpath Diagnostics, Brookfield, Wisconsin, USA

A seventeen year old male had a lesion on the right neck which was clinically thought to represent a benign adnexal neoplasm such as trichoepithelioma. Excisional biopsy was performed, and two patterns of dermal infiltrate were seen. In the superficial papillary dermis, there were nested collections of small round cells which stained positively for S100 and Melan-A, consistent with an intradermal nevus. A second distinct population of cells was seen merging with the nevus and extending throughout the dermis and focally into subcutaneous fat, forming a somewhat poorly circumscribed nodule. These cells were arranged in nests (theques) separated by thickened collagen bundles. They had moderate to
abundant amphophilic and slightly foamy cytoplasm, with round nuclei, indistinct nucleoli, scattered pleomorphism, and infrequent mitoses. Staining demonstrated strongly positive NKI/C3, minimally positive CD68, and negative S100, Melan-A, smooth muscle actin, muscle specific actin, lysozyme, and keratins. These findings suggested a diagnosis of cellular neurothekeoma. The origin of cellular neurothekeoma is not well understood, and many sources have been proposed. Melanocytosis of cellular neurothekeoma has been described, but to our knowledge, there are no reported cases of cellular neurothekeoma merging with a melanocytic nevus. The intimate junction of normal nevus cells with cellular neurothekeoma seen in this case supports a common neural crest origin for the two entities.

**A Rare Case of Cutaneous Blastoid Mantle Cell Lymphoma**

Ata Moshiri, MD, MPH
Ata Moshiri, MD, MPH; Mark Mochel, MD; Paul Haun, MD, MS; Evan Piette, MD; Carrie Kovarik, MD

*University of Pennsylvania, Philadelphia, Pennsylvania, USA*

Our patient is a 75 year old man who in early 2014 developed sinus congestion unresponsive to corticosteroid therapy. Imaging showed a nasopharyngeal mass and left-sided cervical lymphadenopathy, both of which were biopsied, revealing sheets of medium to large atypical cells with pleomorphic nuclei, strongly positive for CD20, CD79a and BCL1 (cyclin D1). Further workup revealed no bone marrow or organ involvement. He was diagnosed with a pleomorphic variant of mantle cell lymphoma (MCL), and after six cycles of bendamustine and rituximab, he achieved a complete clinical and radiographic response by September 2014. His initial therapy was followed by consolidation radiation and maintenance rituximab every two months. In January 2016, he developed a painless nodule on his left buttocks. Biopsy of this lesion revealed a dermal infiltrate of atypical lymphoid cells with scant cytoplasm, large nuclei with irregular contours and heterogeneous chromatin. These stained strongly positive with CD20, CD5 and BCL1. Repeat PET-CT showed no other areas of metabolic activity. MCL comprises less than 10% of non-Hodgkin lymphomas, and less than 1% of these have been reported to have cutaneous involvement, making this case a rare presentation of an uncommon disease. Histologically, the blastoid variant of MCL resembles diffuse large B-cell lymphoma (DLBCL), and both entities typically share a similar immunophenotype (positive for BCL2, MUM-1/IRF4, IgM; negative for CD10, BCL6), making distinction between the two entities very difficult. The distinguishing factors are expression of BCL1 and the canonical t(11;14), the latter of which is not routinely considered in such cutaneous specimens.
Hypertensive Leg Ulcers (Martonell’s ulcer), a Forgotten Entity
Georgina Uberti, MD
Georgina Uberti, MD1; Michael Schowalter, MD1; Anthony P. Fernandez, MD, PhD1; Melissa Piliang, MD1
1Cleveland Clinic, Cleveland, Ohio, USA

Hypertensive ischemic leg ulcers (Martonell’s ulcers) are a unique, under-recognized entity in patients with long-standing, poorly controlled hypertension. Commonly, lower extremity ulcers are associated with vascular arterial disease, venous insufficiency, and vasculitis. We present a challenging case of a 50-year-old-man with a history of hypertension, presenting with a 4 month history of a non-healing, painful leg ulcer, and normal ankle-brakial index (ABI). Histopathologic examination of the lesion revealed ulceration of the epidermis, edema, granulation tissue of the superficial dermis, and significant hyalinized wall thickening of the arterioles. There was minimal luminal patency, consistent with arteriosclerosis. Martonell’s ulcers are typically found in the antero-lateral aspect of the leg, or on the Achilles tendon. The pain is often disproportionate to clinical findings, occurring frequently at night. The ulcers are superficial, with irregular contours, have a necrotic base and inflammatory purple-red edges. Satellite lesions may appear. Infections are a common complication. Histopathologic findings include subcutaneous arteriolosclerosis, showing thickening of the elastic lamina, proliferation of the intimal layer, media hyperplasia with hyalinization and calcinosis. The result is an increase in the thickness of the vessel wall, with narrowing of the lumen. An inflammatory response is secondary to the necrosis that results from progression to tissue ischemia. These findings can be seen in several

AGEP Secondary to Stribild in an AIDS Patient
Aimee Coscarart, MD
Aimee Coscarart, MD1; Buu Duong, MD1; Corey Rougelot, MD1; Michael Lee, MD1; Alun Wang, MD, PhD1
1Tulane Medical Center, New Orleans, Louisiana, USA

Acute generalized exanthematous pustulosis (AGEP) is an acute febrile pustular drug eruption characterized by numerous small pustules arising on extensive edematous erythema. There are few reports of AGEP secondary to antiretroviral therapy in patients with AIDS. We present a case of AGEP in a 45-year-old Caucasian female with AIDS (CD4 count of 13) who presented with a one-week history of worsening pruritic skin rash. Patient had started anti-retroviral therapy with Stribild (emtricitabine/tenofovir/elvitegravir/cobicistat) and prophylaxis with azithromycin one to two weeks prior. The rash presented as extensive erythematous nonfollicular pustular eruptions with intact and flaccid pustules involving the chest, neck, face, ears and scalp. Biopsy revealed subcorneal, intraepidermal and follicular neutrophilic sterile pustules. Patient was taken off all medications and discharged home. Two months later, Stribild was reinitiated. Approximately 1 week after therapy, a similar pustular eruption reappeared and Stribild was discontinued. After eruption resolved, patient was started on lamivudine/zidovudine/atazanavir/ritonavir regimen without adverse reactions. There have been rare reports of AGEP attributed to protease inhibitors of HAART in HIV-infected patients, whereas nucleoside/nucleotide reverse transcriptase inhibitors have not been implicated as causal agents in AGEP. Stribild should be considered when evaluating for possible medications that can induce AGEP.
organs. Calciphylaxis, pyoderma gangrenosum (PG) and vasculitis, are important entities to consider within the differential diagnosis. This is particularly true when a punch biopsy is taken from the base of the necrotic wound, since a superficial biopsy can mimic changes seen in PG. A long narrow but deep to the fascia biopsy will reveal the characteristic stenotic arterioles in the subcutis. Doppler, as well as duplex with reflux studies should be perform to exclude peripheral vascular disease, and venous insufficiency respectively. Martonell’s hypertensive ischemic ulcers should be considered in cases of painful ulcers of the lower extremities. Delays in recognition of this underappreciated etiology of ulcers, may prolong disability, and lead to unnecessary and ineffective treatment.

**Primary Cutaneous Low-grade Neuroendocrine Tumor: An Exceedingly Rare Entity**

Tiffany Chen, MD
Tiffany Chen, MD; Annie Morrison, MD; Joseph Susa, DO; Clay Cockerell, MD

1 University of Texas Southwestern Medical Center, Dallas, Texas, USA

Primary cutaneous low-grade neuroendocrine tumor (NET), also known as carcinoid tumor, is an extremely rare diagnosis. NET commonly arises from the gastrointestinal and pulmonary tracts, but rarely occur in the skin as a low grade neoplasm. Cutaneous NET typically occurs as a high-grade metastatic lesion or primary Merkel cell carcinoma. In the few cases described in literature, primary cutaneous low-grade NET are usually indolent cutaneous nodules, presenting on the head and trunk of elderly patients. Primary cutaneous low-grade NET is histologically similar to its counterparts arising in other anatomic locations: a well-circumscribed nodule composed of cells arranged in nets, islands, and lobules. The neoplastic cells are uniform and round with round-to-oval nuclei displaying characteristic “salt and pepper” stippled chromatin. Mitoses are rare and mitotic index (or Ki67 index) stratifies these lesions into low-intermediate-or-high grade. NET show positive staining with neuroendocrine markers (synaptophysin, chromogranin and CD56). By definition, low grade NET have a Ki-67 proliferative index of less than 3%. The distinction between primary and metastatic NET, however, is not absolute and can be difficult. A primary versus metastatic NET diagnosis relies on clinical exclusion of a NET in other, more common, anatomic locations. Here, we present a case of a primary low-grade NET on the scalp of a 72-year-old female patient. Whole body imaging failed to identify any octreotide-avid lesions elsewhere in the patient. Despite the low histologic grade, two positive cervical lymph nodes were identified with octreotide scan (and pathologically confirmed). This is the 11th reported case of primary cutaneous low grade NET and the 2nd reported case of primary cutaneous low grade NET with nodal metastasis.
Amyloidosis of AL Type Presenting with Large Cutaneous Plaques and a Breast Mass in a Patient with Scleroderma in the Absence of Plasma Cell Dyscrasia

Nariman A. Nawar, MD
Nariman A. Nawar, MD; David M. Burch, MD

1West Virginia University, Morgantown, West Virginia, USA

Various types of amyloid have been described in cutaneous amyloidosis, such as the AA type and the AL type. Cutaneous amyloidosis of AA type results from acute phase reactant protein deposition in skin in association with systemic inflammatory conditions or autoimmune conditions. Cutaneous amyloidosis of AL type results from light chain immunoglobulin deposition and is usually associated with plasma cell dyscrasia or multiple myeloma. This type of amyloidosis commonly presents as small papules or as purpuric rash. Here, we present a case of cutaneous amyloidosis of AL type in a 68 year old female in the absence of known plasma cell dyscrasia. The patient had a history of scleroderma and Sjogren syndrome. She presented with several large cutaneous plaques over extremities and a breast mass. The breast mass core biopsy showed amyloid involving ductal units and blood vessels. Skin punch biopsy revealed plasma cell infiltrate in the mid dermis and amyloid, which was confirmed by Congo red stain. In-situ hybridization characterized the plasma cells as polyclonal and bone marrow examination was negative for plasma cell dyscrasia. However, mass spectrometry of the skin biopsy typed the amyloid as AL. Dermatopathologists need to be aware that AL amyloidosis can present with large plaques as well as the more classic purpura and small waxy papules. AL amyloid should be considered even when there are other possible causes of amyloid, such as that associated with chronic disease or autoimmune disease, and when plasma cell dyscrasia is not evident.

Compound Melanocytic Nevus Arising Within an Organoid Nevus: A Rarely Reported Clinical and Histopathologic Finding in a Girl with Phakomatosis Pigmentokeratotica

Amber Fresco, MD
Amber Fresco, MD; Allison Kutner, MD; Wu Julia, MD; Diana H. Lee, MD, PhD; Bijal Amin, MD

1Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, New York, USA

We present a 14-year-old female with phakomatosis pigmentokeratotica manifested by widespread organoid nevi distributed on her scalp and trunk, a large speckled lentiginous nevus of her trunk, and hypophosphatemic rickets. Clinically, a dark brown verrucous papule was found within a blaschkolinear verrucous plaque situated on a larger tan patch on the patient’s back. Another dark brown verrucous papule was identified within a yellow papillated alopecic plaque on the tempoparietal scalp. Biopsy of the two lesions showed increased number of sebaceous glands in the upper half of the dermis, a papillated epidermis, and proliferation of monomorphous melanocytes arranged as solitary units and small nests within the epidermis, dermo-epidermal junction, and dermis. A compound nevus within an organoid nevus was diagnosed. Phakomatosis pigmentokeratotica is a multi-system congenital disorder characterized by organoid nevi and speckled lentiginous nevi with accompanying neurologic, endocrine, and musculoskeletal disorders. Previous literature has documented numerous benign and malignant secondary proliferations arising in organoid nevi, including trichoblastoma, syringocystadenoma
Pembrolizumab-Induced Widespread Ulcerations in a Patient with Metastatic Melanoma and Squamous Cell Carcinoma

Dinesh Pradhan, MD
Dinesh Pradhan, MD1; Sonal Choudhary, MD1; Arivarasan Karunamurthy, MD1; Timothy J. Patton, DO1; James P. O’toole, MD1; John M. Kirkwood, MD1; Jaroslaw J. Jedrych, MD1; Jonhan Ho, MD1
1UPMC, Pittsburgh, Pennsylvania, USA

Pembrolizumab-induced widespread ulceration is extremely rare. Mostly it is associated with low-grade rash, pruritus and vitiligo. Xerosis, lichenoid dermatitis, psoriasis, oral lichenoid reactions, xerostomia, dysguesia, alopecia, and hair color changes has also been reported. Herein we report a 77-year-old hypertensive male with the past history of metastatic melanoma primarily involving the left thigh in remission after wide excision and tremelimumab therapy and recently excised invasive squamous cell carcinoma originating at the same chronic burn wound site in the left thigh with multiple positive lymph nodes on imaging, who presented to his wound care service with numerous ulcerations involving bilateral lower limb. The patient was on pembrolizumab for approximately 3 months at this stage without any other adverse effects. He also started developing several itchy 5-10 mm erythematous round nodules with white scales over the arms and similar erythematous scaly plaques over the dorsum of the hand. In the ensuing couple of months, the deep ulcers worsened and extensively involved the bilateral upper and lower extremity and the lower abdomen. The bleeding and serous drainage from the wounds increased significantly. He also developed dehydration, anorexia and anemia. Histologic examination of both the upper and lower extremity lesion revealed lichenoid process with mixed inflammation, pseudoepitheliomatous hyperplasia and some squamous atypia. Pembrolizumab therapy was stopped after 7 cycles due to concerning wound issues and failure to thrive and the patient was put on steroids. The lesions improved significantly in 1 month when the abdominal lesion was biopsied. Microscopic examination revealed similar lymphoplasmacytic lichenoid infiltrate with significant squamous atypia. The patient is on follow up for 2 months and is doing well with significant improvement of the lesion. The basis of this lichenoid dermatitis may be enhanced autoimmunity (activation of T-cells targeting antigen presenting keratinocytes) triggered by programmed cell death-1 (PD-1) receptor inhibition. We present this case to highlight this rare adverse event associated with pembrolizumab therapy. Awareness of this finding will help in the management of cancer patients receiving PD-1 inhibitors.
## Fellows' Presentations

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
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<tbody>
<tr>
<td>2:00 p.m. – 2:05 p.m.</td>
<td>Metastatic Malignant Melanoma with Gains of Chromosome Region 22q12 by FISH</td>
<td>Ryan S. Berry, MD</td>
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<td>2:05 p.m. – 2:10 p.m.</td>
<td>Libman-Sacks Endocarditis Presenting as an Initial Symptom of Systemic Lupus Erythematosus</td>
<td>Jose E. Ollague, MD</td>
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<td>2:10 p.m. – 2:15 p.m.</td>
<td>Non-blistering PD-1 inhibitor- induced Bullous Pemphigoid: Entering an Era of Autoimmune Disorders Induced by Checkpoint Blockade</td>
<td>Katherine Roy, MD</td>
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<td>2:15 p.m. – 2:20 p.m.</td>
<td>EBV-associated, Cutaneous, Smooth Muscle Tumor in AIDS Patient</td>
<td>Yevgeniya B. Rainwater, MD</td>
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<td>2:20 p.m. – 2:25 p.m.</td>
<td>Fibroblastic Rheumatism: A Rare But Pertinent Dermatoarthropathy</td>
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<tr>
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<td>Nodular Cutaneous Microsporidiosis in an Immunocompromised Patient</td>
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<tr>
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<tr>
<td>2:35 p.m. – 2:40 p.m.</td>
<td>Amyloidoma of the Skin/Subcutis with Monotypic Plasma Cell Infiltrates: An Unusual Presentation of Primary Cutaneous Marginal Zone Lymphoma?</td>
<td>Ian Marie L. Lano, MD</td>
</tr>
<tr>
<td>2:40 p.m. – 2:45 p.m.</td>
<td>T-cell Acute Lymphoblastic Lymphoma/Leukemia Presenting as a Diffuse Exanthem: A Clinical and Histopathologic Challenge</td>
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<tr>
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<td>ALK1-positive Pediatric Spitzoid Melanoma with Homozygous Deletion of 9p21 (CDKN2A) and Gain of 6p25 (RREB1) by FISH: A Case Report.</td>
<td>Andrew J. Rand, MD</td>
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<tr>
<td>2:50 p.m. – 2:55 p.m.</td>
<td>A Primary Cutaneous Burkitt Lymphoma with Classic Immunohistochemical and Molecular Findings</td>
<td>Aravindhan Sriharan, MD</td>
</tr>
<tr>
<td>2:55 p.m. – 3:00 p.m.</td>
<td>Epithelioid Fibrosarcoma with Collagen Rosettes</td>
<td>Stephanie J.T. Chen, MD</td>
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<tr>
<td>3:00 p.m. – 3:10 p.m.</td>
<td>An Evaluation of the Utility of a Novel Microsatellite Instability Assay in the Workup of Sebaceous Neoplasms</td>
<td>Jay Wofford, MD</td>
</tr>
<tr>
<td>3:10 p.m. – 3:20 p.m.</td>
<td>Utility of Histologic Features of Secondary Syphilis</td>
<td>Alexandra Flamm, MD</td>
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<tr>
<td>3:20 p.m. – 3:30 p.m.</td>
<td>Expression of Metallopanstimulin-1 in the Spectrum of Melanocytic Neoplasms</td>
<td>Maria A. Deschaine, MD</td>
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<tr>
<td>3:30 p.m. – 3:40 p.m.</td>
<td>STAT3 Gene Mutation and Enhanced STAT3 Phosphorylation is Detected in a Subset of Tumor Stage Mycosis Fungoides with Large Cell Transformation</td>
<td>Andy C. Hsi, MD</td>
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<td>3:40 p.m. – 3:50 p.m.</td>
<td>Histopathologic Attributes Associated with MelaFind Classification: A 3-Year Experience with High-Risk Pigmented Lesion Clinic</td>
<td>Vikas Shrivastava, MD</td>
</tr>
<tr>
<td>3:50 p.m. – 4:00 p.m.</td>
<td>The Ciliation Index Distinguishes Invasive Melanoma and Melanoma In-Situ from Associated Dermal Melanocytic Nevi</td>
<td>Ursula E. Lang, MD, PhD</td>
</tr>
</tbody>
</table>
Fellows' Presentations

Metastatic Malignant Melanoma with Gains of Chromosome Region 22q12 by FISH
Ryan S. Berry, MD
Ryan S. Berry, MD\(^1\); William B. Tyler, MD\(^1\); Wells M. Chandler, MD\(^1\); Tammie C. Ferringer, MD\(^1\)
\(^1\)Geisinger Medical Center, Danville, Pennsylvania, USA

Initial studies looking at chromosomal alterations in malignant melanoma (MM) using comparative genomic hybridization have shown losses on chromosome 6q, 8, 9p, 10, 21q and gains at 1q, 4q, 6p, 7q, 8q, 11q, 17q, and 20q. There is little in the literature regarding alterations of chromosome 22 in MM, with only one case report showing amplification of region 22q12. We report a case of metastatic malignant melanoma occurring on the forearm of a 66-year-old female that harbored gains of chromosome region 22q12 by FISH analysis. The patient presented with a lesion on her right forearm of approximately 9 months duration. There was no change in size or color of the lesion. She endorsed a long history of sun exposure without sun protection. She denied a personal and family history of MM. A biopsy of the lesion was performed, which consisted of the deep dermis and subcutis without overlying epidermis. Deep in the dermis was a nodular proliferation of enlarged and atypical epithelioid cells with moderate amounts of cytoplasm and enlarged atypical nuclei with prominent nucleoli. Occasional multinucleated cells were present. At the periphery of the lesion was reactive fibrosis with an accompanying lymphocytic infiltrate and focal nodular aggregates of lymphocytes. Up to 23 mitoses/HPF were identified. The lesional cells showed strong immunohistochemical staining with Melan-A. Given clear cell sarcoma was considered in the differential diagnosis, tissue was sent for FISH analysis looking for the characteristic reciprocal translocation, t(12;22)(q13;q12), which results in fusion of the EWSR1 and ATF1 genes. Dual color break apart probes for EWSR1 (22q12) failed to show rearrangement; however, there were multiple copy number gains (ranging from 3 to 10) in all cells examined, suggesting either partial or whole gains of chromosome 22. To the authors knowledge, only one other case of malignant melanoma harboring amplification of chromosome region 22q12 has been reported in the literature. Similar to the reported case, our patient was older and presented with metastatic disease. The significance of these findings is uncertain at this point, but could potentially serve as a diagnostic aid and/or a marker of prognostic value.

Libman-Sacks Endocarditis Presenting as a an Initial Symptom of Systemic Lupus Erythematosus
Jose E. Ollague, MD
Jose E. Ollague, MD\(^1\); William B. Tyler, MD\(^1\); Victor Marks, MD\(^1\)
\(^1\)Geisinger Medical Center, Danville, Pennsylvania, USA

Background: Acral purpuric lesions usually suggest embolic disorders. It may present due to fragmentation of an atheromatous plaque, bacterial or fungal endocarditis, endovascular catheter fragments and less common atrial myxomas, and aseptic heart valves vegetations as seen in hypereosinophilic syndrome and Libman-Sacks endocarditis. Case Description: A 13 year old African
an uncommon presentation of Libman-Sacks endocarditis, especially as an initial symptom of SLE. It is important for clinicians and pathologists to work in together to ultimately determine the appropriate diagnosis.

Non-blistering PD-1 Inhibitor-induced Bullous Pemphigoid: Entering an Era of Autoimmune Disorders Induced by Checkpoint Blockade

Katherine Roy, MD
Katherine Ron, MD; Nicholas Love, PhD; Bernice Kwong, MD; Jinah Kim, MD, PhD

Stanford University, Stanford, California, USA

Recent advances in immunotherapeutic treatment of cancer have led to development of novel directed therapies including monoclonal antibodies that block the immune checkpoint, such as programmed death 1 (PD-1) and programmed death ligand 1 (PD-L1). Immune-related toxicities have been documented with these drugs including skin eruptions. In fact, cutaneous complications can be seen in up to 20% of patients receiving these agents, and include T-cell mediated process such as lichenoid drug reactions and vitiligo. Recently, cases of bullous pemphigoid (BP) induced by PD-1 inhibitors have been reported, which have demonstrated classic clinical, histologic, and immunofluorescence features. In contrast, here we present a case of an 83-year-old male who developed a generalized eruption present on trunk, extremities, and scalp six weeks after the initiation of anti-PD1 monoclonal antibody therapy for metastatic squamous cell carcinoma of the tongue. The eruption was initially suspected to be a lichenoid process on both clinical and histolomorphologic grounds; however, direct immunofluorescence performed on perilesional skin demonstrated 3+ linear staining for IgG and C3 along the basement membrane zone and along the roof of salt split skin, confirming the diagnosis of bullous pemphigoid. As the eruption progressed, the patient developed blisters and erosions clinically. The mechanism by which the PD-1 inhibitors trigger BP, an autoantibody-driven disease, is unclear, but
perhaps the atypical clinical and histologic features seen in our case are the result of the T-cell stimulation triggered by the drug. Our case highlights the importance of biopsy and immunofluorescence for workup of similar cutaneous eruptions in patients undergoing PD1-inhibitor therapy, as atypical presentations of immunobullous disease may be more likely in this population.

**EBV-associated, Cutaneous, Smooth Muscle Tumor in AIDS Patient**
Yevgeniya B. Rainwater, MD
Yevgeniya B. Rainwater, MD¹; Travis Vandergriff, MD¹
¹UT Southwestern Medical Center, Dallas, Texas, USA

EBV-associated smooth muscle tumors (EBV-SMTs) are rare and occur in immunocompromised children, transplant patients, and patients with HIV. EBV-SMTs are often multifocal with CNS, lung, liver, vocal cord, abdominal wall, and adrenal gland involvement. To date, cutaneous involvement with EBV-SMTs has not been reported. Here we present the first case of EBV-associated, cutaneous smooth muscle tumor in HIV patient. A 42 year old male with HIV/AIDS, non-adherence to anti-retroviral therapy, and hepatitis C presented with a 2-month history of a painful lesion on left thigh. The patient underwent complete excision of a 3 cm mass and histopathology revealed a circumscribed, slightly asymmetric nodule composed of spindled and epithelioid cells arranged in fascicles with branching vascular spaces at the periphery. The spindled and ovoid cells highlighted strongly and diffusely with actin and calponin. Epstein Barr virus in situ hybridization was positive throughout the tumor. The remainder of infectious work up was unrevealing. Based on these finding, the patient was diagnosed with cutaneous EBV-associated SMT. Full-body computed tomography revealed a 4 cm right hilar pulmonary mass that has regressed with reinstitution of anti-retroviral therapy and no other signs of systemic involvement. To our knowledge, this is the first report of unifocal, cutaneous, EBV-associated SMT in HIV/AIDS patient. It is important to consider this unique pathologic entity on differential diagnosis of solitary cutaneous smooth muscle tumors in immunocompromised patient and recommend a systemic work up for multifocal involvement.

**Fibroblastic Rheumatism: A Rare but Pertinent Dermatoarthropathy**
Justin P. Bandino, MD
Justin P. Bandino, MD¹; Nicole Dominiak, MD¹; Kathryn Echols, MD¹; Dirk M. Elston, MD¹
¹Medical University of South Carolina, Charleston, South Carolina, USA

Fibroblastic rheumatism is an exceedingly rare dermatooarthropathy and diagnosis is based on both clinical and histopathologic features. We present a case of a 50-year-old Caucasian female with deep, firm, non-mobile, flesh-colored, dermal and subcutaneous papulonodules slowly enlarging on her predominantly volar fingers and hands. Pertinent prior history includes five-years of seronegative arthritis complicated by idiopathic fibrosing tenosynovitis involving her forearms and hands, a monoclonal IgG kappa protein spike, and failed treatment with adalimumab, infliximab, cyclophosphamide, methotrexate, and prednisone. Clinical suspicion arose for rheumatoid nodules,
multicentric reticulohistiocytosis, deep granuloma annulare, erythema elevatum diutinum, or fibromatosis, and a punch biopsy was thus obtained. The biopsy demonstrated a cutaneous proliferation of bland, plump spindle cells and fibroblasts, superimposed on a background of whorled, ropey collagen within the dermis and septa. Typical volar architecture of eccrine glands and vasculature was largely preserved. A CD34 immunostain was negative. This combination of clinical and histological features is consistent with fibroblastic rheumatism. Fibroblastic rheumatism was first described in 1980, with only rare subsequent reports. Concomitant symptoms may include polyarthritis, joint ankylosis, deformities, and dense dermal fibrosis. In some cases, the cutaneous lesions resolve spontaneously after several months, although the overall tendency is progression toward a disabling, erosive polyarthritis. No specific diagnostic criteria exist, but the combination of the above clinical and histopathological findings in the absence of inflammation make the diagnosis. Rheumatoid factor and related serologic tests are typically negative. An elastin stain may be helpful as this entity typically displaces elastic tissue. Treatment often proves challenging. Systemic prednisone, colchicine, interferon, penicillamine, imatinib, methotrexate, and NSAIDs, as well as intralesional methotrexate or 5-fluorouracil have been used with variable success.

Nodular Cutaneous Microsporidiosis in an Immunocompromised Patient
Emily H. Smith, MD
Emily H. Smith, MD; Pranathi Lingam, MD; Frank Wang, MD; Rajiv M. Patel, MD; May P. Chan, MD; Yvonne Qvarnstrom, PhD; Cynthia S. Goldsmith, MGS; Douglas R. Fullen
1University of Michigan Health System, Ann Arbor, Michigan, USA
2University of Michigan, Ann Arbor, Michigan, USA
3Centers of Disease Control, Atlanta, Georgia, USA

The microsporidia are a group of obligate intracellular parasitic fungi found worldwide naturally infecting domestic and wild animals. Human microsporidiosis is an increasingly recognized multisystem opportunistic infection. The clinical manifestations are diverse with diarrhea being the most common presenting symptom. We encountered a 52 year-old HIV-negative female from rural Indiana with a history of amyopathic dermatomyositis complicated by interstitial lung disease managed on mycophenolate mofetil and hydroxychloroquine. She presented with a seven-month history of recurrent ulcerative subcutaneous nodules on the face, arms and legs as well as intermittent diarrhea and chronic sinusitis. Hematoxylin and eosin stained tissue sections from multiple cutaneous locations demonstrated a superficial and deep lymphocytic and granulomatous dermatitis with focal necrosis. Tissue stains for microorganisms revealed multiple 1-3 micron round to oval structures within the necrotic areas, best highlighted by Giemsa, Steiner, Hucker-Twort and Fite stains. A periodic acid Schiff stain enabled identification of a unique organelle, the polar tubule or polar filament on the oval structures. Electron microscopy demonstrated a diplokaryotic organism containing up to 12 coils of the polar tubule in anisofilar arrangement, confirming microsporidia species. Upon further questioning the patient reported exposure to domestic pets and wild animals near her home, the most likely infectious reservoir. We hypothesize that oral ingestion of spores resulted in primary gastroenteritis with subsequent hematogenous dissemination to her skin facilitated by her immunosuppressed state. The patient was
taken off mycophenolate mofetil and placed on a 21-day course of albendazole with improvement in her lesions. This case is one of very few confirmed cases of cutaneous microsporidiosis to be reported in the literature.

**A Subset of Melanocytic Nevi with Sclerosing and Epithelioid Features and Consistent Gain of Chromosome 15: A New Subtype of Spitz Nevus?**

John Scopetta, MD
John Scopetta, MD1; Joel A. Lefferts, PhD1, Gregory Seidel, MD1; Robert E. LeBlanc, MD1; Shaofeng Yan, MD, PhD1; Gregory Tsongalis, PhD1; Konstantinos Linos, MD1;

1Dartmouth-Hitchcock Medical Center, Geisel School of Medicine, Lebanon, New Hampshire, USA

Conventional nevi show no chromosomal aberrations whereas melanomas exhibit multiple gains and losses as shown in chromosomal microarray analysis. Relatively recently subsets of Spitz nevi/tumors have been shown to have characteristic genomic alterations and reproducible morphologic findings (e.g. BAP1 loss, gains in 11p, gains of 7q, ALK fusion). Since August 2015 we have analyzed 97 samples of difficult melanocytic neoplasms with Single Nucleotide Polymorphism array (SNP array) as part of the work up to reach a definitive diagnosis. We identified four cases with the monoaberration of copy number gain of the entire chromosome 15. We retrospectively reviewed the clinical information and the H&E slides in an effort to identify potential reproducible findings. Clinically the size ranged from 2-7 mm whereas the anatomic sites included the knee (1), arm (1), thigh (1) and upper back (1). The age ranged from 40 to 73 years old and the F:M ratio was 3:1. Three samples were shave biopsies and one was an excision. The margins were positive in two cases and negative in the other two. Three cases were re-excised with one case exhibiting recurrent nevus phenomenon and the remaining two showing no residual. No adverse events have been documented with a follow up ranging from 3 to 9 months. Morphologically all lesions showed striking similarities. They were all dome-shaped and well circumscribed, exhibiting basal keratinocytic hyperpigmentation. Cytologically all four cases showed consistent epithelioid morphology with some pleomorphism and hyperchromasia whereas a characteristic sclerotic background at the deeper aspect was evident. Our data suggest that a subset of nevi with gain of the entire chromosome 15 has reproducible morphologic findings and may represent a subtype of Spitz nevus.
Primary cutaneous marginal zone lymphoma (PCMZL) can be categorized histopathologically as conventional, lymphoplasmacytic, plasmacytic and blastoid types. Lesions previously termed cutaneous immunocytoma or plasmacytoma are now encompassed within the spectrum of PCMZL. The usual clinical presentation of the disease is as erythematous papule(s), plaque(s) and/or nodule(s) on the upper extremities or trunk of an adult. Microscopically, dense dermal infiltrates of small to medium-sized lymphocytes, plasma cells and lymphoid follicles are observed in varying proportions. Amyloidomas have been reported as manifestations of marginal zone lymphomas in mediastinal and intra-abdominal sites but are not generally recognized as a reflection of PCMZL. We report 2 examples of cutaneous/subcutaneous amyloidomas of the leg associated with monotypic plasma cell infiltrates and propose that these are unusual presentations of PCMZL, plasmacytic variant. One case was of a 56 year old woman with a locally recurrent subcutaneous nodule on the left lower leg and the other of a 62 year old man with a soft plaque on the left foot. The lesions were asymptomatic and the patients otherwise well. The histopathological findings in each case were characterized by heavy deposits of amyloid in the skin and subcutis with focal calcification, occasional multinucleated giant cells and aggregations of mature plasma cells. The latter displayed kappa light chain restriction. Clinical investigations revealed no evidence of multiple myeloma or systemic B cell lymphoma. Taking cognizance of similar, rare reports in the literature, we suggest that, as seen at other sites, amyloidomas can be a manifestation of PCMZL.

T-cell Acute Lymphoblastic Lymphoma/Leukemia Presenting as a Diffuse Exanthem: A Clinical and Histopathologic Challenge
Jessica M. Kwock, MD
Jessica M. Kwock, MD; James W. Patterson, MD; Mark R. Wick, MD; Alejandro A. Gru, MD
1University of Virginia Health System, Charlottesville, Virginia, USA

A 14-year-old boy presented with a 6-month history of an asymptomatic exanthem of ill-defined erythematous papules on the trunk and extremities. A punch biopsy was read at an outside hospital as “lymphocytic infiltrate”. One month subsequently, he developed decreased appetite, weight loss, and abdominal and arm pain. He was found to have marked leukocytosis with blasts on peripheral smear and peripheral blood flow cytometry consistent with T-cell acute lymphoblastic leukemia/lymphoma (T-ALL). The blasts were positive for cCD3 and TdT, while negative for CD4, CD8, CD1a and CD34. Additionally, FISH studies showed a rearrangement of the NUP214-ABL1 genes. Evaluation of the patient’s initial biopsy revealed a moderately dense dermal infiltrate comprised of a monotonous population of small round basaloid cells, centered on dermal vessels and adnexal structures, with crush artifact and relative absence of mitoses. Immunohistochemical staining highlighted an infiltrate of TdT, CD3 and CD5 positive cells consistent with T-lymphoblasts. The features were consistent with
ALK1-positive Pediatric Spitzoid Melanoma with Homozygous Deletion of 9p21 (CDKN2A) and Gain of 6p25 (RREB1) by FISH: A Case Report

Andrew J. Rand, MD
Andrew J. Rand, MD1; Marier Hernandez-Perez, MD2; Genevieve M. Boland, MD, PhD3; Daniela Kroshinsky, MD, MPH1; Julia Reimann, MD, PhD1,2

1Tufts Medical Center and Miraca Life Sciences, Needham, Massachusetts, USA
2Miraca Life Sciences, Newton, Massachusetts, USA
3Massachusetts General Hospital, Boston, Massachusetts, USA

ALK rearrangements occur in up to 10% of Spitzoid melanocytic neoplasms. Although some ALK-positive Spitz tumors have been classified as melanoma on histomorphologic grounds, none reported have shown homozygous deletion of 9p21 (CDKN2A) and/or gain of 6p25 (RREB1) by fluorescence in situ hybridization (FISH), which are associated with aggressive clinical behavior. We review the case of a 9-year-old male who presented with a 1.3 cm pigmented nodule on the anterior left thigh, clinically suspicious for an atypical nevus. It was first noticed three years earlier and grew rapidly during the first year to approximately 2.5 cm. In the following year, half of it was torn off with heavy blood loss during a football game, prompting evaluation and a biopsy. Histologic examination revealed a predominantly intradermal Spitzoid melanocytic neoplasm. The hypercellularity, lack of maturation, numerous dermal mitoses (including deep ones), and asymmetry were consistent with Spitzoid melanoma. Homozygous deletion of 9p21 (CDKN2A) (54%) and gain of 6p25 (RREB1) (45%) by FISH provided further support for the diagnosis. Tumor extended to the deep margin and was least 8 mm in thickness with no ulceration. By immunohistochemistry, ALK1 was diffusely positive in tumor cells, consistent with ALK rearrangement. The Ki-67 proliferation index was focally increased, HMB-45 was negative in the dermal component, and BAP-1 was retained. A wide local excision showed no residual melanoma. Excision of a single left inguinal sentinel lymph node revealed small subcapsular foci of metastatic melanoma measuring 0.2 mm in greatest dimension. The completion lymphadenectomy was negative for melanoma in eleven lymph nodes. No other metastatic disease was detected by imaging. Five months after the biopsy, the patient was started on interferon therapy and was doing well. To our knowledge, this is the first reported case of an ALK1-immunoreactive Spitzoid melanocytic neoplasm with homozygous deletion of 9p21 (CDKN2A) and gain of 6p25 (RREB1). Confirmation of ALK rearrangement by FISH is planned. Long-term follow-up will be important to further define the clinical behavior of this unique Spitzoid neoplasm.
A Primary Cutaneous Burkitt Lymphoma with Classic Immunohistochemical and Molecular Findings
Aravindhan Sriharan, MD
Aravindhan Sriharan, MD1; Sonal Chaudhary, MD1; Robert F. Cheek, MD2; Mark J. Vellek, MD3; Jaroslaw Jedrych, MD1; Jonhan Ho, MD, MS1; James Edinger, MD2
1University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA
2Boye and Bynum Pathology Laboratories, P.C., Columbia, Missouri, USA
3Missouri Cancer Associates, Columbia, Missouri, USA

When Burkitt’s Lymphoma has been documented in the skin, it has been as a secondary phenomenon. There is one case in the literature reported as a translocation positive primary cutaneous large cell lymphoma. We report a case of primary cutaneous Burkitt Lymphoma with supporting immunohistochemical and molecular evidence. The patient is a 91 year old woman with no known history of lymphoma, who presented with a 2.8 cm nodule on the ventral abdominal wall. Examination of the biopsy revealed a sharply circumscribed unencapsulated mass centered in the superficial dermis, comprised of crowded cells arranged in sheets with the characteristics “starry sky” appearance. The neoplasm had overlapping small to medium sized nuclei, each with a thin rim of cytoplasm, and many with cytoplasmic vacuoles. There was a very high mitotic rate. Immunohistochemical studies revealed a population of EBER+ B lymphocytes that marked with CD10 and were negative for lymphoblast markers. The percentage of cells marking with ki-67 was above 95%. The lesions cells were positive for c-myc. The diagnosis of Burkitt Lymphoma was confirmed by FISH for myc-IgH. The patient’s history and imaging revealed no prior Burkitt lymphoma and no other site of malignancy. To our knowledge, this is the first case of primary cutaneous Burkitt Lymphoma.

Epithelioid Fibrous Histiocytoma with Collagen Rosettes
Stephanie J.T. Chen, MD
Stephanie J.T. Chen, MD1; Emily H. Smith, MD1; Rajiv M. Patel, MD1; Douglas R. Fullen, MD1
1University of Michigan Health System, Ann Arbor, Michigan, USA

Giant collagen rosettes have been most notably described in a subset of low-grade fibromyxoid sarcomas sometimes referred to as hyalinizing spindle cell tumor with giant rosettes (HSCTGR). Such rosettes were also reported in one case of fibrosarcomatous dermatofibrosarcoma protuberans. We report an exceptional case of epithelioid fibrous histiocytoma with collagen rosettes. A 49-year-old woman presented with a 0.7 cm enlarging papule of the left mandibular angle region. Shave biopsy revealed a circumscribed dermal proliferation of epithelioid cells present within an eosinophilic to basophilic, hyalinized stroma. In areas, constituent cells and stroma formed giant rosettes composed of brightly eosinophilic, fibrillary collagen and bland epithelioid cells with pale, bubbly cytoplasm and bland nuclei. Mitotic figures were not observed. Immunostains demonstrated tumor cells to be positive for CD68 (strong), factor XIIIa (moderate to weak), NKI/C3 and S100 (subset, weak), while Melan-A, tyrosinase, MiTF, CD34, CD163, EMA, cytokeratin (MNF116), p63, smooth muscle actin, desmin and GFAP were negative. PGP9.5 staining was equivocal. The histologic differential diagnosis included epithelioid fibrous histiocytoma, superficial low-grade fibromyxoid sarcoma (HSCTGR), myoepithelioma and cellular neurothekeoma. Myoepithelioma was excluded given the lack of EMA, GFAP, cytokeratin and smooth muscle actin expression. Cellular neurothekeoma was considered less likely given the extent of CD68 and factor XIIIa expression, equivocal PGP9.5 staining and lack of smooth muscle actin and MiTF
immunoreactivity. Lack of Melan-A, tyrosinase and MiTF excluded a melanocytic tumor or PEComa. A superficial variant of low-grade fibromyxoid sarcoma (HSCTGR) was ruled out. To our knowledge, this is the first report of collagen rosettes in an epithelioid fibrous histiocytoma.

An Evaluation of the Utility of a Novel Microsatellite Instability Assay in the Workup of Sebaceous Neoplasms
Jay Wofford, MD
Jay Wofford, MD1; Greg Hosler, MD1; Kathy Murphy, PhD1
1ProPath, Dallas, Texas, USA

Muir-Torre Syndrome (MTS) is a heritable condition caused by mutations in DNA mismatch repair genes, including MLH1, MSH2, MSH6, and PMS2. Patients with MTS frequently develop sebaceous neoplasms, which can be diagnosed readily by histology. Currently, adjunct diagnostic testing can be performed on sebaceous neoplasms to evaluate for MTS, including immunohistochemistry (IHC) and, less commonly, microsatellite instability (MSI) by molecular methods. The purpose of this study was to compare the utility of a newer MSI molecular test (long mononucleotide repeat or LMR) with that of a standard MSI test and with IHC. We performed IHC (for MLH-1, MSH-2, MSH-6, and PMS-2), a standard MSI molecular test, and the newer LMR assay on 61 sebaceous neoplasms from 46 patients. A total of 33 tumors returned valid results for all 3 modalities. The three modalities had concordant results in 25 (75.8%) of the tumors, with discordant results in 8 (24.2%). Of the 25 tumors with concordant results, 19 (76%) had loss of IHC staining (a positive result) as well as positive MSI on both the standard and LMR assays. The remaining 6 (24%) tumors were negative for all 3 testing modalities. Among the 8 tumors with discordant results, 5 (62.5%) exhibited loss of IHC staining, a negative standard MSI analysis, but had a positive result for MSI using LMR. Two (25%) of the tumors with discordant results exhibited loss of IHC staining but had negative results on both MSI testing modalities. One tumor (25%) had positive IHC staining (a normal result), a negative standard MSI test, but had a positive MSI result using LMR. Overall, MSI analyses from both molecular tests correlated well with IHC results, but also identified cases with discordant results. Furthermore, the newer MSI assay (LMR) appears to be more sensitive for detecting MSI in cases where the standard MSI analysis was normal but IHC indicated an abnormality. These findings highlight a need to re-examine the role of molecular MSI testing in the workup for MTS.

Utility of Histologic Features of Secondary Syphilis
Alexandra Flamm, MD
Alexandra Flamm, MD1; Eun Ji Kwon, MD2; Viktoryia Kaziouskaya, MD3; Dirk M. Elston, MD4
1University of Pennsylvania, Philadelphia, Pennsylvania, USA
2Dermpath Diagnostics New York, Port Chester, New York, USA
3SUNY Downstate Medical Center, Brooklyn, New York, USA
4Medical University of South Carolina, Charleston, South Carolina, USA

Background: The incidence of primary and secondary syphilis in the United States has more than doubled since its lowest recorded rate. Given the wide variety of clinical manifestations and often-inconsistent reliability of serological tests, there have been increases in dermatopathological specimens for syphilis diagnosis, however the histopathologic features of syphilis also vary. Previous studies of
secondary syphilis identified the frequency of many of these features, however their utility in comparison to other entities in the differential are unknown. Objective: To determine the utility of histopathologic features characterizing secondary syphilis in comparison to other entities in the clinical and histologic differential. Methods: A multicenter retrospective analysis of biopsy-proven cases of secondary syphilis, mycosis fungoides (MF) and pityriasis rosea (PR) was performed. Cases were categorized as having or lacking 12 histologic features often seen in secondary syphilis. Results: 106 cases of secondary syphilis, 106 cases of PR and 101 cases of MF were collected. Compared to PR, syphilis was more likely to have neutrophils in the stratum corneum and reticulated effacement of the rete ridges (LR+ 7.3 and 6.7). Conclusion: Plasma cell infiltrate, reactive lymphocytes with ample cytoplasm (LR+ 28.5 and 14.3) and endothelial swelling (LR+ 4 and 7.3). Compared to PR, syphilis was more likely to have neutrophils in the stratum corneum (LR+ 7.3) and effacement of the rete ridges (LR+ 6.7). Conclusion: Plasma cell infiltrate, reactive lymphocytes and endothelial swelling are statistically significant findings that can differentiate secondary syphilis from MF and PR. Neutrophils in the stratum corneum and rete ridge effacement may also be helpful differentiating factors in the case of PR. Future Directions: We aim to compare cases of pityriasis lichenoides to syphilis as well.

Expression of Metallopanstimulin-1 in the Spectrum of Melanocytic Neoplasms
Maria A. Deschaine, MD
Maria A. Deschaine, MD1; Jane L. Messina, MD1,2; Anthony Maglocco, MD2; Daryoush Saeed-Vata, MD2
1University of South Florida, Tampa, Florida, USA
2Moffitt Cancer Center, Tampa, Florida, USA

Background: Increased serum and tissue expression of metallopanstimulin-1 (MPS-1) has been demonstrated in melanoma as well as other neoplasms. Higher expression of MPS-1 is associated with more aggressive, higher stage melanoma. However, there is little in the literature exploring the expression of MPS-1 in the spectrum of melanocytic neoplasms, including dysplastic nevi and this difference has yet to be quantified using an immunofluorescence (IF) assay. In this pilot study we quantified the level of MPS-1 to evaluate differences in expression among benign nevi, dysplastic nevi, and malignant melanoma. Design: Thirty archived cases, including 10 invasive melanomas, 2 melanoma in situ, 8 dysplastic nevi (6 mild, 1 moderate, 1 severe), and 10 nevi (1 junctional, 4 compound, 2 dermal, 1 special site, two blue), were selected. MPS-1 expression was studied via an Aqua assay on whole tissue section slides using a monoclonal MPS-1 antibody (1:1000, clone N11), and quantified via an Automated Quantitative Software Analysis (AQUA) system targeting melanocytes. Results: MPS-1 was more strongly expressed in melanomas compared to both benign and dysplastic nevi, with mean AQUA scores of 122.88, 23.73, and 19.47, respectively (p= 0.0005, p=0.0004). There was no statistical difference between AQUA scores from dysplastic nevi compared to benign nevi (p= 0.34). Conclusion: The distribution pattern of MPS-1 demonstrates that it is more strongly expressed in melanomas compared to both benign and dysplastic nevi, while no significant difference exist between dysplastic and non-dysplastic nevi. Based on our data, the expression of MPS-1 can be reliably quantitated and potentially used to distinguish malignant melanocytic neoplasms from both dysplastic and benign nevi.
Expansion of the study cohort, as well as inclusion of diagnostically challenging, “borderline” lesions such as Spitzoid proliferations is planned.

**STAT3 Gene Mutation and Enhanced STAT3 Phosphorylation is Detected in a Subset of Tumor Stage Mycosis Fungoides with Large Cell Transformation**

Andy C. Hsi, MD
Andy C. Hsi, MD¹; Andras Schaffer, MD, PhD¹
¹Washginton University Dermatopathology Center, St. Louis, Missouri, USA

Mycosis fungoides (MF) is the most common cutaneous T-cell lymphoma. While many MF cases exhibit an indolent course, progression to tumor stage with large cell transformation (LCT) can occur, resulting in significant morbidity and mortality. Currently, there are no targeted therapies for advanced MF. The purpose of this study was to discover new potentially targetable driver mutations in MF, using whole exome sequencing and immunohistochemistry. Three pairs of tumor MF (2 with LCT) and normal tissue (2 lymph nodes and 1 liver) from the same patients were sequenced. After subtracting germline polymorphisms that were present in both tumor MF and normal tissues, all mutations unique to the tumor MF samples were compared with previously published somatic cancer mutations using the COSMIC database for significant recurrent mutations. Of the 477 mutations identified, a STAT3 Y640F mutation that has been implicated in multiple hematologic neoplasms was seen in one of the MF with LCT specimens. The Y640F mutation results in constitutive phosphorylation of STAT3 (pSTAT3), leading to JAK-independent activation of downstream oncogenic pathways. Next, we aimed to assess the expression of pSTAT3 in MF progression using immunohistochemistry. CD3/pSTAT3 dual staining was performed on 20 cases of patch/plaque stage MF and 33 tumor stage MF, including 24 cases with LCT. A positive case is defined as pSTAT3 staining in ≥ 10% of the CD3-positive lesional cells. Positive CD3/pSTAT3 coexpression was seen in 2 cases of patch/plaque MF (10%), 3 cases of tumor MF without LCT (33%), and 13 cases of MF with LCT (54%). The overall pSTAT3 expression was low in patch/plaque MF (median = 2.5% of CD3+ cells; range 0-30%) and tumor MF without LCT (median = 5%; range 0-30%), while MF with LCT showed an increased level of pSTAT3 staining (median = 15%; range 0-85%). The results imply that STAT3 Y640F mutation and STAT3 phosphorylation might be critical for MF progression in a subset of patients and thus may serve as a potential therapeutic target.

**Histopathologic Attributes Associated with MelaFind Classification: A 3-Year Experience with High-Risk Pigmented Lesion Clinic**

Vikas Shrivastava, MD
Vikas Shrivastava, MD¹; Phillip Bailin, MD¹; Jennifer Elliott, RN¹; Wilma F. Bergfeld, MD¹; Steven D. Billings, MD¹; Melissa Piliang, MD¹; Anthony Fernandez, MD, PhD¹; Jennifer S. Ko, MD, PhD¹
¹Cleveland Clinic, Cleveland, Ohio, USA

MelaFind is a non-invasive computer-assisted system to aid in melanoma diagnosis. We have histologically evaluated consecutive Melafind-selected (high disorganization scores, n=253 of 923 (27%)
scanned) biopsies obtained in our high risk pigmented lesion clinic (3 years). Biopsies were scored based on 12 histologic features known to be associated with dysplasia/malignancy. Diagnoses, with frequency and histologic scores, included: compound nevus (104; 3.2±1.7), atypical compound nevus (ACN) - mild dysplasia (48; 4.7±1.5), ACN- moderate to severe dysplasia (12; 7.6±1.8), junctional nevus (JN) (9; 3.2±1.8), junctional lentiginous nevus (22; 2.8±1.3), atypical JN- mild dysplasia (19; 5.2±1.9), atypical JN-moderate to severe dysplasia (1; 7±0), melanoma in-situ (6; 9.3±1.5), invasive melanoma (5; 10.7±0.8), and other (24; 1.3±1.2). Atypical histologic criteria included: dermal fibroplasia (177/253, 70%), melanoderma (169/253, 66.8%), bridging (165/253, 65.2%), poor circumscription (119/253, 47%), shouldering (93/253, 36.8%), inflammation (91/253, 36%), cytologic atypia (75/253, 29.6%), asymmetry (59/253, 23.3%), upward migration (15/253, 5.9%), and nonmaturation (3/253, 1.2%). The most common reasons for biopsy, in the absence of worrisome histologic features, were: combined nevus with lentigo or seborrheic keratosis, and melanoderma. The histologic lesion score differed significantly depending on the diagnoses and Melafind score (benign n=34, 3.3±1.5; mildly atypical n=134, 4.8±1.6; moderately to severely atypical n=26, 7.4±1.7; and in-situ or invasive melanoma n=22, 9.9±1.4; p<.005 in each case). Lesions with relatively few histologic criteria of atypia were not reliably diagnosed as dysplastic (range of scores in benign nevi= 0-7). Despite Melafind’s proven utility in reducing the number of skin biopsies, many benign histologic attributes can lead to a high-risk Melafind score. Knowledge of these attributes should increase the bidirectional confidence level when making such clinicopathologic correlations in high risk patients.

The Ciliation Index Distinguishes Invasive Melanoma and Melanoma In-Situ from Associated Dermal Melanocytic Nevi
Ursula E. Lang, MD
Ursula E. Lang, MD1; Nicholas R. Love, PhD2; Christine Cheung, BS3; Timothy H. McCalmont, MD4; Jinah Kim, MD, PhD3
1Stanford Medical Center, San Francisco, California, USA
2Stanford School of Medicine, Stanford, California, USA
3Stanford Medical Center, Stanford, California, USA
4University of California San Francisco, San Francisco, California, USA

Background: Our understanding of melanoma precursor lesions and the potential for genetic heterogeneity within a single lesion, has developed as a result of advances in the field of molecular diagnostics. These combined lesions can pose a diagnostic challenge when deciding the line between benign and malignant. Primary cilia are ubiquitous sensory organelles that have essential functions in cellular proliferation, differentiation, and development. The ciliation index (percentage of ciliated melanocytes) has recently been shown to reliably differentiate melanoma, which fail to ciliate, from melanocytic nevi, which retain primary cilia. Objective: To evaluate the ciliation index within combined melanocytic lesions containing both melanoma and associated dermal nevus. Methods: We collected 10 cases of paraffin embedded tissues, containing melanoma and associated nevus components, and subjected them to immunofluorescence microscopy. Melanocytes were highlighted with Sox10 and costained with gamma-Tubulin and acetylated alpha-Tubulin to highlight the basal body and cilium,
respectively. The number of melanocytes retaining cilia under high-power microscopy was examined. Results: The melanoma component had average of 4% ciliation (SD: 7%), while the associated nevus component had an average of 59% ciliation (SD: 17%). There was a significant decrease in number of cilia in the melanoma versus nevus components in each of these cases (p<0.00001). Conclusions: These data show that primary cilia may be a reliable means of distinguishing benign from malignant components within a single lesion. The ciliation index may be a helpful tool in distinguishing challenging cases of combined lesions of melanoma in-situ with a dermal nevus component from invasive melanoma.
## Oral Abstract Session 2

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:30 p.m. - 1:40 p.m.</td>
<td>Skin Biopsy Trends and Associated Health Care Utilization</td>
<td>Toshi Ghosh, MD</td>
</tr>
<tr>
<td>1:40 p.m. - 1:50 p.m.</td>
<td>Dual Expression of MYC and Beta-adrenergic Receptors in Cutaneous Angiosarcoma</td>
<td>Laura Gray Pruitt, MD</td>
</tr>
<tr>
<td>1:50 p.m. - 2:00 p.m.</td>
<td>Direct Immunofluorescence (DIF) Testing in Vasculitis - A Single Institution Experience with Henoch Schönlein Purpura</td>
<td>Patrick Feasel, MD</td>
</tr>
<tr>
<td>2:00 p.m. - 2:10 p.m.</td>
<td>Increasing Concordance for Atypical Melanocytic Lesions Using NDER, a Novel Web Application</td>
<td>Greg Cheeney, MD</td>
</tr>
<tr>
<td>2:10 p.m. - 2:20 p.m.</td>
<td>Genomic Profile of Pigmented Epithelioid Melanocytic Lesions</td>
<td>Jarish N. Cohen, MD, PhD</td>
</tr>
<tr>
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<td>Melissa Pulitzer, MD</td>
</tr>
<tr>
<td>2:30 p.m. - 2:40 p.m.</td>
<td>Loss of Retinoblastoma Protein Expression in Pleomorphic Fibroma: An Immunohistochemical and Genomic Analysis</td>
<td>Brian R. Hinds, MD</td>
</tr>
<tr>
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</tr>
<tr>
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</tr>
</tbody>
</table>
Oral Abstract Session 2

Skin Biopsy Trends and Associated Health Care Utilization
Toshi Ghosh, MD
Toshi Ghosh, MD; Lindsey R. Sangaralingham, MPH; Stephanie R. Anderson, BA; Niley D. Shah, PhD; Margot S. Peters, MD; Nneka I. Comfere, MD; Mayo Clinic, Rochester, Minnesota, USA; OptumLabs, Cambridge, Massachusetts, USA

Background: Partial biopsies of skin tumors, defined as specimens obtained without intent of complete removal, are prevalent in dermatopathology practice. Incomplete biopsy may result in lack of specific pathologic diagnosis or incorrect diagnosis, which may lead to under- or overtreatment, particularly additional procedures associated with morbidity, cost, and patient dissatisfaction. Yet, there are limited guidelines for appropriate skin biopsy practices. Design: To assess trends in skin biopsy type and impact on resultant health care utilization, we performed a retrospective cohort analysis of 6,508,062 skin tumor biopsies obtained between 2003 and 2013 using OptumLabs Data Warehouse, a database including administrative claims data on over 100 million privately insured and Medicare Advantage enrollees. Biopsy types, performing medical specialties, and subsequent health care utilization were assessed. Results: There were more than double the number of skin biopsies in 2013 compared with 2003 (287,088 vs. 785,524), and per capita utilization increased 100% (from approximately 175 to 350 per 10,000 patients). Partial biopsies comprised the predominant biopsy type during both years: 48% in 2003, 49% in 2013. Most biopsies were performed by dermatologists: 73% in 2003, 82% in 2013. During the six months after biopsy, health care utilization for dermatological care was slightly greater for procedures (30% in 2003, 36% in 2013), as compared to clinical follow-up visits (28% in 2003, 32% in 2013). Conclusion: To our knowledge, this study appears to be the first to assess skin biopsy trends by biopsy type and documents that partial samples constitute the largest proportion of all skin tumor biopsies over a 10-year study period. During the six months following biopsy, there was progressively increasing and slightly higher procedural health care utilization for dermatological concerns compared with clinical follow-up over the study period. These trends may be attributable to incomplete or incorrect diagnoses generated by incomplete biopsies.

Dual Expression of MYC and Beta-adrenergic Receptors in Cutaneous Angiosarcoma
Laura Gray Pruitt, MD
Laura Gray Pruitt, MD; Nathaniel Slater, MD; Paul Googe, MD; University of Tennessee Medical Center, Knoxville, Tennessee, USA; Knoxville Dermatopathology Laboratory, Knoxville, Tennessee, USA

Background: Angiosarcomas are a rare and typically aggressive malignancy of vascular origin with a poor prognosis even following multimodal therapy. Given the rarity of these tumors, they remain understudied and potential aberrant signaling pathways are not well characterized. Both radiation
related and non-radiation related primary cutaneous angiosarcomas have been shown to overexpress MYC, a proto-oncogene involved in the regulation of cell proliferation. Beta-adrenergic receptor expression has also been demonstrated in cutaneous angiosarcomas, and beta-blockade has been recently reported to decrease the proliferative index of cutaneous angiosarcomas. To our knowledge, there are no prior immunohistochemical studies investigating co-expression of beta-adrenergic receptors and MYC in these tumors. Methods: We reviewed Hematoxylin and Eosin stained sections of eleven cases of primary cutaneous angiosarcomas and stained each with antibodies to beta-adrenergic receptors 1 and 2 and MYC. Immunohistochemistry results were compared with the histologic grade of the tumors. Results: Cases studied came from patients with a median age of 72 (range 61 – 84), 6 females (55%) and 5 males (45%), one of whom was known to have prior radiation exposure. Cases had a mean histologic grade of 1.8 (range 1 – 3), with 5 specimens (45%) taken from the scalp, and the remainder from face, trunk, and extremities. All cases examined were found to express beta 2 adrenergic receptor, and 9 of 11 (82%) also expressed beta 1 adrenergic receptor. MYC expression was detected in 7 total cases (64%), with 6 cases (55%) demonstrating co-expression of MYC along with beta 1 and beta 2 adrenergic receptors. All 4 cases negative for MYC expression came from the scalp, with a mean histologic grade of 1.25. Conclusion: In this series of cutaneous angiosarcomas, there is a high degree of co-expression of beta-adrenergic receptors and MYC. Future studies may further elucidate the pathways involved in co-expression of MYC and beta-adrenergic receptors in cutaneous angiosarcomas and possible therapeutic implications.

Direct Immunofluorescence (DIF) Testing in Vasculitis - A Single Institution Experience with Henoch Schönlein Purpura
Patrick Feasel, MD
Patrick Feasel, MD¹; Steven Billings, MD¹; Anthony Fernandez, MD¹; Melissa Piliang, MD¹; Wilma Bergfeld, MD²; Jennifer Ko, MD¹
¹Cleveland Clinic, Cleveland, Ohio, USA

DIF panels typically consist of IgG, IgA, IgM, C3 and fibrinogen, and frequently yield negative results. Cases submitted for DIF with available histology and “vasculitis” in the provided clinical information were queried for reported DIF results (2010-2014). Electronic medical records were reviewed for clinical suspicion of Henoch-Schönlein purpura (HSP). Vasculitis was the given indication for DIF studies in 20% of all cases (258/1318). Among these, HSP was clinically suspected in 95 of 258 cases (37%). When HSP was suspected, DIF was relatively high yield (35/95, 37% positive and 60/95, 63% negative/non-specific), with 100% of DIF-positive cases showing immunoreactivity for IgA and leukocytoclastic vasculitis (LCV) by H&E. The majority of cases submitted for vasculitis had no real suspicion for HSP (163/258, 63%). In this setting, DIF was relatively low yield, with 21/165 (13%) positive cases, and 142/165 (87%) negative/non-specific cases. When HSP was not suspected and DIF was positive, 13 of 21 cases (62%) showed LCV by H&E, while other diagnoses with positive (although not diagnostic) DIF included vasoocclusive disease, interface dermatitis, and linear IgA disease. Most importantly, among cases diagnosed as LCV (74), 100% showed classic H&E findings of perivascular neutrophilic inflammation with leukocytoclasia and vascular damage. Of these, 20 (27%) had positive DIF and 54 (73%) had negative or
non-specific findings. In summary, a high percentage of DIF is performed for vasculitis (20%). When HSP is suspected, the yield of DIF is relatively high, and IgA can be used as the sole immunoreactant. All HSP cases showed H&E findings of LCV, a broader, H&E-based histopathologic diagnosis that can have positive, negative, and non-specific DIF results. As such, DIF is best utilized when real clinical suspicion for HSP exists.

**Increasing Concordance for Atypical Melanocytic Lesions Using NDER, a Novel Web Application**

Greg Cheeney, MD
Greg Cheeney, MD¹; Nicholas P. Reder, MD, MPH¹; David Zlotnick, MD¹; Evan George, MD, PhD¹

¹University of Washington, Seattle, Washington, USA

Background: Atypical melanocytic lesions represent a diagnostically challenging and clinically meaningful biological spectrum with distinct molecular underpinnings. Diagnostic discordance of melanocytic lesions leads to increased costs, turn-around time, and patient safety issues. Diagnostic concordance can be improved by training, even among experienced sub-speciality pathologists. We developed a software program, called NDER, to improve concordance in this difficult area of dermatopathology. Methods: Digitized whole-slide images of melanocytic lesions were annotated with regions of interest (ROI) and classified into five categories: benign, mild dysplastic features, moderate dysplastic features, severe dysplastic features, and melanoma in-situ or malignant melanoma. NDER displays these ROIs briefly (average: 4 seconds), forces users to classify the image, and then gives users immediate feedback. An adaptive algorithm determines the time that each subsequent image is displayed with over 100 ROIs displayed in the module. A pilot study of 9 trainees was performed. Lesions were grouped into three categories (benign, mild and moderately dysplastic, and severely dysplastic and MIS/MM) for analysis. Accuracy was defined using gold-standard evaluation by an experienced dermatopathologist. A paired t-test compared pre-test to post-test (different ROIs) accuracy, and Fleiss’ kappa was used to assess inter-observer agreement. Results: Users had large improvements in pre-test vs. post-test accuracy (59% vs. 84%, p<0.005). The effect size (Cohen’s d = 1.68) was very large, where 0.2 is a small effect, 0.5 moderate, and 0.8 large. Inter-observer agreement improved from 0.35 pre-test to 0.63 post-test (Fleiss’ kappa). On average, the module lasted 20 minutes. Qualitative feedback was positive including favorable attitudes towards usability and engagement. Conclusions: NDER is a novel web app that rapidly increases accuracy and evaluates for diagnostic proficiency. There was significant improvement from pre-test to post-test, with large effect size. NDER is an efficient, adaptive method of increasing concordance for melanocytic lesions. NDER can be used not only for training, but also for quality assurance amongst established pathologists. Further studies with larger cohorts are needed.
Genomic Profile of Pigmented epithelioid melanocytic lesions
Jarish N. Cohen, MD, PhD
Jarish N. Cohen, MD, PhD1; Nancy M. Joseph, MD, PhD1; Philip E. Leboit, MD1
1University of California, San Francisco, San Francisco, California, USA

The term ‘pigmented epithelioid melanocytoma’ (PEM) has been proposed for heavily pigmented melanocytic lesions with predominant epithelioid morphology, a propensity for local lymph node involvement, and only rare systemic spread. The category was created to include Carney complex-associated and sporadic epithelioid blue nevi, and animal-type melanoma. There has been question as to whether the category is homogeneous, and whether PEM are simply blue nevi with more pigmentation than usual. There are conflicting studies regarding the loss of protein expression of regulatory subunit of protein kinase alpha (PRKAR1A, the defective gene in Carney complex) in PEM. One study showed uniform loss of expression of PRKAR1A by immunohistochemistry. However, the genetics of PEM have been little investigated. We identified several dozen PEM, largely from the consultation files of one of the authors, and have begun to study their molecular alterations. 5 of several dozen cases have been analyzed to date. Patient ages ranged from 9-59 (median 44). DNA was extracted from matched normal and lesional tissue, and targeted sequencing of approximately 500 cancer-associated genes was performed, followed by analysis of somatic mutations, copy number changes, and gene structural rearrangements. 2 cases harbored protein kinase C alpha (PRKCA) gene fusions with two distinct partners: RNF13-PRKCA and ATP2B4-PRKCA. The case with the ATP2B-PRKCA fusion also demonstrated a canonical hotspot mutation in RAC1 and a truncating mutation in PTCH1. Of the other 3 cases, 2 had no clear driver alterations and 1 had a BRAF mutation and a PPM1D mutation. These 3 cases without PRKCA fusions demonstrated candidate driver alterations of uncertain significance including inversions in the PRKAR1A gene, and mutations in PRKAR1A, CTNNB1, and HRAS. Very few copy number alterations were identified in these cases, which is consistent with the relatively docile clinical behavior of PEM. Overall, this preliminary study suggests that PEM are low grade melanocytic neoplasms that harbor recurrent alterations in protein kinase A and protein kinase C genes, as well as additional non-synonymous oncogenic driver mutations. Our data lend credence to the postulate that PEM are a distinct subset of melanocytic neoplasm, but that the group is molecularly heterogeneous.

Mutational Profile of Combined Squamous and Merkel Cell Carcinoma is Comparable to de novo Squamous Cell Carcinoma but Not Pure Merkel Cell Carcinoma
Melissa Pulitzer, MD
Melissa Pulitzer, MD1; Abhinita Mohanty, MS1; Michael Berger, PhD1; Shay Warren, BS1; Nikhil Shyam, MD1; Thomas Wiesner, MD1; Peter Louis, BS1; Sasinya N. Scott, PhD1; Helen Won, BS1; Travis Hollmann, MD, PhD1; Klaus J. Busam, MD1; Heinz Kutzner, MD1
1Memorial Sloan Kettering Cancer Center, New York, New York, USA
2Dermatopathologie Friedrichshafen, Friedrichshafen, Germany

Merkel cell carcinoma with squamous differentiation i.e. combined squamous cell carcinoma/Merkel cell carcinoma (cSCC/MCC) is characterized by the absence of Merkel cell polyomavirus (MCPyV), high
Loss of Retinoblastoma Protein Expression in Pleomorphic Fibroma: An Immunohistochemical and Genomic Analysis

Brian R. Hinds, MD
Brian R. Hinds, MD; Alfredo Aguiló, MD; Jeff North, MD

1University of California San Francisco, San Francisco, California, USA
2Navarra Hospital, Pamplona, Spain

The RB1 gene encodes a tumor suppressor protein (RB) which is lost in a subset of soft tissue tumors, namely spindle cell/pleomorphic lipoma, cellular angiofibroma, and mammary-type myofibroblastoma. The atypical, multinucleated cells of pleomorphic lipoma are enigmatic in origin and resemble the cells seen in pleomorphic fibromas (PF). We examined RB expression in 17 PFs and also assessed the tumors with p16 and ki-67 staining. We observed a female predominance in PF (13 females and 4 males) with a mean age of 45 and an anatomic predilection for both the trunk and proximal extremities. Histopathologic features include a dome-shaped to polypoid silhouette in most cases, with variable myxoid to sclerotic stroma. Pleomorphic, multinucleate cells with large nuclei, scant cytoplasm and small nucleoli are characteristic of PF. RB staining was absent in the constituent cells of all lesions. Conversely, p16 overexpression was observed in the majority of tumors (82%). The ki-67 proliferative index was uniformly low and mitotic figures were infrequent [n=1]. Array-based comparative genomic hybridization was performed on one PF and showed loss of the long arm of chromosome 13 (13q14.2;Rb1) and short arm of chromosome 17 (17p13.1;tp53). Our study indicates loss of RB protein expression.
represents a fundamental event in the pathogenesis of PFs, shown by means of both protein expression and chromosome 13q14 loss. Abnormalities in the Rb and p53 pathways are evident in the pleomorphic cells in PF. The uniform loss of RB expression in this series suggests that PF belongs to the family of other ‘Rb-omas’.

Mismatch Repair Deficiency as a Low-Frequency Driver Event in Anorectal Melanoma
Basil A. Horst, MD
Basil A. Horst, MD1; Susan J. Hsiao, MD, PhD1; Hui Min Yang, MD1; David F. Schaeffer, MD2; David N. Horst, MD3; Mahesh M. Mansukhani, MD1
1Columbia University Medical Center, New York, New York, USA
2University of British Columbia, Vancouver, British Columbia, Canada
3Ludwig-Maximilians-Universitaet Munich, Munich, Germany

Introduction: Anorectal melanoma is a rare and highly lethal malignant neoplasm, comprising less than 2% of melanomas and 3% of all anal tumors. The prognosis is poor with a five-year survival rate of less than 20%. Underlying genetic alterations in anorectal melanoma are poorly defined. Although microsatellite instability (MSI) has been found to correlate with tumor progression in cutaneous melanomas, limited data on defects in mismatch repair (MMR) proteins and mutational status of MMR genes precludes distinction between epigenetic inactivation and primary mutational events in most studies. The purpose of this study was to investigate the mutational profile in a cohort of anorectal melanomas. Methods: Fifteen cases of anorectal melanoma were retrieved from the archives of three academic institutions, with approval of respective Institutional Review Boards. Representative tumor areas were microdissected from FFPE tissue sections, and extracted DNA was subjected to targeted exon sequencing. Expression of mismatch repair proteins MLH1, MSH2, MSH6 and PMS2 was assessed by immunohistochemistry. MSI testing for five mononucleotide markers was performed using a fluorescent PCR-based assay. Results: Activating KIT mutations represented the predominant recurrent mutational event, detected in 5 of 15 anorectal melanomas (33%). Interestingly, one case showed a pathogenic mutation in MLH1 (G67R), which has previously been reported in individuals with hereditary non-polyposis colon cancer (HNPCC)/Lynch syndrome. Allele frequency estimates were consistent with a heterozygous mutation. Immunohistochemical analysis for MMR protein expression demonstrated loss of MLH1 and of its dimerization partner, PMS2. PCR testing confirmed microsatellite instability in 5 of 5 loci tested (MSI-H). Clinical features of HNPCC were absent, making a MLH1 germline mutation unlikely. Conclusions: Our findings confirm the predominance of activating KIT mutations in anorectal melanoma. Furthermore, these data extend the spectrum of sporadic, microsatellite-unstable tumors carrying MMR gene mutations to include anorectal melanomas, thereby contrasting with findings in sporadic MSI-H colorectal carcinomas which generally lack MLH1 mutations.
T-cell Receptor High-throughput Sequencing (TCR-HTS) Distinguishes a Lymphomatoid Drug Reaction from CTCL

Nick R. Love, PhD
Nick R. Love, PhD1; Lanny Kirsch, MD2; Youn Kim, MD1; Jinah Kim, MD, PhD1

1Stanford University School of Medicine, Stanford, California, USA
2Adaptive Biotechnologies, Seattle, Washington, USA

Distinguishing cutaneous T-cell lymphoma (CTCL) from lymphomatoid drug reactions may be challenging, especially in the setting of novel experimental immunotherapies. Here, we report three patients with recalcitrant, biopsy-proven CTCL who underwent experimental anti-CCR4 immunotherapy. During therapy, the patients developed erythematous eruptions on the head, neck and upper trunk in a photo-exposed distribution without the classic morbilliform features that typically characterize a drug eruption. The differential diagnosis included drug reaction or recurrent/progressive disease. Thus, critical, time-sensitive clinical management decisions hinged on an accurate diagnosis in this unique setting. Biopsies of the eruptions demonstrated an atypical T cell infiltrate with evidence of significant exocytosis of atypical lymphocytes into the epidermis. However, the immunophenotypic features demonstrated CD8 predominance, suggestive of a reactive process. Despite this, T-cell receptor polymerase chain reaction (TCR-PCR) studies demonstrated clonality, supporting a diagnosis of CTCL. To resolve this ambiguity, we utilized high-throughput sequencing of T-cell receptor (HTS-TCR), a novel diagnostic adjunct that quantifies the T-cell repertoire via sequencing. Using HTS-TCR, we found no dominant TCR clone in these cases, confirming a diagnosis of a lymphomatoid drug reaction, allowing the patients to continue their anti-CCR4 therapy. Taken together, these studies demonstrate the utility of HTS-TCR in establishing true T-cell clonality to promote diagnosis. Our preliminary results suggest that standard TCR-PCR may lack the specificity to consistently distinguish between reactive and neoplastic conditions, and thus, HTS-TCR may be a more accurate and useful diagnostic tool.
### Oral Abstract Session 3

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30 a.m. - 7:40 a.m.</td>
<td>Fontana-Masson Stain in Fungal Infections</td>
<td>Puja K. Puri, MD</td>
</tr>
<tr>
<td>7:40 a.m. - 7:50 a.m.</td>
<td>Adipophilin Expression in Cutaneous Malignant Melanoma</td>
<td>Masakazu Fujimoto, MD, PhD</td>
</tr>
<tr>
<td>7:50 a.m. - 8:00 a.m.</td>
<td>Can Mass Spectrometry Imaging Predict the Clinical Behavior of Atypical Melanocytic Neoplasms?</td>
<td>Rossitza Lazova, MD</td>
</tr>
<tr>
<td>8:00 a.m. - 8:10 a.m.</td>
<td>Correlation Between Human Papillomavirus Status on Condylomata in Women and Risk of Cervical Dysplasia on Papanicolaou Smear: A Case-control Study</td>
<td>Julia S. Lehman, MD</td>
</tr>
<tr>
<td>8:10 a.m. - 8:20 a.m.</td>
<td>Immunological Characterization of Sentinel Lymph Nodes Involved by Metastatic Melanoma</td>
<td>James J. Abbott, BS</td>
</tr>
<tr>
<td>8:20 a.m. - 8:30 a.m.</td>
<td>Gene Expression Signature as an Ancillary Method in the Diagnosis of Desmoplastic Melanoma</td>
<td>Loren E. Clarke, MD</td>
</tr>
</tbody>
</table>
Oral Abstract Session 3

Fontana-Masson Stain in Fungal Infections
Puja K. Puri, MD
Puja K. Puri, MD; Alan D. Proia, MD, PhD; Kelly L. West, MD, PhD
1Laboratory Corporation of America, Research Triangle Park, North Carolina, USA
2Duke University Medical Center, Durham, North Carolina, USA
3Ball Dermpath, Greensboro, North Carolina, USA

Background: The Fontana-Masson stain is used to identify dematiaceous fungi in tissue sections that have been processed for histopathology, and the result often guides initial speciation and antifungal treatment. However, there is evidence that non dematiaceous fungi including several angioinvasive species may react with this stain, as well. There are very few studies in the current literature addressing this issue. Objective: Our aim is to classify the staining patterns of the more commonly encountered fungal pathogens. In doing so, we hope to generate data that will be of use to the pathologist attempting to accurately speciate fungal forms in routine histopathologic examination. Methods: We identified 132 cases of culture proven mycoses. We stained the corresponding surgical pathology tissue with two different Fontana-Masson protocols and recorded the intensity and distribution of fungal staining. Results: There was a large degree of variability in staining, and numerous non dematiaceous fungi showed Fontana-Masson positivity, including Zygomycetes, Aspergillus and Fusarium spp. Limitations: The study was limited in the number of cases identified and studied. Of the 132 cases identified, 112 cases had adequate tissue left after sectioning deeper into the block. Conclusion: Non-dematiaceous fungi, including angioinvasive species, frequently stain with Fontana-Masson. The course of anti-fungal treatment should not be based on the result of this stain alone.

Adipophilin Expression in Cutaneous Malignant Melanoma
Masakazu Fujimoto, MD, PhD
Masakazu Fujimoto, MD, PhD; Ibu Matsuzaki; Shin-ichi Murata, MD, PhD
1Wakayama Medical University, Wakayama, Japan

The lipogenic pathway is upregulated in cancer cells, including melanomas. However, the pathologic significance of cellular lipids in melanocytic lesions is unclear. In the present study, we evaluated intracytoplasmic lipids in melanocytic nevi and malignant melanomas, by immunohistochemical analysis of adipophilin (ADP), which is a member of proteins surrounding intracytoplasmic lipid droplets. A total of 100 primary cutaneous melanocytic lesions including 33 melanocytic nevi (MN), 17 melanoma in situ (MIS), and 50 invasive melanomas (IM) were immunostained for ADP. Then the intensity score (IS) and proportional score (PS) of ADP staining in each case were recorded semi-quantitatively from 0, 1+, 2+, to 3+. As a result, high ADP expression (IS 2+/3+ and PS 2+/3+) was observed in 27 cases, which consisted of 1 MN and 26 melanomas (3 MIS and 23 IM) (p<0.01). Among the IM, high ADP expression was more common in pT3/T4 (63.3%) than pT1/T2 (23.8%) (p=0.01), and stage III/IV (76.9%) than stage I / II.
In conclusion, most of the melanocytic lesions with high ADP expression were malignant melanomas in our cohort. Therefore, ADP might serve as a sensitive diagnostic marker for malignant melanoma. Additionally, it may be a useful prognostic marker for malignant melanoma, because high ADP expression was positively correlated with advanced stage IM.

Can Mass Spectrometry Imaging Predict the Clinical Behavior of Atypical Melanocytic Neoplasms?
Rossitza Lazova, MD
Rossitza Lazova, MD1; Erin H. Seeley, PhD2
1Yale University School of Medicine, New Haven, Connecticut, USA
2Protea Biosciences Inc., Morgantown, West Virginia, USA

Background: In a previous study using Mass Spectrometry Imaging we discovered differences on a protein level between benign melanocytic nevi and malignant melanomas. Objective: To investigate whether Mass Spectrometry Imaging (MSI) can help predict which Atypical Melanocytic Neoplasms (AMN) will have a benign clinical course and which will have poor prognosis. Methods: Formalin-fixed, paraffin-embedded tissue samples from 9 patients diagnosed with AMN were prospectively subjected to mass spectrometric analysis. A diagnosis of either melanoma or nevus was rendered based on proteomic signature, which diagnosis was then correlated with clinical behavior. In addition, MSI was performed retrospectively on 6 cases of AMN in children ranging from 2 to 16 years of age. Results: MSI classified 9/9 cases of AMN from the prospective group as benign. Of these patients 6/9 had positive sentinel lymph nodes (SLN) and one patient had 3 positive nodes on completion lymphadenectomy (CLDN). All 6 AMN in children analyzed retrospectively were also diagnosed as benign by MSI. Two of these patients had positive SLN, and one of them had positive nodes on CLDN. The follow-up ranged from 3.5 to 14 years with all patients alive and with no evidence of disease. Conclusions: Mass Spectrometry Imaging can be helpful as an ancillary diagnostic modality in difficult melanocytic neoplasms. It shows potential in predicting the clinical behavior of Atypical Melanocytic Neoplasms. Further studies are needed with larger number of cases to determine whether MSI will be a clinically useful tool in these cases.

Correlation Between Human Papillomavirus Status on Condylomata in Women and Risk of Cervical Dysplasia on Papanicolaou Smear: A Case-control Study
Julia S. Lehman, MD
Julia S. Lehman, MD1; Michelle Duvall, MD1
1Mayo Clinic, Rochester, Minnesota, USA

Background: Condylomata are squamous papillomas that typically result from infection by human papillomavirus (HPV). HPV in situ hybridization (ISH) for low-risk or high-risk serotypes is performed on squamous papillomas from the genital region at our institution. It is unknown whether positivity for HPV by ISH in condylomata in women predicts risk for cervical dysplasia or other HPV-related complications (e.g. cervical, vaginal, vulvar, or anogenital dysplasia or cancer; genital squamous cell
carcinoma). Aim: To evaluate whether HPV status in condylomata in women correlates with the development of other HPV-related complications. Methods: We identified all skin biopsies from the genital, perineal, or perianal regions that underwent HPV ISH testing (2004-2014) for low- and high-risk serotypes in women who had also undergone Papanicolaou (Pap) smear testing at our institution either before or after skin biopsy testing. Specimens showing diagnoses incompatible with condyloma (e.g. squamous cell carcinoma, acantholytic acanthoma) were excluded. We recorded skin biopsy HPV ISH results, Pap smear results, and other potentially HPV-related diagnoses. Results: Of 147 skin biopsy specimens, 60 (41%) tested positive for HPV ISH [53 (88%) low risk, 7 (12%) high risk]). We identified no difference in the frequency of Pap smear abnormalities in patients with HPV-positive skin specimens compared with HPV-negative skin specimens (35% vs. 34% respectively; p=0.94), nor in patients with high-risk HPV-positive compared with low-risk HPV-positive skin specimens (14% vs. 38% respectively; p=0.19). Moreover, no association between high-risk or low-risk HPV status on skin specimens and other HPV-related complications was observed (14% vs. 6% respectively; p=0.39). Conclusions: This study did not identify a correlation between HPV status in condyloma and cervical dysplasia or other HPV-related complications. Our data imply that prediction of other HPV-related complications is insufficient to justify HPV ISH testing on genital papillomas. While validation from larger studies is required, these data may contribute to discussions regarding appropriate-use criteria for HPV tissue testing on genital squamous papillomas.

Immunological Characterization of Sentinel Lymph Nodes Involved by Metastatic Melanoma
James J. Abbott, BS
James J. Abbott, BS1; Meghan Buckley, MS2; Laura Taylor, MD1; Phyllis Gimotty, PhD2; Paul Zhang, MD1
1The Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA
2The University of Pennsylvania, Philadelphia, Pennsylvania, USA

Introduction: One of the most important prognostic factors in early stage melanoma is sentinel lymph node (SLN) status. However, the significance of lymph node morphology related to immune response is still being determined. We examined the micromorphometric immunological pattern to metastatic melanoma in SLN biopsies and completion lymph node (CLN) dissections and their relation to 5-year overall survival. Methods: Retrospective cohort of 49 patients from 1996 to 2005 with a positive SLN who underwent CLN dissection were studied. Micromorphometric characteristics such as follicular center count per profile (FCC), sinus histiocytosis, metastatic size and location, tumor infiltrating lymphocytes (intranodal), paracortical dendritic cells, germinal center reaction, and overall morphology were recorded on positive SLN and negative CLN. Comparison of Kaplan-Meier survival curves used the exact log rank statistic. Results: In the high FCC (n5-51) versus the low FCC (n2 mm and nodal capsular extension had significantly lower 5-year survival (both <0.001). Conclusion: Nodal micromorphometric features (i.e. FCC) are likely related to host immune response to metastasis and are associated with clinical outcomes. In addition to evaluating the size of metastases and capsular involvement, quantitative evaluation of lymphoid follicular centers might provide additional prognostic information.
Gene Expression Signature as an Ancillary Method in the Diagnosis of Desmoplastic Melanoma

Loren E. Clarke, MD
Loren E. Clarke, MD1; Jason D. Pimentel, MD2; Hillary Kimbrell, MD1; Klaus Busam, MD3
1Myriad Genetics, Inc., Salt Lake City, Utah, USA
2Henry Ford Hospital, Detroit, Michigan, USA
3Memorial Sloan Kettering Cancer Center, New York, New York, USA

Background: A 23-gene signature was recently developed for use as an adjunct to histopathology in distinguishing benign from malignant melanocytic neoplasms. The signature produces a score that classifies lesions as positive (likely malignant), negative (likely benign), or indeterminate. Objective: The objective of this study was to assess the sensitivity and specificity of the gene signature in the differentiation of desmoplastic melanoma (DM) and its variants from benign simulators such as sclerotic and desmoplastic variants of melanocytic nevi. Methods: The database of a commercial laboratory was searched for all cases for which the submitting dermatopathologist used one or more of the following terms within the diagnosis or differential diagnosis fields: Desmoplastic; sclerosing / sclerotic; and fibrosing / fibrotic. Forty cases were identified. H&E-stained sections of all 40 were reviewed independently by two dermatopathologists and diagnoses were assigned. An additional 10 lesions were retrieved from the pathology archives of a tertiary cancer center and submitted (blinded to initial diagnosis) for gene expression testing. The final diagnoses for all cases were supported by one or more of the following: a) Histopathologic features; b) follow-up / outcome information; and / or c) other ancillary tests such as array-based comparative genomic hybridization. Results: The final cohort included 20 DM or DM variants and 27 melanocytic nevi. The gene expression score was positive (malignant) in 15 of the 20 melanomas, negative (benign) in four, and indeterminate in one. The score was negative (benign) in 24 of the melanocytic nevi and indeterminate in the remaining three. Conclusion: These results reflect the performance of the gene signature in differentiating desmoplastic melanoma and its variants from benign simulators.