Poster Presentation

Session I

Poster 1

ANTIPHOSPHOLIPID ANTIBODY SYNDROME TRIGGERED BY LEVAMISOLE-TAINTED COCAINE: CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Antiphospholipid antibody syndrome is characterized by occlusive vasculopathy secondary to anticardiolipin or lupus anticoagulant antibodies. This disorder may be triggered by underlying infection, drugs, surgery, and genetic predisposition. Cocaine contaminated with levamisole may be a new cause of this phenomenon. Case report: A 52-year old female presented on three separate hospital admissions with retiform purpura of the extremities and with cutaneous necrosis of the nasal tip, ears and cheeks. Skin biopsy confirmed extensive thrombotic vasculopathy. Anticardiolipin antibodies and anti-neutrophil cytoplasm antibodies (ANCA) were detected. Reversible leukopenia was documented on all three hospital admissions. The patients' cutaneous lesions and neutropenia improved following therapy with pulse IV steroids, anticoagulation therapy, and drug abstinence. Literature review: Neutropenia following levamisole use has been described since the 1970s. Levamisole-induced skin necrosis has also been previously described. Levamisole is a widely used veterinary antihelmintic agent and human antineoplastic agent. Levamisole adulterated cocaine has been increasingly common in North America since 2005. A single report details 2 patients with retiform purpura following levamisole adulterated cocaine use. Our case highlights the unique clinical reversibility of this phenomenon upon drug abstinence. Conclusions: We strongly suspect exposure to levamisole as a potential trigger to an underlying genetic propensity for antiphospholipid antibody syndrome. The relative ubiquitous contamination of levamisole in North American cocaine as well as the reported clinical findings of retiform purpura and neutropenia should prompt physicians to consider adulterated cocaine use as causative of this relatively new phenomenon with potential serious complications.

Category: New clinical phenomenon important in Dermatology

Poster 3

A NOVEL DEFECT IN FIBRILLIN-1 DEPOSITION BY DERMAL FIBROBLASTS CLINICALLY PRESENTING AS ACQUIRED CUTIS LAXA IS REVERSIBLE WITH DEXAMETHASONE AND LOSARTAN TREATMENT

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Acquired cutis laxa is a rare condition of unknown etiology associated with monoclonal gammopathies and autoimmunity. We present a healthy 35 year-old female with an acute onset of elastolysis presenting as focal plaques of loose sagging skin in the context of a monoclonal gammopathy. A functional assessment and a detailed immunohistochemical analysis of lesional and non-lesional primary cultures of biopsy-derived dermal fibroblasts obtained from this patient was performed. Patient-derived fibroblasts deposited normal collagen fibers however elastic fiber deposition was poor. Lesional elastic fibers were structurally abnormal and lacked fibrillin-1, a major component of the microfibrillar scaffold. The normally secreted elastin was assembled on a fibulin-1 scaffold instead. The resulting structures resembled those in the skin of patients with Marfan syndrome (fibrillin-1 deficiency). Interestingly, patient fibroblasts maintained in the presence of autologous serum deposited excessive extracellular fibrillin-1 that aggregated with elastin and decorated thin elastic fibers. These aberrant structures resembled the distorted elastic fibers of Pseudoxanthoma Elasticum (PXE). Patient fibroblasts resumed deposition of normal microfibrils following treatments with dexamethasone and losartan, and the combination of these two drugs induced the most potent deposition of fibrillin-1 and restored production of normal elastic fibers. The observed microfibrillopathy was due to a secondary defect in the assembly of fibrillin-1 molecules onto the microfibrilar polymer rather than to a primary fibrillin-1 deficiency. These observations suggest defective elastic tissue deposition in addition to inflammatory destruction. The reversibility of impaired elastic fiber formation suggests a new therapeutic approach to the prevention and treatment of acquired elastolysis.

Category: Pilot/exploratory experiments

Poster 5

INTRALESIONAL CANDIDA ANTIGEN FOR COMMON WARTS IN PEOPLE WITH HIV
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Verrucae vulgares or common warts are caused by various subtypes of human papilloma virus. This epidermal infection is found in higher prevalence in immune-suppressed patients such as those with HIV infection. Acquired deficits in cell-mediated immunity from HIV contribute to their persistence. Spontaneous clearance may take years. Treatment is sought because of wart persistence, spread within the same individual and risk of transmission to others. At the HIV Dermatology Clinic of the BC Centre for Excellence in HIV/AIDS, warts refractory to standard patient- and physician-applied modalities were treated with intralesional Candida antigen. Clearance was achieved in 3 out of 7 patients while 4 out of 7 did not respond due to lack of effectiveness or inability to tolerate treatment. Adverse events included injection site redness, pruritus and pain. This is the first reported case series using Candida antigen for HPV warts in HIV+ individuals. The use of Candida antigen represents a simple and novel approach to the management of treatment-refractory warts. This case series provides a foundation for future larger, randomized trials.

Category: Pilot/exploratory experiments

Poster 7

CELLULITIS: MAKING THE DIAGNOSIS

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BACKGROUND: Cellulitis is an acute infection of the dermis and subcutaneous tissue, often presenting as a warm, tender, and swollen lower limb. Without specific diagnostic criteria, cellulitis is diagnosed clinically. The differential includes: lymphedema, stasis dermatitis, Well's Syndrome, deep venous thrombosis (DVT), erysipelas, acute gout, and necrotizing faciitis. Misdiagnosis may prolong symptoms and facilitate inappropriate antibiotic use.
METHOD: 1) Analysis of the current diagnostic pathway for 99 patients diagnosed with lower limb cellulitis at a major Vancouver teaching hospital Emergency Department (ED). 2) Observational study of the active diagnostic and treatment process of similarly-presenting patients at the same ED. **RESULTS:** 1) Presentation: 69%, 65%, and 57% of cases were positive for erythema, edematous, or warmth and pain, respectively. 14% included bilateral disease. 2) History: History of presenting illness (HPI) and past medical history (PMHx) were not recorded in the majority of cases. 3) Investigations: Wound cultures and white blood cell (WBC) counts were independently ordered in 1/3 of cases; with 52% positive and 88% normal results, respectively. Doppler ultrasound (DUS) was ordered for suspected DVT. 4) Observational study: Diagnostic observations usually included erythema, warmth, and pain. A validated treatment pathway (including antibiotic resistance considerations) was reliably utilized.
CONCLUSION: Cellulitis was diagnosed at the ED with inconsistent considerations of the clinical presentation, HPI, PMHx, and most investigational results. The differential was often limited to DVT, even with bilateral leg involvement. An established treatment pathway was consistently implemented. These results suggest a potential need for diagnostic ED guidelines for lower limb cellulitis.

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

Poster 9

APPLICATION OF SOLID ROUGH SKIN PHANTOMS FOR LASER SPECKLE DEVICE TESTING

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Background: Laser speckle pattern remitted from skin contains information on skin morphology. In order to fully utilize speckles for skin roughness measurement and skin lesion differentiation, we must model light interaction in skin and calibrate the laser speckle devices using phantoms.

Objectives: 1) To evaluate physical properties of our phantoms and compare them to those of normal human skin. 2) To test the workability of laser speckle devices for measuring phantom roughness using both linear and circular polarized light. **Methods:** 1) Silicone skin phantoms controlling light scattering and absorption were fabricated with standardized surface roughness values. 2) Surface roughness of these phantoms was measured using profilometry and their attenuation coefficients were theoretically calculated and compared to those known for normal skin. 3) Laser speckle data were collected for these phantoms using linear and circular polarization. Speckle contrast was calculated for each pattern and experimental curves of contrast vs. surface roughness were plotted. **Results:** 1) Phantom surface roughness and total attenuation coefficient were similar to those in normal skin. 2) The comparison between theoretical and experimental curves on contrast vs. roughness showed that the speckle device perfectly measured roughness for pigmented phantoms with strong absorption. For scattering phantoms with no absorption, we encountered a systematic error introduced by bulk scattering that should be addressed in future studies. **Clinical Significance & KT:** Phantoms simulating physical properties of skin allow us to model speckle formation for various skin conditions. Eventually, this knowledge will help us develop a non-invasive device for skin disease diagnosis.

Poster 11

QUANTIFICATION IN CLINICAL DERMATOLOGY
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Accurate estimation of size, number, and surface area is critical in dermatology. Dermatologists must accurately estimate these parameters to facilitate diagnosis, prognostication, and monitoring of response to treatment; for example, body surface area is a key factor in diagnosing erythroderma and toxic epidermal necrolysis. Previous studies on estimation of body surface area have found a trend toward overestimation of body surface area. There were no published studies on accuracy in estimation of size and number. In the clinical setting, we have found that observers tend to overestimate percentage surface area and underestimate size and number. In order to evaluate this, 10 resident participants viewed a series of forty slides for ten seconds each. The participants were asked to estimate surface area, size, or number in each of the slides. Participants significantly underestimated size for small objects such as coins (p<.01). There was a trend towards underestimation of size with large objects such as a journal; however, this was not statistically significant. Surface area was significantly overestimated by participants (p<.01). Participants were most accurate at estimating number, with no significant bias toward underestimation or overestimation. Given this tendency toward bias in estimation of size and surface area, clinicians who are aware of this may compensate with techniques to aid in more accurate estimation. It may also be beneficial for training in estimation techniques to be included in Dermatology training programs.

Poster 13

GENERALIZING COMMON SKIN IMAGING ANALYSIS TASKS USING PROBABILISTIC MODELS

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Background: Many tasks in skin imaging can be generalized into a single formulation: "for each pixel in the image, assign a label from a set of mutually exclusive labels". This generalization encompasses such tasks as detecting occluding artifacts, segmenting lesions and identifying dermoscopic structures. **Purpose:** To explore mathematical models capable of performing this generalized task, and to explore ways to automatically infer model parameters given a set of image/label example pairs so that the system can quickly "learn" new tasks. **Methods:** The first model is based on maximum a-posteriori (MAP) estimation. It uses linear discriminant analysis to automatically determine model parameters. We call this the MAP model. The second model is based on conditional random fields (CRFs), and uses maximum likelihood estimation and regularized gradient descent to determine model parameters. We call this the CRF model. **Results:** We have taught the MAP model how to detect occluding hair, with performance comparable to more specialized algorithms. We aslo taught the framework how to segment skin lesions. The performance was compared to 5 other previously published methods. Our framework performed comparably to four and outperformed the fifth. We then apply the CRF model to the same tasks and achieve slightly better accuracies; however the training time (time needed to infer model parameters) increases from minutes to hours. **Conclusions:** Probabilistic models, with automatic and empiric ways to determine model parameters is a promising way to automatically learn and perform a variety of tasks in skin imaging.

Category: Early experiments with well defined objectives.

Poster 15

THE VALUE OF INTERNATIONAL ELECTIVES FOR DERMATOLOGY RESIDENTS: AN ANALYSIS OF CASES SEEN DURING OVERSEAS ELECTIVES

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BACKGROUND: Overseas volunteerism is becoming increasingly popular in Dermatology. However there is limited information in the literature regarding the preparedness of North American dermatologists to work in resource-limited settings in developing countries. One way to increase competency in this setting is by completing international electives during residency.

This study serves to tabulate and analyze cases seen during a four-week elective in Delhi, India and a six-week elective in Gabarone, Botswana. METHOD: Cases encountered during a four-week elective at the All India Institute of Medical Sciences in Delhi, India and during a six-week elective at the Princess Marina Hospital in Gabarone, Botswana were documented, tabulated and analyzed. RESULTS: Of 443 patient encounters during a 4 week elective in India, the most common dermatoses were eczema, psoriasis and acne. Regional specific dermatoses seen included leprosy, cutaneous TB and phyrnoderma. Of 498 patient encounters during a 6 week elective in Africa, the most common diagnoses included eczema, acne and superficial fungal infections. Regional dermatoses seen included oculocutaneous albinism, measles and acne keloidalis nuchae. CONCLUSION: The majority of cases seen were common skin conditions. However even in the treatment of common dermatoses, the day-to-day practice of dermatology varies significantly across continents due to differences in populations served, co-morbidities, environmental exposures and medical resources. Additionally, overseas electives allow exposure to regionally specific dermatoses that are uncommon presentations in North American training settings. International electives undertaken during Dermatology residency are therefore both educationally enriching and valuable preparation for overseas volunteerism.

Category: Early experiments with well defined objectives/hypotheses

Poster 17

INTEGRIN BETA6-DEFICIENT MICE SHOW ENHANCED KERATINOCYTE PROLIFERATION AND RETARDED HAIR FOLLICLE REGRESSION

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Integrin $\alpha v \beta 6$ is an epithelial-specific receptor that binds and activates latent transforming growth factor-$\beta 1$ (TGF-$\beta 1$). TGF-$\beta 1$ has been implicated as an endogenous inducer of hair follicle regression during hair cycling. We hypothesized that $\alpha v \beta 6$ integrin-mediated TGF-$\beta 1$ signaling regulates hair regeneration and hair follicle involution. In wild-type (WT) mice, the expression of integrin $\alpha v \beta 6$ was strongly upregulated in the outer root sheath (ORS) during early hair regeneration and was specifically enhanced in the hair follicle bulge region. Expression gradually decreased in late anagen and remained restricted to the bulge region in the catagen and telogen stage hair follicles. $\beta 6$ integrin knock-out ($\beta 6-/-$) mice presented with accelerated hair regeneration and retardation of hair follicle regression compared to WT controls. Hair follicles from $\beta 6-/-$ mice contained significantly higher numbers of proliferating Ki67-positive keratinocytes than WT follicles at an identical cycle stage. The $\beta 6-/-$ follicles also demonstrated significantly reduced levels of TGF-$\beta 1$ expression and Smad2 phosphorylation during early anagen and anagen-catagen transition. Our study indicates that $\alpha v \beta 6$ integrin plays an important inhibitory role in keratinocyte proliferation in both hair follicles and interfollicular epidermis. Thus, downregulated TGF-$\beta 1$ signaling in $\beta 6-/-$ mice may impact bulge niche stem cell behavior, which suggests a possible manipulation target in the functions of epidermal stem cells. Suppressing $\alpha v \beta 6$ integrin expression may provide useful therapeutic tools for human hair growth disorders.

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

Poster 19

14-3-3 EXPRESSION PROFILE IN HUMAN KERATINOCYTES IS ALTERED BY DERMAL FIBROBLASTS

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Epidermal-mesenchymal communication plays an integral role in epithelialization and wound healing. In healthy skin, enzymes such as matrix metalloproteinases (MMPs) help maintain structural integrity by balancing extracellular matrix (ECM) synthesis and degradation. Previously, keratinocyte-derived factors such as 14-3-3 σ were shown to modulate MMP-1 expression in fibroblasts. However, the capacity of fibroblasts to influence 14-3-3 expression in keratinocytes is largely unknown. We hypothesize that in a double-paracrine fashion, fibroblast-derived factors possess the capacity to influence the 14-3-3 expression profile in keratinocytes. Co-culture systems consisted of keratinocytes seeded on 6-well plates with dermal fibroblasts seeded on inserts. Cell-lysates and conditioned media samples were collected and analyzed by western blot; total mRNA was extracted and evaluated by qPCR. Cells were cultured in the presence of several MAPK inhibitors to elucidate the mechanism responsible for 14-3-3 σ induction in keratinocytes stimulated with fibroblast-conditioned medium. A significant increase in the intracellular levels of 14-3-3 γ and σ proteins in keratinocytes was observed when co-cultured with fibroblasts, along with a significant upregulation of all four 14-3-3 isoforms (β, η, γ, σ) at the gene level. Co-cultured keratinocytes release significantly higher levels of 14-3-3 σ than keratinocytes cultured alone. Addition of MAPK inhibitors resulted in significant inhibition of 14-3-3 σ induction in co-cultured keratinocytes. This study suggests that dermal fibroblasts may influence 14-3-3 expression in human keratinocytes. These findings have strong implications for mitigating fibrosis in resistant or non-healing wounds such as burns and ulcers as well as further progressing our understanding of the complex and dynamic wound remodeling process.

Category: "Early experiments with well defined objectives/hypotheses."

Poster 21

TRANSCRIPTION FACTOR RBP-J-MEDIATED SIGNALING REGULATES EPIDERMIS/HAIR FATE, WHICH IS ESSENTIAL FOR SUPPRESSING BASAL CELL CARCINOMA FORMATION AND INDUCING HAIR FOLLICLE FORMATION

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Hair follicles (HF) and basal cell carcinomas (BCCs) can be regarded as ordered and disordered skin appendages respectively. They may utilize similar molecular mechanisms of growth. We

examined the similarities and differences in gene expression by microarrays between nodular BCCs and HFs including the bulge region which has been identified as a potential primary source of BCCs. Microarray data was validated using quantitative PCR, immunohistochemistry and in vitro studies. Two differentially expressed gene sets were identified by significance analysis of microarray (SAM) in BCC and HF versus skin epithelium respectively. Subsequently, multiple signaling pathway analyses were conducted. The results indicated that Notch and Hedgehog signaling pathways were active in the growth of both HF and BCCs. However, Notch signaling, including tumor suppressor genes *NOTCH1*, *NOTCH2*, ligands *JAG1*, *JAG2*, signaling inhibitor *NUMB*, and downstream Notch pathway genes *DTX1*, *DTX2*, RBP-J, *LFNG*, *HR,* and *HES7*, all showed significant differential expression in BCCs compared to HF. The data suggests downstream gene expression in the Notch signaling pathway is suppressed in BCCs. We tested the effect of transcription factor RBP-J and found transcription factor RBP-J-mediated signaling regulates suppress basal cell carcinoma cell growth and induce cell apoptosis *in vitro*. Our data suggest that RBP-J serves as a tumor suppressor in BCC and RBP-J deficient in BCC had lost tumor repression activity. Modulation of the Notch pathway may be a focus for the development of BCC treatments.

Early experiments with well defined objectives/hypotheses

Poster 23

ASSESSSING THE ROLE OF SOX4 IN SKIN PHOTOAGING
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UV-induced collagen degradation and keratinocyte hyper-proliferation are the main causes of skin photoaging. NF-κB is activated by UV-irradiation, enhancing the expression of matrix metaloproteinase-1 (MMP-1). Moreover, fibroblast growth factor beta (bFGF) is induced in skin by UV, leading to keratinocyte proliferation. We recently reported that trancription factor Sox4 suppresses NF-κB-p50 expression in melanoma cells. We hypothesize that Sox4 inhibits photoaging by suppression of bFGF and NF-kB. In aim 1, we will determine if Sox4 inhibits proliferation of keratinocytes after UV irradiation. HaCaT keratinocytes will be transfected with control vector or Sox4 plasmid and irradiated with various doses of UVA and UVB. Cell proliferation will be studied by sulforhodamine B assay, flow cytometry and analysis of the expression of cyclins. In aim 2, we will investigate if Sox4 inhibits UV-induced expression of bFGF. HaCaT cells and fibroblasts will be transfected with Sox4 and irradiated with UV. Then expression of bFGF will be determined by RT-PCR and ELISA. We will use EMSA or ChIP assay to investigate if Sox4 binds to bFGF promoter region to suppress the expression of bFGF. In aim 3, we will determine if Sox4 inhibits the expression of NF-kB and its downstream target genes involved in photoaging. HaCaT and fibroblasts will be transfected with Sox4 and irradiated with UV. Expression of NF-κB, IL-1, TNFα and MMP-1 after UV will be examined by RT-PCR, Western blot, and ELISA. This project aims to explore molecular mechanisms of skin photoaging which may lead to better strategies for prevention and treatments.
Category: Pilot/exploratory experiments

Poster 25

COOPERATION OF ING PROTEINS AND *SWI/SNF* CHROMATIN REMODELING COMPLEX IN REPAIR OF UV-DAMAGED DNA

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UV radiation (UVR), the major environmental risk factor for the development of skin cancers including melanoma, induces DNA lesions which are repaired by the NER pathway. Therefore, it is important to understand how NER is regulated. The remodeler SWI/SNF including hSNF5 subunit has been shown to enhance repair of a mononucleosome reconstituted with an acetylaminofluorene-guanosine (AAF-G) lesions in the core. Also, this complex enhances the repair of photolesions in nucleosomes as measured by lesion specific phage T4 endonuclease, and enhances accessibility to repair factors *in vivo*. Recently, it has been shown that its core subunits SNF5 and SNF6 interact with the NER lesion detection complex Rad4-Rad23 *in vivo*, suggesting that ATP-dependent chromatin remodeling factors are recruited to the damage sites to facilitate NER. We have previously demonstrated that ING proteins (ING1b and ING2) play a key role in repair events of ultraviolet damaged DNA and significantly enhance NER. Recently, we also found that they enhance histone H4 acetylation, chromatin relaxation and recruitment of XPA to damaged sites after UVR, indicating that ING proteins may facilitate NER by chromatin remodeling. We demonstrated that ING1b cooperates with ATP-dependent chromatin remodeling SWI/SNF complex in chromatin relaxation after UV. In this study, we will investigate the novel role of ING proteins as chromatin remodeling regulators in NER.

Early experiments with well defined objectives/hypotheses

Poster 27

SELF-REPORTED SKIN HEALTH IN HIV INFECTED PATIENTS

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Background: In persons living with HIV, skin infections are highly prevalent and are often the earliest clinical signs observed. Appropriate management of skin conditions in HIV patients requires an understanding of factors influencing patient outcomes. The current research explores associations of self-reported skin health in the HIV population. **Methods:** A prospective cohort of HIV-infected patients referred to dermatology specialists was invited to complete a questionnaire assessing quality of life, treatment adherence self-efficacy, and functional social support. It also included an item for self-reported skin health, which was correlated to physician-rated skin severity and laboratory CD4 count. Each psychosocial variable was compared across groups of self-reported skin health to determine associated factors. **Results:** 37 of 40 (92.5%) surveys distributed to HIV-infected patients were returned. No relationship was observed between patient-reported skin health and physician-rated skin severity (r=0.108, p=0.548). Similarly, no correlation existed between patient-reported skin

health and laboratory CD4 count (r=-0.027, p=0.878). However, aggregate scores for quality of life and adherence self-efficacy differed between groups of self-reported skin status (p=0.006 and p=0.004 respectively). Qualitative responses emphasized that patients conceal health information from close friends/family and skin problems exacerbate existing health concerns. **Conclusions:** Patient-reported skin health was notassociated with objective clinical data as in other populations, but instead, with treatment adherence and quality of life. Assessing how patients feel about their own skin health might help address barriers to treatment and improve overall health outcomes. HIV dermatologists have a privileged opportunity to offer additional interventions and resources for patient well-being.

Category: Pilot experiments

Poster 29

CONNEXIN-43 REGULATES KEY GENES INVOLVED IN SCAR FORMATION

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Objectives: Excessive scar formation is an unwanted outcome of wound healing. In scars, fibroblasts are responsible for deposition of the collagen-rich extracellular matrix, the hallmark of scars. During wound healing, fibroblasts communicate via cell-cell adhesions mediated by gap junctions (GJ). Connexin-43 (Cx43) is the most abundant GJ protein expressed by fibroblasts. Interestingly, blocking of its function accelerates wound granulation tissue formation *in vivo*, but little is known about the role of Cx43 in scar formation. We hypothesized that Cx43 regulates expression of key genes involved in tissue repair. **Methods:** To find out gene expression changes that associate with GJ-mediated cell-cell communication, fibroblasts were cultured in high and low densities, and expression of Cx43 and key anti-fibrotic and pro-fibrotic genes were analyzed using real-time PCR, Western blotting, and immunostaining. To find out whether blocking of Cx43 affects fibroblast phenotype, high-density cultures were treated with a peptide that specifically blocks Cx43 function (GAP27), and gene expression was analyzed as above. **Results:** In high-density cultures there was an increase in the proportion of Cx43 molecules that were phosphorylated compared to low-density cultures. This was associated with alterred gene expression of key wound healing molecules by fibroblasts. Blocking of Cx43 in the high-density cultures resulted in upregulation of anti-fibrotic and downregulation of pro-fibrotic genes. **Conclusion:** Cell-cell communication mediated by Cx43 regulates key genes involved in wound healing and scar formation in fibroblasts. Blocking of Cx43 promotes expression of genes that may promote scarless wound healing in skin.

Category: Early experiments with well defined objectives/hypotheses

Poster 31

HYPERFERRITINEMIA - A POTENTIALLY USEFUL MARKER IN A NUMBER OF CRITICAL DERMATOLOGICAL CONDITIONS ASSOCIATED WITH MACROPHAGE ACTIVATION SYNDROME

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Introduction and objective: Macrophage activation syndrome (MAS) is a severe, potentially like-threatening condition caused by excessive activation and proliferation of well-differentiated macrophages. Sustained macrophage activation results in tissue infiltration and the production of high levels of TNF-a, IL-1 and IL-6 which play a major role in tissue damage leading to multiorgan dysfunction. Here we describe a series of cases of cutaneous disorders associated with MAS. These include panniculitis-like T-cell lymphoma, adult-onset Still's disease (AOSD) and Kikuchi-Fujimoto syndrome. Clinical features and cutaneous manifestations of each of these conditions are reviewed. Hyperferritinemia is an important laboratory hallmark of MAS that has received little attention to date. We propose that ferritin levels can serve as a reliable marker of disease onset and progression. **Methods and results:** in this retrospective case series we followed several patients with three distinct cutaneous diseases: panniculitis-like T-cell lymphoma, AOST and Kikuchi-Fujimoto syndrome. We correlated the disease activity at diagnosis and throughout the course of treatment with serum ferritin levels and found that ferritin was dramatically elevated, often to over 10,000 ng/ml (normal 10-150 ng/ml) during the disease flare. Furthermore, a good correlation between the ferritin level and response to therapy was found, with a rapid decrease in ferritin associated with a favorable course of MAS. **Conclusions:** Hyperferritinemia may serve as a sensitive and specific laboratory marker of a number of dermatoses associated with MAS and may be a useful indicator of disease activity, response to therapy and prognosis.

Category: this is a review of several clinical cases.

Session II

Poster 2
QUANTITATIVE EVALUTION OF PIGMENTED SKIN LESIONS USING NEAR-INFRARED FLUORESCENCE IMAGING

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Objective: Recent studies show that melanin exhibits stronger autofluorescence than other tissue components under near-infrared (NIR) excitation. Our objectives are: (i) to quantitatively evaluate NIR fluorescence intensities for a variety of common pigmented skin lesions; and (ii) to assess the relationship between NIR fluorescence intensity and melanin content. **Method:** NIR fluorescence images were captured using our prototype NIR fluorescence imaging device. Diffuse reflectance spectra were collected to quantify visual luminosity and estimate relative

melanin content. Non-parametric analyses were used to compare relative fluorescence between lesion types. Linear regression models were used to correlate NIR fluorescence with relative melanin content and luminosity. **Results:** Of 144 pigmented skin lesions imaged, 126 sets of images (87.5%) were included in our analyses. Mean relative fluorescence ratios were significantly different amongst pigmented lesions (p<0.001). Mean relative fluorescence was lower in vitiligo (mean [SD] = 0.81 [0.64]), and vascular lesions (0.83 [0.22]), and higher in malignant melanomas (1.18 [0.24]) and seborrheic keratoses (1.69 [0.48]). Regression analysis identified a linear relationship between NIR fluorescence and melanin content (r = 0.441, p = 0.013) whereas no significant relationship was observed with luminosity. **Conclusion:** We confirm that NIR fluorescence intensities vary among lesion types. NIR fluorescence is directly related to melanin content instead of luminosity. Our results provide insight for an objective and direct *in vivo* method of imaging and discriminating melanin from other components of pigmentation in the skin. NIR fluorescence imaging offers a non-invasive approach for enhanced clinical evaluation for patients with pigmented skin lesions.

Category: Pilot/exploratory experiments

Poster 4

EXPRESSION OF MIRNA PROCESSING FACTOR DICER IN CUTANEOUS MELANOMA AND ITS ROLE IN CELL INVASION

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Deregulated expression of miRNAs and their processing factors is a hallmark of cancer. Although altered expression of several miRNAs has been reported in melanoma, the expression profile of miRNA processing factors such as Dicer in this cancer is unknown. In this study we examined the expression of Dicer protein in different stages of melanocytic lesions. Using tissue microarray and immunohistochemistry, we evaluated cytoplasmic Dicer expression in 30 normal nevi, 87 dysplastic nevi, 262 primary melanomas, and 135 metastatic melanomas. Our data revealed that expression of Dicer has a significant but inverse correlation with progression of melanoma (*P*<0.001). Accordingly, the number of samples with moderate-strong staining for Dicer was reduced from 76.6% in normal nevi to 60.9% in dysplastic nevi, 63.3% in primary melanoma and 48.8% in metastatic melanoma. The expression of Dicer was also negatively correlated with the American Joint Committee on Cancer (AJCC) staging of the melanoma biopsies (*P*<0.001). The reduced Dicer expression was correlated with a poorer overall and disease-specific 5-year survival of melanoma patients (*P*=0.006 and *P*=0.007 respectively). Furthermore, Dicer expression was an independent prognostic factor to predict patient outcome (multivariate Cox regression *P*=0.005). We also knocked down Dicer expression in MMRU melanoma cells and found that it enhances the invasion ability of MMRU cells by 2-fold in Boyden chamber matrigel invasion assay. Our results demonstrate the critical role of miRNA machinery in the progression of melanoma, suggesting that Dicer may be a suitable prognostic marker for human melanoma patients as well as a potential therapeutic target.
Category: Early experiments with well-defined objectives/hypotheses

Poster 6

ROLE OF RED BLOOD CELLS IN WOUND HEALING

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Wound healing is a complex & intricate process that involves the coordinated efforts of an enormous number of unique tissues & cell lineages. During the inflammatory phase of wound healing, a blood clot that functions as a temporary extracellular matrix (ECM) for cell migration & proliferation is established. The role(s) of red blood cells (RBC) which are one of the most predominate cell types during inflammation & the formation of the primary blood clot remain unclear- RBCs are known as inert bystanders in wound healing. Our aim was to determine the effects of RBC intracellular proteins on the expression of ECM components in dermal-fibroblasts (DF) & to identify the elements involved in the underlying signaling pathway. The intracellular protein levels (IPL) of matrix metalloproteinases (MMP)-1, 2, 3, & type-1 collagen in DG treated with RBC lysate for 24 hours, were analyzed through western blotting (WB). Similarly, the effect of inhibitors for three MAPK pathways on RBC induced MMP-1 expression by DF was tested. RBC lysate significantly augmented and reduced the IPL of all three MMPs and type-I collagen, respectively. Moreover, it was found that only PD98059, a specific inhibitor of ERK1/2 activity, inhibited the activation of DF MMP-1 IPL by RBC. Additionally, RBC treatment resulted in increased ERK1/2 phosphorylation in DF. These findings demonstrate that RBCs contain some anti-fibrogenic factors that potentially affect ECM remodeling, through ERK1/2 pathway and could pave the way for designing novel treatments for fibrotic disorders such as pulmonary fibrosis & hypertrophic scars in wound healing.

Category: Early experiments with well defined objectives/hypotheses

Poster 8

HAIR FOLLICLE IMMUNE PRIVILEGE AND THE POTENTIAL ROLE OF SOMATOSTATIN

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Immune privilege (IP) is a phenomenon in which tissues are not attacked by the recipient's immune system after incompatible transplantation. It is observed in the cornea, brain, and placenta. Decreased MHC Class I, impairment of antigen presenting cells, and increased expression of immunosuppressants may explain the protection. A few experiments in the last 40 years have led to the belief that IP is present in the anagen hair follicle (HF). However, there have been few quantitative or functional studies. Our hypothesis is that cells in the HF bulb strongly exhibit IP. Our lab examined IP-related mRNA expression in human HFs by quantitative RT-PCR. Microdissection was conducted on five HF samples, separating bulb and sheath regions, and ten control epidermal samples. Briefly, out of 44 genes, we found several HLA Class I and Class II genes strongly downregulated in the HF. Non-classical HLA-G was

significantly upregulated in sheath (7.64-fold) and bulb (5.57-fold). Immunosuppressive secretory factors were significantly upregulated such as CCL2 in sheath (2.8-fold) and somatostatin (SST) in sheath (5.88) and bulb (94.23). SST is an anti-inflammatory neuropeptide secreted in the pancreas, intestine, and eye aqueous humour. In immunohistochemistry, SST was strongly expressed in HF sheath layers compared to epidermis. By ELISA, preliminary results show a trend of greater SST detected in sheath cell culture than epidermal and bulb, but need to be confirmed by additional testing. Clinical Significance: Discovering a functional mechanism for IP in HFs may have implications for inflammatory hair loss diseases and even in tissue transplantation.

Category: Early experiments with well defined objectives/hypotheses.

Poster 10

RELATIONSHIP BETWEEN VITILIGO LESIONAL TRANSCRIPTOME SIGNATURES AND THERAPEUTIC RESPONSE TO COMBINED NARROW BAND PHOTOTHERAPY AND TOPICAL TACROLIMUS THERAPY

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Objectives: Vitiligo is the most common depigmentation disease affecting humans. The narrow band ultraviolet light therapy and topical tacrolimus therapy being widely accepted therapies. This study was to examine the relationship between vitiligo lesional molecular signatures and clinical phenotypes after the ultraviolet B and topical tacrolimus therapy. **Materials and Methods:** Seventeen subjects with non-segmental vitiligo were recruited with informed consent to donate skin biopsies for transcriptome analyses. These subjects underwent treatment, that consistent of twice-trice weekly narrow band UVB phototherapy and twice daily topical 1% tacrolimus cream. The skin biopsies with more than 30% repigmentation by 6 months were compared with those that showed less than 10% repigmentation in terms of lesional disease onset, as well as lesional gene expression signatures. Statistical analysis were performed using t-test using SPSS, with significance set at $p<0.05$. **Results:** Of the 17 patients, 11 had more than 30% repigmentation at 6 months after the combination therapy, whereas the 6 had less than 10% repigmentation. Most of the patients with good response also had short onset of the lesional skin at the time of biopsies. Further, although statistically non-significant, the molecular signatures of good therapeutic response and recent lesional onset were highly similar, both consisting of higher residual melanocyte markers (> 2 to 3 fold higher) and increased presence of inflammatory markers such as NK cell signatures, including KLRK1. **Conclusion:**. This study suggests there is a need to start vitiligo therapy at the earliest opportunity when there are still residual melanocytes left.

Category: Early experiments with well defined objectives/hypotheses

Poster 12

REDUCED TIP60 EXPRESSION AS A PREDICTIVE BIOMARKER FOR ADVANCED MELANOMA AND PATIENT OUTCOME

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Purpose: The tumor suppressor Tip60 plays a major role in transcription, DNA damage response, apoptosis and cancer development. We investigated the role of Tip60 in melanoma pathogenesis and assessed the prognostic value of Tip60 expression on melanoma patient survival. **Experimental Design:** Two sets of tissue microarrays were constructed consisting of 448 cases of melanomas (201 for the training set and 247 for the validation set) and 105 cases of nevi. The TMA was assessed for Tip60 expression by immunohistochemistry. The Kaplan-Meier method was used to evaluate the patient survival, and univariate and multivariate Cox regression models were performed to estimate the harzard ratios (HR) at five-year follow-up. **Results:** Tip60 expression was significantly reduced in metastatic melanoma compared to normal nevi ($P = 0.045$), dysplastic nevi ($P = 0.047$) and primary melanoma ($P = 0.001$). Tip60 expression correlated with AJCC stages (I-II vs III-IV, $P = 0.001$) and tumor thickness (≤ 4.00 vs. >4.00 mm, $P = 0.037$). Reduced Tip60 expression was associated with a poor five-year disease-specific survival in primary melanoma ($P = 0.016$) and metastatic melanoma patients ($P = 0.027$). Furthermore, Cox regression analyses indicated that Tip60 expression was an independent prognostic marker for primary ($P = 0.002$) and metastatic melanomas ($P = 0.035$). **Conclusions:** Reduced Tip60 expression is significantly associated with thick primary melanoma and metastatic melanoma, as well as poor patient prognosis. **Clinical implication:** This study suggests that Tip60 may serve as a potential biomarker for advanced melanoma and patient outcome.

Category of this study: Pilot/exploratory experiments

Poster 14

ASYMMETRIC DEPTH OF BoNT-A INJECTION IN THE GLABELLA

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Introduction: Botulinum toxin type A (BoNT-A) can be used to achieve a modest brow lift. The theorized mechanism is that it results from inactivation of the brow depressors[1]. Expert consensus is that increased injection depth delivers more BTX-A to the depressors and causes increased lift. Conversely, shallow injections have greater effect on the superficial, brow elevating, frontalis. This technique is applied to the correction of brow height asymmetry but no studies exist demonstrating the theory. Methods: A retrospective analysis was performed on photographs of 23 women in this single centre trial. Subjects were included if they had

investigator identified eyebrow height asymmetry. At baseline, subjects received4 units BoNT-Ain5 glabellar injection sites. Deep injections into the medial corrugator were performed on the side where increased brow lift was desired and shallow injections on the opposite side. Photographs were performed at baseline and week 4 for comparison measurements at the midpupillary line, outer edge, and canthus. Results: There was no significant difference at 4 weeks in the change in brow height between the sides that received deep vs. shallow BoNT-A injection. Conclusion: It has been hypothesized that lateral brow lift following glabellar injection of BoNT-A is actually caused by an inactivation of the inferomedialfrontalis and a compensatory increase in the resting tone of the remainder of the frontalis muscle[3]. This may partially explain why a superficial injection can also lead to brow lift. The lack of significant difference may be due to the easy diffusion of the drug between muscle layers.

References
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Category: Early experiments with well defined objectives/hypotheses

Poster 16

REDUCED EXPRESSION OF THE TUMOR SUPPRESSOR FBW7 IN HUMAN MELANOMA
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FBW7 (F-box and WD repeat domain-containing 7) is a member of the F-box family of proteins, which function as interchangeable substrate recognition components of the SCF ubiquitin ligases. FBW7 binds to key regulators of cell division and growth, including cyclin E, MYC, JUN and Notch. Most FBW7 substrates are proto-oncogenes that are broadly implicated in the pathogenesis of human cancers. FBW7 is widely considered as a tumor suppressor, and it has been reported that loss of FBW7 function leads to chromosomal instability, probably owing to hyperactivation of its oncogenic substrates. To investigate the role of FBW7 in human melanoma, we used tissue microarray technology and immunohistochemistry to examine the expression of FBW7 in melanocytic lesions at different stages. The results showed that FBW7 expression is significantly reduced in primary melanoma and metastatic melanoma, compared with normal and dysplastic nevi (p<0.05). We also found significant lower expression in advanced primary melanoma (AJCC stage III-IV) than melanoma at AJCC stage 1-II (p=0.027). Furthermore, we showed a strong correlation between negative FBW7 expression and a worse 5-year survival in melanoma patients (p=0.031). Moreover, we found the significant reduction

(60%) of mRNA level of FBW7 in several melanoma cell lines compared with normal melanocytes. Our in vitro studies showed that overexpression of Fbw7 in MMRU melanoma cell line do not affect the cell proliferation. Interestingly, we found Fbw7-γ promoted MMRU cell migration in wound healing assay. Overall, our data indicate that Fbw7 is a potential therapeutic target for melanoma treatment.

Early experiments with well defined objectives/hypotheses

Poster 18

EFFECT OF LOSS OF *NF1* ON PIGMENTATION

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Loss of neurofibromin is pleiotropic, affecting a number of cell types. We have found that an ENU-induced point mutation ($Nf1^{Dsk9}$) or a targeted knockout of one *Nf1* allele specifically and uniformly darkens the mouse dermis by increasing the number of melanocytes. To observe the effect of loss of *Nf1* on pigmentation, we made a melanocyte specific homozygous knockout of *Nf1* on a C57BL/6J mouse background. We also observed that the $Nf1^{Dsk9/Dsk9}$ mutants show a unique population of glial-melanocyte bipotential cells at E11.5. A melanocyte-specific knockout of *Nf1*showed a significant hyper pigmentation of the tail dermis in the *Mitf-Cre/+;Nf1^{flox/flox}* homozygotes compared to $Nf1^{Dsk9/+}$ mice, with no change in epidermal pigmentation. This suggests a cell autonomous mechanism of dermal hyper pigmentation in the homozygote caused by the loss of *Nf1* in melanocytes. In contrast to the $Nf1^{Dsk9/+}$, the *Mitf-Cre/+;Nf1^{flox/+}* mice did not show dermal hyper pigmentation. This indicates either that the loss of *Nf1* in melanocytes acts in a non-cell autonomous mechanism in the heterozygote, or that the knockout is required in an earlier precursor of melanocytes. In $Nf1^{Dsk9/Dsk9}$ embryos, 50% of the cells expressing *Dct* showed colocalization with *Blbp*. This suggests that $Nf1^{-/-}$ mutants show presence of a unique population of bipotential glial-melanocyte cells. Neurofibromatosis type I patients manifest Café-au-lait macules (CALMs), uniform hyper pigmentation, disfiguring neurofibromas (often pigmented). Our study will help us discover the mechanisms by which Nf1 regulates melanocytes using an in vivo model. We hope to better understand the role of *Nf1* during glial and melanocyte development.

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

Poster 20

HIRSUTISM CLINICAL PRESENTATION, PATHOGENESIS, AND TREATMENT APPROACHES

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Hirsutism is a disorder of excessive growth of terminal hairs in androgen-dependent areas in women. Hirsutism is a common condition affecting about 5%-10% of women of childbearing age. More than 70% of hirsutism is caused by polycystic ovary syndrome (PCOS). Other causes include idiopathic hirsutism, nonclassic adrenal hyperplasia, ovarian or adrenal androgen secreting tumors, Cushing's syndrome, acromegaly, hyperprolactinemia, and drugs. History and examination are important. Laboratory investigation is essential in women with moderate to severe, sudden onset or rapidly progressing hirsutism. Identification of the underlying etiology does not alter management, but detects patients at risk for infertility, endometrial carcinoma and cardiovascular diseases. Treatment of hirsutism should be long term and should include cosmetic as well as pharmacological interventions such as oral contraceptives and antiandrogens. Treatment must consider not only amelioration of hirsutism but also treatment of the underlying etiology and of any metabolic associations**.**

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

Poster 22

GRANULOMATOUS CICATRICIAL ALOPECIAS

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Granulomatous cicatricial alopecias (GCA) are a group of diseases in which hair loss appears after the pilosebaceous follicle is destroyed by a granulomatous infiltrate. GCA can be classified into non- infectious granuloma disorders, which include sarcoidosis, necrobiosis lipodica and granuloma annulare, and infectious disorders including tuberculosis and leprosy. Lesions of cutaneous sarcoidosis of the scalp may resemble discoid lupus erythematosus. There are less than 35 cases with scalp involvement in English-language literature. Subcutaneous granuloma annulare present with skin-colored nodules mainly affects children in the first decade. Its typical sites are on pretibial surfaces and feet, buttocks, and scalp. The non scalp lesions are usually mobile because they are attached to underlying fascia while on the scalp they are attached to underlying periosteum and usually not mobile. Necrobiosis lipoidica (NL) of the scalp is very rare, and a review of the literature revealed 42 cases. The scalp lesions may be more annular or serpiginous in configuration and are less atrophic compared with classic NL on shin. Leprosy of the scalp is very rare because hairy scalp has higher skin temperature than other parts of body, and a review of the literature revealed only 10 cases. There are two cases of lupus vulgaris and one case of papulonecrotic tuberculid with scalp lesion reports in literature.

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

Poster 24

TRANSCRIPTOME ANALYSES REVEAL HEIGHTENED NATURAL KILLER CELL ACTIVITY IN THE LESIONAL AND PERI-LESIONAL SKIN OF GENERALIZED VITILIGO

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Objectives: Vitiligo is the most common depigmentation disease affecting humans, and is characterized by the death of melanocytes. The pathogenesis of vitiligo is currently unclear. The objectives of the current study are to characterize the molecular signatures of lesional and non-lesional skin of vitiligo patients in comparison with skin from normal individuals. **Materials and Methods:** Seventeen subjects with non-segmental vitiligo and 18 normal individuals participated in the study. Full-thickness biopsies were obtained from the skin of vitiligo patients and normal individuals. Transcriptome analyses were performed on the mRNA prepared from these skin biopsies using Agilent whole genome array containing 41 thousand gene probes. In addition, skin biopsies were used for explant culture of natural killer cells, which are analyzed by flow cytometry and confirmed by immunofluorescence. **Results:** Twenty seven genes were decreased by at least two folds in the lesional skin of vitiligo, most of these encode for melanocyte markers. Of the 13 genes that were strongly up-regulated in lesional skin compared with both normal and peri-lesional skin, 4 of these are in the killer cell lectin-like receptor (KLR) family. Explant cultures of skin biopsies showed dramatically increased NK cells in lesional and non-lesional skin from vitiligo patients in comparison with normal skin, a finding confirmed with immunofluorescence microscopy. **Conclusion:** This is the largest-to-date transcriptome analyses of vitiligo-affected skin. The results uncovered strong evidence for the presence of natural killer cells in vitiligo skin and highlighted the potential role they might play in the destruction of melanocytes.

Category: Basic Science Research

Poster 26

POAMS: POST OPERATIVE ANXIETY IN MOHS SURGERY. EFFECT OF ANXIETY ON PATIENT SATISFACTION WITH THE POST-OPERATIVE OUTCOMES OF MOHS MICROGRAPHIC SURGERY.

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Pre-operatively, patients undergoing Mohs Micrographic Surgery (MMS) for facial cancer exhibit anxiety about the presence of the cancer. Post-operatively, many patients show even greater anxiety associated with the degree of reconstruction required and expected long-term

cosmetic result. In a small percentage of patients, they may regret having had the surgery performed. Using a single-blinded prospective study, with patient volunteers derived from those presenting to the Skin Care Surgery Centre between November 2010 and December 2011, we wish to more fully document the varying anxiety levels in patients undergoing MMS of the face both pre-operatively, and 6 months or greater post-operatively. We hypothesize that by 6 to 12 months post-operatively, greater then 90% of patients demonstrate anxiety levels below baseline levels for both cancer and cosmetic result. In adjunct, we hypothesize that patients with underlying mood disorder(s) will exhibit greater anxiety both pre and post-operatively, and this will impact on their perception of the progression of the post-operative course and final cosmetic result. Finally, we will determine if patient age, gender, level of education, type of reconstruction, location and length of scar impact on post-operative anxiety and perceived final cosmetic result. With quantitative knowledge of patient's anxiety levels through-out the pre and post-operative course we hope to be able to more specifically address pre and post-operative counselling to minimize anxiety levels.

Category: A/B- early experiments

Poster 28

UTILIZATION AND ADMINISTRATION OF UVA-1PHOTOTHERAPY IN THE VGH PSORIASIS AND PHOTOTHERAPY CLINIC

Judith Gerbrandt, Sunil Kalia, Jennifer Howe, Kurt Pachal, Elaine Stebbing, Martina Slezkova, Martin Tsai, Helena Yang, Soodabeh Zandi, Harvey Lui.

Introduction: A new commercial UVA-1 unit has been installed at the VGH Skin Care Centre. This study reviews patient demographics and diagnoses selected for treatment as well as the unique dosimetry and treatment courses using this device. **Methods:** Patients received UVA-1 treatment between November 1, 2009 to November 30, 2010 with a multi-lateral UVA-1 ML24000 phototherapy unit. Efficacy was evaluated after 20 treatments and at 2 month intervals thereafter. UVA-1 dosimetry was based on treatment parameters recommended in literature. **Results:** Diagnoses included morphea (8), scleroderma (2), lichen sclerosis (1), eosinophilic fasciitis (1), and mastocytosis (1). Of the 13 patients who underwent treatment. 10 patients fully tolerated the first-course dose (60 J/cm^2, 5 days each week over 4 weeks), 2 required dosage adjustment, and 1 did not complete treatment. One patient has undergone a second course of treatment 130J/cm^2 (daily for 6 weeks), due to an incomplete response with first course. The effects of treatment varied between patients and diagnoses. Results, other than deep tanning, were usually delayed in onset. **Conclusions:** The dosimetry protocol reported in literature appears to be appropriate for our device. Sufficient data and clinical experience has been collected to formulate a patient information and education handout.

Poster 30

siRNA KNOCKDOWN OF AMINOPEPTIDASE N/CD13 ALTERS ECM GENE EXPRESSION IN DERMAL FIBROBLASTS

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Introduction: Of the many processes that contribute to matrix remodeling in the skin, epithelial-mesenchymal interactions are central to the formation of ECM by dermal fibroblasts. Aminopeptidase N (APN) or CD13 has recently been proposed as a cell-surface receptor responsible for the stratifin-mediated matrix metalloproteinase-1 (MMP-1) upregulation in fibroblasts. Interestingly, the fibroblast expression of APN is potently stimulated by stratifin and keratinocyte-conditioned medium (KCM), suggesting a regulatory role for APN in epithelial-mesenchymal communication and matrix remodeling. **Methods:** The present study evaluated the impact of APN modulation on the ECM gene expression profile of fibroblasts upon KCM stimulation. Specifically, dermal fibroblasts were transiently transfected with APN-specific siRNA and treated with KCM. The gene expression profile of the fibroblasts was evaluated using an ECM-specific oligonucleotide array and confirmed by Western blotting. **Results:** The result showed that transient knockdown of APN in fibroblasts affects the KCM-mediated expression of key ECM components and adhesion molecules such as fibronectin, tenascin-C, MMP-1, MMP-2, MMP-3, and MMP-12. The APN regulation of fibronectin and the selective MMPs appears to be associated with the receptor-mediated signal transduction independently of its peptidase activity. However, inhibition of the APN enzymatic activity by bestatin significantly reduced the tenascin-C expression in fibroblasts. **Significance:** The overall effect of APN-mediated downregulation of fibronectin production and upregulation of tenascin-C, MMP-1, MMP-2, MMP-3, and MMP-12 in fibroblasts suggests an important role for APN in the regulation of keratinocyte-mediated ECM remodeling. Understanding the regulation of APN/CD13 will help us to learn more about epidermal-mesenchymal interactions and find therapies for ECM-related skin diseases.

Poster 32

THE ROLE OF SMALL LEUCINE-RICH PROTEOGLYCANS IN WOUND HEALING

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Scarring in skin is associated with an increased accumulation of collagen in the extracellular matrix (ECM) as a response to increased activity of transforming growth factor-β1 (TGF-β1), butalsoother mechanisms are likelyinvolved. Since wound healing in the oral mucosa (OM) results in scarless healing, comparing the pericellularmicroenvironments in OM and skin may provide novel information about the factors that regulate scar formation. Small leucine-rich proteoglycans (SLRPs) are important components of the pericellular ECM.Theyalso modulate activity of TGF-β1 and collagen accumulation. Our general hypothesis is that the composition of SLRPs in the ECM of OM is distinct from skin, and this promotes gene expression in fibroblasts

that is conducive for scarless healing in the OM. Using an *in vivo*-like cell culture model, we will generate oral mucosal fibroblast (OMF)- and skin fibroblast (SF)-derived 3D ECM and characterize their TGF-β1, SLRP and typeI collagen composition. In order to unravel their function,SLRP abundance in the 3D ECM will be modulated using molecular biology techniques. The effects of the modified 3D ECM on gene expression and key cell functions will then be assessed. We expect to find out that reduced abundance of SLRPs results in upregulation of expression of profibrotic genes, abnormal collagen accumulation and increased activity of TGF-β1. Our research will help at understanding the molecular mechanisms in scar formation and contribute to the development of novel anti-scarring therapies.

Category: Early experiments with well defined objectives/hypotheses