ORAL PRESENTATION

(8:40 AM)

CLINICAL RECOGNITION OF MELANOMA BY DERMATOLOGISTS AND NON-DERMATOLOGISTS

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BACKGROUND: The incidence of melanoma is increasing annually in Canada. Consequently there has been a rise in the number of patients presenting with pigmented skin lesions to dermatologists and non-dermatologists. OBJECTIVE: This retrospective study is designed to assess the ability of physicians of different specialties to accurately recognize melanoma. METHODS: Pathology reports of biopsies submitted to Vancouver Coastal Health with a clinical diagnosis of melanoma were reviewed (January - July 2013). The clinical diagnoses made by dermatologists, general practitioners and family physicians (GP/FP), and all other specialists were correlated with the final histopathological diagnosis. RESULTS: The dermatologists, GP/FP's and all other specialists achieved diagnostic accuracies of 24.75% (50 of 205), 3.52% (9 of 240) and 12.75% (14 of 107), respectively. Dermatologists diagnosed the most melanoma (50) and had the highest diagnostic accuracy (24.75%). The clinical diagnosis rendered by GP/FP's matched the histopathological diagnosis in only 3.52% of biopsies. GP/FP's also diagnosed the lowest number of melanomas (9) and biopsied the most skin lesions (240). All other specialists performed better than GP/FP's in accuracy (12.75%) but only performed half as well as dermatologists. CONCLUSION: Although the diagnostic accuracy of dermatologists was significantly better than the other groups, the majority of patients with suspicious skin lesions present to a family or general practitioner first. Thus, there is considerable value in providing more training and education to non-dermatologists as it can have a meaningful impact on patient care.

Category: Early experiments with well defined objectives/hypotheses

(8:51AM)

IDENTIFYING KERATINOCYTE DERIVED COLLAGEN INHIBITORY FACTORS TO TREAT HYPERTROPHIC SCAR AND KELOID

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Two extremes of the wound healing process represent serious pathologic conditions: non-healing and over-healing. There exist a multitude of strategies that effectively address early stages of wound healing; however, there are no specific modalities to target or signal wound healing cessation. Consequently, patients continue to deposit matrix long after the wound has technically healed. Over healing such as post-burn hypertrophic scarring (HSc) and keloid are disfiguring and devastating, resulting in bulky, itchy and inelastic scars that pose serious functional and cosmetic problems for recovering burn patients. Our working hypothesis has been that mesenchymal-epithelial communication is critical in exchanging information between keratinocytes and fibroblasts. Keratinocyte releasable factors function as either stop signals at the late-stage of wound healing or by modulating the expression of key Extra-Cellular Matrix

(ECM) components. To test this hypothesis, we established a keratinocyte/fibroblast co-culture in vitro model, and have since identified two sets of keratinocyte releasable anti-fibrogenic factors for dermal fibroblasts. The 1st set of these factors stimulate the expression of Matrix Metalo-Proteinase (MMP-1, 3) while the 2nd set of the factors suppresses the expression of key ECM components like type I and III collagen. In tandem these two sets of factors stand to elucidate a clear picture of how to regulate or stop wound healing in such a way to improve/prevent hypertrophic scars and keloid. As such, the main goal of this study is to identify these keratinocyte releasable anti-fibrogenic factors, their motifs, functionality and their therapeutic benefits in wound healing.

Category: Early experiments with well-defined objectives/hypotheses

(9:02 AM)

ALLERGIC CONTACT DERMATITIS AND ATOPY

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Atopy is a genetic predisposition to the development of allergic reactions and the increased production of IgE upon exposure to environmental antigens. Clinical manifestations of atopy include asthma, atopic dermatitis (AD) and allergic rhino conjunctivitis (ACR). Allergic contact dermatitis (ACD) is a T-cell mediated cutaneous delayed-type hypersensitivity (CDTH) reaction to topical allergens. We hypothesized that the prevalence of ACD would be higher among patients with a history of atopy and with a familial predisposition to atopy. For this study, we reviewed the patch test database of the UBC Contact Dermatitis Clinic from 2008 to 2012. A personal history of asthma, AD and ACR was recorded. In addition, a family history was obtained and manifestations of atopy in family members were noted. A total of 1515 patients were included in this study. Our data show that the odds ratio of a positive patch test with a personal history of atopy was 1.39, while the odds ratio of a positive patch test with a family history of atopy was 1.69. Patients with a personal history of atopy also reacted to greater number of allergens with 28 % reacting to 4 or more allergens compared with 23 % in patients with no history of atopy. We conclude from our study that patients with a personal or family history of atopy have an increased risk of ACD and that atopic patients react to a greater number of allergens. These results provide further evidence for the link between atopy and ACD.

Category: Applied/functional experiments (animal models of disease and in vivo studies, etc)

(9:13 AM)

NOTCH/RBP-J SIGNALING PATHWAY GENES ARE SIGNIFICANTLY DIFFERENTIALLY EXPRESSED IN HAIR FOLLICLES AND BASAL CELL CARCINOMAS

Feng-Tao Shi[1], Mei Yu[1], David Zloty[1], Robert H. Bell[2], Eddy Wang[1], Noushin Akhoundsadegh[1], Gigi Leung[1,], Anne Haegert[2], Nicholas Carr[3], Jerry Shapiro[1], Kevin John McElwee[1]
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Multiple reports suggest that a significant subset of basal cell carcinomas (BCCs) are directly derived from hair follicles (HF). In some respects, hair follicles can be defined as "ordered" skin appendage growths, while BCCs can be regarded as "disordered" skin appendage growths. We examined the similarities and differences in gene expression between HF and BCCs to define common and unique signaling pathways expressed in each type of skin appendage. Human nodular BCCs and non-follicular skin epithelium were obtained from patients undergoing surgical resection, while HFs were collected from scalp biopsies of normal individuals undergoing cosmetic procedures. Selected genes were validated using quantitative Real-time PCR, immunohistochemistry, and *in vitro* assays. Two differentially expressed gene sets in BCC and HF versus skin epithelium were identified by significance analysis of microarray (SAM). Subsequently, multiple signaling pathway analyses were conducted. The results indicated that specific molecular mechanisms involved in the process of self renewal, such as Notch and Hedgehog signaling pathways were active in both HF and BCCs. However, Notch signaling, including tumor suppressor genes NOTCH1/2, ligands JAG1/2, signaling inhibitor NUMB, and downstream Notch pathway genes DTX1, DTX2, RBPSUHL, LFNG, HR, and HES7, all showed significant differential expression in BCCs compared to HF. The data suggests downstream Notch signaling pathway gene expression is suppressed in BCCs while highly expressed in HF. Elements of the notch pathway could be targets for the treatment of BCCs and potentially in hair follicle engineering.

Category: Early experiments with well defined objectives/hypotheses

(9:24 AM)
SKIN LOCALIZED T REGULATORY CELLS PRODUCE PRO-FIBROTIC CYTOKINES IN SYSTEMIC SCLEROSIS SKIN

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T regulatory cells (Tregs) are defined by constitutive FOXP3 expression and are critical for self-tolerance. Conversion of Tregs to a cytokine-producing phenotype has been described in several autoimmune diseases, and may play a role in a number of inflammatory skin conditions. Systemic sclerosis (SSc) is an autoimmune disorder with extensive skin involvement for which there is no specific treatment. We aim to determine the role of Treg plasticity in the pathogenesis of SSc. 4mm skin biopsies taken from SSc patients and healthy controls (HC) for immunofluorescence or isolation of T cells after short-term culture for cytokine analysis. PBMCs were evaluated in parallel for cytokine production and skin homing marker expression. We found no difference in the proportion of Tregs in the skin or blood of SSc patients compared to HCs. Tregs in SSc skin produced significantly more pro-fibrotic IL-4 and IL-13. Tregs in SSc blood did not make Th2 cytokines, but did express more Th2-associated CCR4, particularly in the skin-homing CLA+ population. This is more pronounced in diffuse disease. Histology shows IL-33, a Th2-polarizing cytokine, is proximal to T cells in SSc skin, and inflammatory cytokines increase IL-33 mRNA in SSc fibroblasts. Accordingly, addition of IL-33 to HC skin during matrix culture increases the percent of IL-13+ Tregs. Overall, Th2-like Tregs are polarized in SSc skin,

potentially through local action of IL-33, allowing them to contribute to fibrosis via IL-4 and IL-13. Th2 and skin-homing markers on circulating Tregs are potential biomarkers and treatment targets for SSc.

Category: Early experiments with well defined objectives/hypotheses.

(9:35 AM)

MULTIPHOTON FLUORESCENCE IMAGING OF CUTANEOUS MELANINS BY STEPWISE CONTINUOUS WAVE LASER EXCITATION

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A novel potential approach to discriminating benign pigmented skin lesions from melanomas is by stepwise multiphoton excitation fluorescence. In stepwise fluorescence, a real intermediate excitation state energy level exists between ground and excited state so that only two or more orders of magnitude lower excitation intensity is needed to obtain the same population density of the fluorescent level as compared with conventional simultaneous excitation. To date, melanin has been the only substance in the skin demonstrated to exhibit the stepwise excitation phenomenon. This property provides a relatively specific method for cutaneous melanin detection. Unlike simultaneous multiphoton excitation fluorescence generated by ultrafast femtosecond (fs, $1x10^{-15}$ second) lasers, stepwise fluorescence excitation can be generated by continuous wave (CW) lasers, significantly reducing the instrumentation costs. We are interested in studying the melanin stepwise effect by both stepwise two-photon and stepwise three-photon fluorescence spectroscopy and imaging. Subsequent studies will extend this technology to *in vivo* human skin imaging and spectroscopy for clinical diagnosis. We have employed a multimodality spectroscopy and imaging system using both CW and fs laser excitations at 785nm for studying melanin. The spectra of synthetic melanin powder and Sepia-derived melanin powder have been measured as references. The images and spectra of human white hair and black hair demonstrated that stepwise fluorescence generates melanin specific signals. Planned future work includes obtaining stepwise spectra/images of melanins from different pigmented skin lesions *ex vivo* and then realizing stepwise fluorescence imaging of melanins in pigmented skin lesions *in vivo*.

Category: Early experiments with well defined objectives/hypotheses

(11:40 AM)

THE MOST COMMON CO/CROSS REACTANTS IN P-PHENYLENEDIAMINE ALLERGIC PATIENTS AND THE IMPACT ON AVAILABLE ALTERNATIVE HAIR DYES

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P-phenylenediamine (PPD) is a common component of hair dyes and is also a common contact sensitizer. Given the rates of sensitization, hair dyes containing alternatives to PPD have been developed. Here we attempt to determine if contact sensitization to the co/cross reactants found in these alternative hair dyes limit their use by PPD allergic patients. We reviewed all patch test results of patients presenting to the UBC Contact Dermatitis Clinic between January 2008 and June 2013. Patients were patch tested with a screening series of 65-80 allergens and supplemental allergens as indicated. The American Contact Dermatitis Society Contact Allergen Management Program (CAMP) database was queried for hair dyes without PPD and each of the most common co/cross reactants. The most common co/cross reactants, constituting statistically significantly greater than 1% of PPD positive patients, were nickel (24%), ammonium persulfate (18%), cobalt (16%), p-toluenediamine sulphate (15%), 4-aminophenol (14%), fragrance mix I (12%), toluenediamine base (9%), fragrance mix II (7%), *myroxylonpereirae* resin (7%), glycerylthioglycolate (7%), 3-aminophenol (6%), black rubber mix (6%), thiuram mix (6%) and carba mix (6%). The CAMP database contained 17 PPD free dyes. Cross reacting to 4-aminophenol restricted available dyes to 16. Positivity to any of the fragrances restricted patients to 1 non-permanent dye. Patients allergic to PPD are commonly allergic to other chemicals found in hair dyes. Patients that are PPD allergic and also react to fragrances are severely restricted in their choices of hair dye. This research will help patients by creating awareness amongst hair dye manufactures of the need to produce fragrance free, PPD free hair dyes.

Category: Early experiments with well-defined objectives/hypotheses

(11:51 AM)

ONE-YEAR REVIEW OF THE "SCREEN" (SKIN CANCER POST- TRANSPLANT) CLINIC: WHAT WE HAVE LEARNED

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The SCREEN Clinic is a new skin-cancer screening clinic that is fully integrated into the renal transplantation clinic at St. Paul's Hospital in Vancouver, BC. Transplant patients (primarily renal; some heart) screened during a 12-month period were stratified into low, medium and high-risk groups based on detailed history and skin examination. The purpose of this review was to determine characteristics of patients at risk, to specify types and locations of skin cancers, and to identify areas for patient and physician education. Of 122 high-risk patients identified and followed, 48(39%) were diagnosed with new skin cancers. 72% were Caucasian, 2% were Metis and 2% were Asian. 67% were male, 53% had a previous history of skin cancer, and 85% were aware of their increased skin cancer risk.123 skin cancers were identified. Of these, 33(27%) were basal cell carcinomas and 90(73%) were squamous cell carcinomas. 27% of the squamous cell carcinomas were invasive. Common locations included arm (8%), neck (8%), hand (7%) and scalp (7%). Actinic keratosis occurred in 60%. 28% reported using only 1-2 bottles of sunscreen per year. 13% never used sunscreen. Sunscreen was commonly applied to the face (51%), back (46%) and back of neck (41%), while the lips (19%) and chest (17%) were areas most neglected.

We have diagnosed new skin cancers in over 1/3 of our high-risk population. Caucasian males were found to be most at risk. Squamous cell carcinoma accounted for the majority of tumours with over 25% demonstrating invasion. Although skin cancer awareness was high, sunscreen use was limited.

Abstract Category: Pilot/Exploratory experiment

(12:02 PM)

INVESTIGATION OF HUMAN AUTOANTIGEN EPITOPES IN AUTOIMMUNE HAIR LOSS DISORDER ALOPECIA AREATA

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Alopecia areata (AA) is believed to be an autoimmune disease that results in non-scarring, inflammatory cell-mediated hair loss. Both CD4 and cytotoxic CD8 T-cells (CTLs) have been found to be important for the onset and progression of AA both in humans and rodent AA models. Hair follicular (HF) keratinocyte and/or melanocyte antigen are suspected potential targets of auto-reactive CTLs, but the specific epitopes have not yet been identified. We investigated the potential for a panel of known epitopes, expressed by human HF keratinocytes and melanocytes, to induce activation of CTLs. Peripheral blood mononuclear cell (PBMC) populations isolated from AA affected and healthy subjects with HLA-A2 serotypes were cultured with synthetic HLA-A2 restrictive peptides. The frequency of CTL activation in PBMC populations was measured by using enzyme-linked immunosorbent spot (ELISpot) assays where activated IFNgamma secreting cells are visible as spots. Specific peptide sequences for trichohyalin, MART-1 and tyrosinase related protein-2 (TRP2) induced significantly higher frequencies of response in AA CTLs compared to healthy controls. Apoptosis assays revealed conditioned media from AA PBMCs stimulated with trichohyalin peptides can elevate the expression of apoptosis markers in primary HF keratinocytes whereas comparable studies with control PBMCs had less effect. The data indicate that AA affected subjects present with an increased frequency of CTLs responsive to antigen epitopes originating from keratinocytes and melanocytes. In addition, HF keratinocytes can undergo apoptosis from the soluble factors secreted by CTLs activated by these epitopes. Potentially, trichohyalin could be specific targets for CTLs that induce AA in humans.

Category: Applied/functional experiments

(12:13 PM)

DART CLINIC REVIEW: EXPERIENCES FROM A COMBINED DERMATOLOGY AND RHEUMATOLOGY CLINIC

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The combined Dermatology and Rheumatology (DART) Clinic is a novel multi-disciplinary teaching clinic in Vancouver, where patients with both skin and rheumatologic issues are concomitantly assessed by both specialties. We retrospectively reviewed the charts of all DART patients for the two-year period, July 2011 to June 2013. The data collected included patient age, gender, dermatologic and rheumatologic diagnoses, biopsies performed, treatment, and number of follow-ups. A total of 320 patients were seen (248 female, 72 male). Mean age was 49 years for men and 47 years for women. Most common rheumatologic diagnoses were systemic lupus erythematosus (58 cases seen), rheumatoid arthritis (49), psoriatic arthritis (41) and undifferentiated connective tissue disease (25). Most common dermatologic diagnoses were dermatitis (60), psoriasis (40), cutaneous lupus (25), alopecia (21), and infections (16). 78 patients had biopsies. The majority of our patients were females with diagnoses of systemic lupus erythematosus or rheumatoid arthritis. Skin conditions seen were both related and un-related to the underlying rheumatologic diagnosis. Dermatitis, a non-rheumatologic-associated condition, was very common, possibly due to its high incidence in the general population and a clinical appearance that may be suggestive of connective tissue disease. Our data also supports that lupus patients often present with skin conditions unrelated to their underlying lupus. Both rheumatologists and dermatologists can benefit from being aware of the skin conditions that rheumatologic patients are experiencing. Information gathered from this review will be used for quality improvement and to help guide the education of physicians in our clinic.

Study Category: Pilot/exploratory

(12:24 PM)

THE ROLE OF BIN1 TUMOR SUPPRESSOR ISOFORMS IN REGULATION OF PROLIFERATION, APOPTOSIS AND TUMOR FORMATION OF HUMAN CUTANOUS T-CELL LYMPHOMA CELLS *IN VITRO* AND *IN VIVO*

Sharmin Esmailzadeh[1], Youwen Zhou[2] and Xiaoyan Jiang[1]
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Cutaneous T-cell lymphomas (CTCLs) represent a group of lymphoproliferative disorders characterized by homing of malignant T-cells to the surface of skin. The goal of this project is to investigate the role of BIN1 in pathogenesis of CTCL. BIN1 is an adaptor protein with more than ten isoforms; some of which have tumor suppressor activity in solid tumors. However, the role of BIN1 in regulation of hematopoiesis and lymphomagenesis remains unknown. We have shown that BIN1 expression level is significantly lower in CTCL patients versus controls. To investigate the role of BIN1 in CTCL, two isoforms were overexpressed in CTCL cell lines,

Hut78 and HH. Overexpression of BIN1 isoforms led to significant reduction in cell proliferation and significant increase in spontaneous and FAS-ligand-induced apoptosis in Hut78 and HH cells. Significant reduction in protein expression level of c-FLIP (inhibitor of FAS apoptosis pathway) and upregulation of downstream cleaved caspase-8 and caspase-3 was demonstrated in BIN1-transduced cells, suggesting that BIN1 isoforms induce apoptosis by downregulating the expression of c-FLIP which leads to downstream activation of FAS apoptosis pathway. Furthermore, subcutaneous injection of control empty-vector HH cells into immunodeficient mice formed local tumors within 1.5 months, whereas no tumor was found in mice injected with BIN1-transduced HH cells. These findings suggest tumor suppressor activities for BIN1 isoforms in CTCL cell lines, using *in vitro* and *in vivo* assays. Ultimately, a deeper insight into roles of specific genes and signaling pathways involved in CTCL development may identify new molecular targets for more effective treatment options.

Category: Early experiments with well defined objectives/hypotheses

(12:35 PM)

RAPIDLY ABSORBABLE VERSUS NON-ABSORBABLE SUTURES FOR MOHS MICROGRAPHIC SURGERY REPAIR ON THE FACE (RAVNAS): A RANDOMIZED CONTROLLED SPLIT-SCAR STUDY

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Background and aim: This study is being carried out to assess equivalence of scar outcome for two suture materials (rapidly absorbable polyglactin 910 (VicrylRapide™) and non-absorbable nylon monofilament (Ethilon™)) commonly used for wound closure on the face in dermatologic and Mohsmicrographic surgery (MMS). **Study design and methods:** Prospective randomized controlled split-scar observer-blinded study. One hundred consecutive patients attending for MMS on the face were included in the study. Each participant's final surgical wound/scar was divided in two, with each half (superior/medial or inferior/lateral) randomly assigned to each study arm receiving either material. Scar analysis was performed by DMZ at one-week, two-month and six-month intervals with the Stony Brook Scar Evaluation Scale (SBSES), Visual Analogue Scale (VAS) and Wound Evaluation Scale (WES). Clinical photographs were takes, and the final six-month assessment will additionally be performed by two independent observers (SH and AS). **Interim results:** Sixty-six participants have been recruited (40 male, 26 female). The mean age is 69.8 years. The average scar length was 71.7 mm. One week follow-up data is available for 47 participants. The mean SBSES, VAS and WES were 3.0, 81.2 and 5.0in the rapidly absorbable suture group and 3.2, 80.3 and 4.8 in the non-absorbable suture group, respectively. Two-month data is available for ten participants. The mean SBSES, VAS and WES were 3.8, 78.5 and 4.8 in the rapidly absorbable suture group and 4.1, 82.4 and 4.8 in the non-absorbable suture group, respectively. Full statistical analysis comparing both study arms will be performed when recruitment and follow-up is complete by late 2014. If these findings show that a rapidly absorbable suture provides an equivalent scar outcome for facial surgery, patients will benefit from a decreased number of clinic visits, and discomfort, associated with suture removal.

Category: Applied/functional experiments

(1:40 PM)

FEASIBILITY OF USING SUNLIGHT EXPOSURE TO OBTAIN THE RECOMMENDED LEVEL OF VITAMIN D IN CANADA

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Vitamin D is an important hormone and deficiencies of it have been strongly linked to osteoporosis, and implicated in breast cancer and cardiovascular disease. This study aims to assess the feasibility of using sunlight exposure in Canada to meet the daily recommended level of vitamin D given differences in average ultraviolet radiation (UVR) levels, skin colour, amount of skin exposed, and adherence to sun protection guidelines. Ultraviolet index (UVI) data for 13 Canadian sites was obtained from Environment Canada. Using Holick's rule, sun exposure times required to synthesize 1000 IU of vitamin D for type II and type V skinned individuals exposing $1/4^{th}$ or $1/8^{th}$ of their body surface area were calculated for each hour of the year and classified according to whether the UVI was ≥3 (when sun protection guidelines are advised) or <3. Darker skinned individuals and those exposing less of their skin to the sun were found to require higher sun exposure times to obtain adequate vitamin D levels, with few opportunities existing outside of those when sun protection is advised. During the fall and winter months and in sites located more north, it was found that even with fair skin and a large amount of skin exposed, UVR levels are too low for individuals to rely solely on sun exposure to obtain enough vitamin D within one time period. This study stresses that while sun exposure is an important source of vitamin D, Canadians should look to other safe sources to meet vitamin D requirements year-round.

Category: Pilot/exploratory experiments (for study design, hypotheses creation, etc)

(1:51 PM)

PROGNOSTIC ROLE OF BRAF IN MELANOMA DISEASE PROGRESSION AND PATIENT SURVIVAL: PROTEIN EXPRESSION VS. GENE MUTATION

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Alteration in *braf* expression and activity is the most prevalent oncogenic event in melanoma development. However, the effect of *braf* mutation on patient survival, as the final outcome, is a matter of controversy. We investigated the effect of *brafV600E* mutation on patient survival and then evaluated the prognostic value of BRAF protein expression level in different stages of melanoma and its correlation with *brafV600E* mutation. Using meta-analysis in a pool of 674 patients, we revealed that *brafV600E* mutation increases the risk of mortality in melanoma patients by 1.7 times (95% CI, 1.37-2.12). In addition, our investigation on 370 patient samples showed a remarkable stepwise increase in BRAF protein expression level in primary and metastatic melanoma compare with normal samples ($P=1.8\times10^{11}$). High BRAF expression was significantly correlated with thicker tumors, ulceration and higher American Joint Committee on Cancer (AJCC) stages (P=1.5×10-7, 1.5×10-5, 3.6×10^{13}, respectively). In primary melanoma

cases, patients with high BRAF expression had significantly worse overall (P=0.009) and disease-specific five-year survival (P=0.007). While there was a trend for higher prevalence of *brafV600E* mutation in patients with high BRAF protein expression, no significant correlation was observed between protein expression and BRAF mutation. Furthermore, univariate-Cox-regression analysis confirmed high BRAF protein expression as a strong risk factor for poor patient survival in primary melanoma (HR2.08 overall survival; HR2.39 disease-specific survival). We found *brafV600E* mutation an absolute risk factor for melanoma and revealed a novel prognostic value for BRAF protein expression in primary melanoma. However there was no significant correlation between these two factors.

Study category: (3) Applied/functional experiment

(2:02 PM)

PHOTOTHERAPY-INDUCED LICHENOID PAPULES OF VITILIGO

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Background: Narrowband ultraviolet B (NB-UVB) is a very effective vitiligo treatment; however, its long-term effects in vitiligo are unknown. We report four patients who developed lichenoid papules (LPs) only in vitiliginous skin after prolonged NB-UVB exposure. Methods: Retrospective review of vitiligo NB-UVB charts was conducted for the period from 2006 to 2013. Data collected included demographics, vitiligo characteristics, clinicopathologic features of LPs, and NB-UVB parameters. Results: A total of 127 patients received NB-UVB over the duration specified. Four patients (3%) developed erythematous-violaceous papules within vitiligo patches; none of them was on photosensitizing medications. Two patients were Caucasian (male and female) and two were East Asian (both females). Mean age at onset of LPs was 48 years (range 29-66). Mean duration of vitiligo was 16 years. All four patients had generalized vitiligo with a mean surface area of involvement of 10% (range 9-10%). Of the 127 patients, 16 had a cumulative dose of more than 100 J/cm^2. All four patients who developed LPs were from this group. However, none of the patients who received <100 J/cm^2 cumulative dose of NB-UVB developed these papules. Histologic findings of LPs included hyperakeratosis, hypergranulosis, lichenoid infiltrate, and sawtooth rete ridges. The mean duration to resolution of LPs after discontinuing NB-UVB was 5 months. However, recurrence was observed soon after restarting NB-UVB. Conclusion: LPs developed in 25% (4/16) of vitiligo patients who received a cumulative dose of > 100 J/cm^2 of NB-UVB. This might possibly be an immune or phototoxic response to prolonged exposure to NB-UVB.

Category: Observational study
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(2:13 PM)

IMMUNE MECHANISMS UNDERLYING THE TOLEROGENIC EFFECTS OF INTRAPERITONEAL INJECTION OF SKIN FIBROBLASTS

Mohsen Khosravi-Maharlooei, SanamSalimi-Elizei, Reza Jalili, Ruhangiz T. Kilani, Aziz Ghahary

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Introduction. We aimed to see whether the immune tolerance induced by intra-peritoneal (IP) injection of indolamine 2,3 dioxygenase (IDO)-expressing skin fibroblasts is based on generation of tolerogenic antigen presenting cells at the site of injection. **Methods.** Ten million C57BL/6 (B6) fibroblasts, B6 IDO-fibroblasts, B6 splenocytes and C3H/HeJ (C3H) fibroblasts were injected into the peritoneal cavity of C3H recipient mice. After 2 and 9 days, the peritoneal lavage (PL) cells were checked regarding the expression of co-stimulatory (CD80) and co-inhibitory molecules (PD-L1, PD-L2 and B7H4) on dendritic cells (DCs) and macrophages. PL cells of recipient mice were cultured and their ability to generate regulatory T cells (Tregs) in vitro was assessed. After 9 days, Tregs were evaluated withinthe spleen, mesenteric lymph node (MLN) and axillary lymph node (ALN) of recipient mice. **Results.** DCs and macrophages within the PL of fibroblast-treated groups expressed a significantly higher ratio of co-inhibitory/co-stimulatory molecules compared to splenocyte-treatedand non-treated groups. In vitro, PL cells of fibroblast-treated groups significantly enhanced the percentage of Tregs. There was no significant difference between allogenic vs. syngenic and regular vs. IDO-expressing fibroblasts. However, the percentage of Tregs in MLN and ALN of recipient mice only increased in IDO-fibroblast-treated group. **Conclusion.** IP-injection of fibroblasts induces tolerogenic DCs and macrophages. While these cells are able to induce Tregs in vitro, presence of IDO is essential for Treg induction in vivo. We are going to test this strategy in skin transplantation model, which can be used to save the lives of burn patients.

Category: Applied/functional experiments (animal models of disease and in vivo studies, etc)

(2:24 PM)
SEASONAL AND GEOGRAPHIC TRENDS IN TANNING
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Background: The incidence of skin cancer remains high and continues to rise. Tanning has been linked to causing skin cancer. Although tanning practices are assumed to be seasonal, seasonal patterns in tanning have not been systematically evaluated. This study utilizes internet search query data to test the hypothesis that tanning varies by season and contrary to general understanding peaks before active summer months. Methods: Internet search query data were obtained from Google Trends. Monthly normalized search volumes (NSV's) were determined for the term "tanning" and "tanning salons", from January 2004 to December 2013. Using cosinor analysis, and Kruskal-Wallis one-way analysis of variance, seasonal and geographic effects were tested for data from Canada, United States and Australia. Results: Time series revealed peaks in NSV's in March-April and troughs in October-November in Canada and the United States. The peaks and troughs in NSV's from Australian data were out of phase by 6 month as compared to the northern hemisphere counterparts, consistent with a seasonal pattern. Cosinar analysis revealed statistically significant seasonal effects on NSV's in all countries. The analysis of variance showed no significant difference between the three countries. Conclusion: Currently the Canadian educational campaigns that educate people about the hazards of tanning begin in May or June. This study suggests interest in tanning practices to be highest in the months preceding summer (April or March) and prior to the onset of these campaigns. Further studies are needed to

confirm these findings, but these results support having educational campaigns being initiated earlier during the year.

Category: Early experiments with well defined objectives/hypotheses

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THYMOCYTE SELECTION-ASSOCIATED HIGH MOBILITY GROUP BOX PROTEIN (TOX) PROFOUNDLY DISRUPTS CELLULAR PROLIFERATION AND APOPTOSIS IN CUTANEOUS T CELL LYMPHOMA

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TOX is a transcription factor essential for early T cell development, and is tightly shut off upon T cell maturation. Normal mature $CD4^+$ T cells do not express TOX. Previous studies showed that $CD4^+$ T cells in cutaneous T cell lymphoma (CTCL) ectopically express TOX. The objective of this study is to examine if aberrant TOX expression contributes to CTCL pathogenesis. In three CTCL cell lines (Hut78, HH, and SZ4), ectopic TOX expression was reduced by lentiviral-shRNA-mediated TOX gene knock-down. In all three cell lines, this resulted in dramatic reduction of cellular proliferation, increased apoptosis, and decreased colony formation in 3D cultures. In addition, expression of several tumor suppressor genes, including FOXO3, were found increased upon TOX knock-down in comparative transcriptome analysis between TOX-suppressed cells and control CTCL cells. Pathway analysis of the differentially-expressed genes uncovered activation of apoptotic pathway upon TOX suppression. These findings were confirmed by quantitative PCR. Thus, our results indicate that ectopic expression of TOX confers growth advantage and apoptosis resistance to CTCL cells by suppressing the transcription of multiple tumor suppressors. Therefore abolishing TOX activity may be a promising treatment strategy for CTCL.

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