POSTER #1

ROLE OF THE TUMOR SUPPRESSOR ING4 IN APOPTOSIS OF HUMAN MELANOMA CELLS

Jun Li and Gang Li
Department of Dermatology and Skin Science, Jack Bell Research Centre, University of British Columbia, Vancouver, British Columbia, Canada

The Inhibitor of Growth (ING) family proteins are novel tumor suppressors which are involved in various biological activities, including regulation of transcription, cell cycle checkpoints, DNA repair, and angiogenesis. ING proteins contain several conserved domains, suggesting that they may share common biological functions. ING4 was shown to diminish colony-forming efficiency, suppress loss of contact inhibition, and arrest cell cycle at G2-M phase. We previously reported that ING4 expression is decreased in malignant melanoma and the reduced ING4 expression is correlated with melanoma tumor thickness, ulceration and poor patient survival. To further elucidate the mechanism by which ING4 inhibits melanoma progression, we investigated the effect of ING4 overexpression on apoptosis of melanoma cells. We found that ING4 overexpression alone promotes morphologic changes associated with apoptosis, notably chromatin fragmentation and the formation of apoptotic bodies. In both wild-type p53 (MMRU) and mutant p53 (PMWK) melanoma cell lines, ING4 overexpression resulted in significantly higher percentage of apoptotic cells when compared with the empty vector. Overexpression of ING4 also enhanced chemodrug-induced apoptosis in both MMRU and PMWK melanoma cells. Furthermore, ING4 overexpression induced UVB-mediated apoptosis in melanoma cells in the presence or absence of functional p53, indicating that ING4 plays an important role in cellular response to UV. Taken together, our data suggest that reduced ING4 expression leads to defects in the apoptotic pathways of melanoma cells. Clinical significance and KT: Our data indicated that restoration of ING4 inhibits human melanoma progression and can be used as a potential target for novel melanoma therapy.

POSTER #2

TUMOR SUPPRESSOR ING1B MAINTAINS GENOMIC STABILITY UPON UV-INDUCED REPLICATION STRESS

Ronald PC Wong, Leon H Lin, David W Chen and Gang Li
Department of Dermatology and Skin Science, Jack Bell Research Center, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, British Columbia, Canada

Genomic instability plays an important role in cancer development. Human genome is susceptible to genetic alterations such as chromosome rearrangement during replication. Individuals with genetic defects in genes involved in DNA replication and repair

pathways are predisposed to cancers. Ultraviolet (UV) irradiation is the major environmental risk factor for skin cancers. UV lesions present on DNA template block progress of replication fork. Prolonged stalling of replication leads to genomic instability and contributes to cancer development. Tumor suppressor ING1b has been shown to be reduced or mislocalized in various cancers. It is shown to be involved in UV response, but the exact role has not been elucidated. In this study, we found that depletion of physiological level of ING1b sensitized cells to UV. ING1b depleted cells exhibited a prolonged S phase arrest and defect in recovery from UV-induced replication blockage. Moreover, ING1b depletion increased H2AX phosphorylation, which is a hallmark for DNA double strand breaks, and formation of aberrant chromosome structures after UV irradiation. Our data suggest a novel tumor suppressive function of ING1b in the maintenance of genomic stability after UV irradiation. Clinical Significance and KT: This study leads to a better understanding of the mechanism involved in preserving genomic stability. It has implications in developing new strategies for skin cancer prevention and detection.

POSTER #3

EXPRESSION OF SNAIL1 DOES NOT CORRELATE WITH THE PROGRESSION OF MELANOMA CANCER AND SURVIVAL OF THE PATIENTS

Seyed Mehdi Jafarnejad[1], Magdalena Martinka[2], and Gang Li[1]
[1]Departments of Dermatology and Skin Science and [2]Department of Pathology, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, British Columbia, Canada

Invasive behaviour of melanoma is due in part to epithelial-mesenchymal transition (EMT), in which epithelial cells lose contacts with their neighbours and assume migratory characteristics. EMT can be promoted by snail family transcriptional repressors. Snail1 has been implicated in triggering EMT during epithelial cancer progression and metastasis by direct repression on the transcription of the cell adhesion molecule E-cadherin. In the present study, we used tissue microarray (TMA) technology and immunohistochemistry to evaluate the expression of snail1 in different stages of human melanocytic lesions and analyzed the correlation between snail expression and clinicopathologic variables and patient survival. Formalin-fixed, paraffin-embedded tissues from 47 dysplastic nevi, 90 primary melanomas, and 46 metastatic melanomas were used for this study. We checked the specificity of the Anti-snail1 antibody with western blot and stained the TMA slides. The stained cores were scored based on the intensity and percentage of the cells positive for Snail1 expression. The data were analyzed by chi-square and t-test or Spearman test in the case of patient survival. Our data revealed no significant correlation between the expression of snail1 and progression of melanoma or survival of the patients. In addition, we did not detect any significant correlation between the expression of snail1 and clinicophatological features such as age, gender, tumour thickness, ulceration, tumour subtype and location of the

melanoma specimens. These results suggest that Snail1 does not play a significant role in the initiation and progression of melanoma.

POSTER #4

CYTOKERATIN EXPRESSION IN A RABBIT MELANOMA METASTASIS ANIMAL MODEL AND HUMAN LYMPH NODE NEGATIVE CUTANEOUS PRIMARY MELANOMAS

Susan M. Poelman[1], Shawn Maloney[2], Jean-Claude Marshall[2], Miguel J. Burnier, Jr. [2]
Divisions of Dermatology[1] and Department of Ophthalmology[2], McGill University

Purpose of the study: Cytokeratin (CK) expression is associated in vitro with an aggressive phenotype, increased metastatic potential, and poor overall survival in a variety of tumors. We sought to examine CK expression in vivo, both in a rabbit animal model, and in human primary cutaneous melanomas, and its association with metastasis development. Methods: Fifteen albino rabbits were immunosuppressed with cyclosporine and inoculated with human cutanous melanoma cells in the suprachoroidal space. Over 12 weeks, 1 rabbit was sacrificed per week and tumor samples collected. CK expression was also compared between primary melanomas from patients who developed metastatic disease (n=11) and those who did not develop metastatic disease within 5 years (n=25). Both rabbit and human tumor specimens were stained with cytokeratins 8 & 18. Results: There was decreased expression in CK 8 in rabbit lung metastases compared with primary tumors and bone marrow derived malignant cell sample cytospins, while CK 18 expression was increased in lung metastasis compared with primary tumors. We found no significant association between CK positivity in human tumors and the development of metastasis (P=1.75). Conclusions: Our animal model results suggest that CK8 downregulation and CK18 upregulation in melanoma cells may regulate metastasis to lung. We did not find an association between CK expression and the development of metastatic disease in patients with lymph node negative cutaneous melanomas in this study, suggesting the rare event of metastasis in these patients is determined by CK-independent mechanisms.

POSTER #5

SCREENING FOR MELANOMA AND NON-MELANOMA SKIN CANCER WITH ANNUAL CUTANEOUS EXAMINATION: REVIEW OF OUTCOMES & COMPLIANCE

Shannon Humphrey[1], Katie Beleznay[3], Tim K. Lee[1,2], Jason Rivers[1]
[1]Department of Dermatology and Skin Science, University of British Columbia. [2]Cancer Control Research, BC Cancer Agency. [3]Faculty of Medicine, University of British Columbia

Justification: Annual Cutaneous Examination (ACE) is recommended by many dermatologists as a screening method for early detection of melanoma and non-melanoma skin cancers (NMSC) in patients with increased risk for these lesions. There is no conclusive evidence to support this practice. Objectives: 1) To determine if patients targeted for ACE develop melanoma or NMSC at a greater rate than those not targeted for ACE. 2) To determine if patients targeted for ACE develop melanoma or NMSC at a greater rate than the general population. Methods: A retrospective chart review was performed for patients seen by the same dermatologist over a 10-year period (1991-2001) with the diagnosis of either benign neoplasm of the skin or melanoma. Clinical data was available until 2006 allowing at least 5 years of follow-up. Charts were reviewed to determine if the recommendation for ACE was made. Clinical data was extracted including subsequent histologically confirmed skin cancer diagnoses. Results: Seven hundred fifty three charts were reviewed in patients with the diagnosis benign neoplasm of the skin, of whom 195 patients were targeted for ACE (25.9%). During the follow-up period among the ACE group 75 skin cancers were detected in 31 patients (15.9%) while 18 skin cancers were detected in 15 patients (2.7%) among the non-ACE group. One hundred sixteen charts were reviewed in patients with melanoma. A total of 116 skin cancers were detected in 53 patients (47%) in the melanoma group. Conclusion: In this study, more skin cancers were detected in the ACE group than the non-ACE group.

POSTER #6

HAIR DISOCCLUSION USING MATCH FLITERING AND DYNAMIC THRESHOLDING

Nhi Nguyen[1], Tim K. Lee[1,2] and M. Stella Atkins[1]
1: School of Computing Science, Simon Fraser University. 2: Department of Dermatology and Skin Science, University of British Columbia

The main challenge in automatic skin cancer detection is the correct segmentation and classification of moles, often occluded by hair in images obtained with a dermoscope. We propose a new method for hair disocclusion in such images based loosely on previous methods in retinal blood vessel segmentation. Our method includes applying a match filter on a gray level image to amplify the hair, based on the empirical observation that hair has near Gaussian profile across its width over all its length. To identify the hair along its length, we treat hair as piece-wise linear. Then we use thresholding (dynamic thresholding using local entropy) to segment the hair from the background and build a binary hair mask. The last step is to redraw the parts of the image that are occluded by hair. Potential solutions for this step are linear interpolation and in-painting. Our goal is to outperform DullRazor, the popular software with the same purpose, and to work on a variety of hair types such as light and fine hairs, which DullRazor cannot identify. Clinical Significance and KT: Our method can be used as the first stage towards an automated skin cancer diagnostic system, where distracting

artifacts such as hair and dark marker lines are eliminated from dermoscopic images in a preprocessing step before segmentation and analysis of skin lesions. Our method can also be extended to work for automated hair counting software in hair research.

POSTER #7

***IN VIVO* CONFOCAL RAMAN SPECTROSCOPY FOR SKIN DISEASE DETECTION AND CHARACTERIZATION—PRELIMINARY RESULTS FROM A MURINE TUMOR MODEL**

Hequn Wang, Naiyan Huang, Jianhua Zhao, Harvey Lui, Haishan Zeng
The Laboratory for Advanced Medical Photonics (LAMP), Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute and Cancer Imaging Department, BC Cancer Research Center, Vancouver, BC, Canada

Background and Objective: The confocal principle provides a powerful method for performing non-invasive, depth-resolved tissue evaluation because of its optical sectioning capability. Raman spectroscopy measures molecular vibrations and can provide fingerprint-type specific signatures for molecular identification. Our objective is to combine these two complementary techniques to achieve non-invasive, depth-resolved biochemical analysis of the skin *in vivo* for improving skin cancer detection and evaluation. Materials and Methods: A confocal Raman spectrometer system with a special probe for reducing involuntary body movements has been built for depth-resolved biochemical analysis of the skin *in vivo.* The skin of 15 anesthetized mice bearing squamous cell carcinoma (SCC) subcutaneous tumors was scanned axially from the stratum corneum to mid dermis. After this, the skin from the measurement sites was excised and H&E stained. Results and Conclusions: The axial resolution of the system within tissue was be 12.6 microns. Raman spectra with good signal-to-noise ratio were obtained within 15 seconds under 27-mW of excitation light exposure to the skin surface. Raman spectra of mouse epidermis and dermis differed significantly. Obvious changes in Raman spectra for the dermal layers were also evident between normal and tumor-bearing skin. We are aiming to now combine this spectrometer system combined with a confocal imaging module in the near future to not only improve the non-invasive clinical diagnosis of skin cancers, but also help delineate their margins.

POSTER #8

CO-CULTURE OF FIBROBLASTS EMBEDDED IN COLLAGEN GEL WITH KERATINOCYTES SHOWED DIFFERENTIAL EXPRESSION OF MMP-1 AND MMP-3 IN COMPARISON TO MONOLAYER CO-CULTURE SYSTEM

A. Lai, M. Li, A. Ghahary
BC Professional Firefighters' Burn and Wound Healing Research Lab, University of British Columbia, Vancouver, BC, Canada

Introduction: Following the inflammatory phase of wound healing, cellular interactions become dominated by the interplay of keratinocytes with fibroblasts, which greatly impacts on the molecular constitution of the extracellular matrix (ECM). In this study, we ask the question of whether fibroblasts embedded within three-dimensional collagen scaffold respond differently to keratinocyte releasable factors in comparison to monolayer co-cultured fibroblasts. Methods: Primary human fibroblasts were seeded either as monolayer culture or into 3D scaffolds, and co-cultured with keratinocytes for 24 hours. mRNA and protein expression patterns of fibroblasts in the co-culture systems were examined by microarray and PCR analyses, and Western blot analysis. Results: Co-culturing fibroblasts with keratinocytes induced the expression of MMP-1 and MMP-3, and the increase in expression was even more prominent in the 3D collagen martrix than in the monolayer culture system. Also, MMP-3 was more releasable from the co-cultured fibroblasts compared to MMP-1. Interestingly, in contrary to MMP-1 whose expression was easily detectable in the cell lysate, MMP-3 was found mainly in conditioned medium. Clinical Significance and Knowledge Translation: Besides MMP-1 and MMP-3, the genes that exhibited the most dramatic increase in expression are either implicated in ECM degradation or associated with cell-cell signaling. The fact that the degree of increase was more prominent in the physiologically relevant 3D co-culture system affirms the impact of cross talk between keratinocytes and fibroblasts in vivo, and provides further insight into the roles of keratinocye releasable factors in fibroblasts, especially in the processes of tissue remodeling and wound healing.

POSTER #9

CARBON NANOTUBE ASSISTED LASER THERMOTHERAPY OF SKIN CANCERS – PILOT PROOF-OF-PRINCIPLE STUDY IN A MURINE MODEL

Naiyan Huang, Harvey Lui, Jianhua Zhao, Mladen Korbelik, Hequn Wang, Haishan Zeng
The Laboratory for Advanced Medical Photonics (LAMP), Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia & Vancouver Coastal Health Research Institute and Cancer Imaging Department, BC Cancer Research Center

Single-walled carbon nanotubes (SWNTs) absorb light over a broad wavelength range and can efficiently translate absorbed energy into heat. SWNTs exhibit strong Raman optical signals, thereby facilitating non-invasive *in vivo* monitoring within tissue. Our objective is to develop a novel laser thermotherapy technique that combines SWNTs and NIR laser light for skin cancer treatment. We hypothesize that intratumoral injected SWNTs can absorb 785 nm NIR laser light and generate sufficient heat to raise the tumor temperature by over 10°C, thereby killing cancer cells and eradicate the tumor via hyperthermia. The SWNTs distribution and tumor temperature can be monitored non-invasively and in real-time by Raman spectroscopy and IR thermometry respectively, in

order to facilitate accurate dosimetry. The hypothesis will be tested with a squamous cell carcinoma (SCCVII cells) in C3H/HeN mouse model. At first, the pharmacokinetics of SWNTs will be studied using Raman spectroscopy to determine the optimum time point for light treatment. For treatment SWNTs are administrated by intratumoral injection, followed by immediate laser irradiation. Different doses of SWNTs and light will be studied. After treatment, the tumor volume will be measured every other day for three months to determine if it is cured. To date we have treated one SCC-bearing mouse (1 mg/ml SWNTs, 200 mW/cm^2 light, 10 min irradiation) and found that significant damage to the tumor appeared 24h after the treatment with clear necrosis being apparent after 48h.

POSTER #10

FRONTAL FIBROSING ALOPECIA

Isabel Restrepo, Abdullateef Alzolibani, Nina Otberg, Kevin McElwee, Magdalena Martinka*, Jerry Shapiro
Department of Dermatology and Skin Science, *Department of Pathology, University of British Columbia, Vancouver, BC, Canada

Frontal fibrosing alopecia (FFA) is characterized by progressive scarring recession of the frontal and temporal hairlines. We report 35 new cases, all women, diagnosed with FFA, based on clinicopathologic correlation, presenting at the University of British Columbia Skin Care Centre. Hair loss measurements were taken from right and left canthus, eyes, and from the glabella to the receding hair line every month in order to evaluate progression and response to the current treatment. A 4mm scalp punch biopsy was taken from the frontal hairline in all patients. There were a total of 35 woman patients between 21 and 78 years old, with FFA: 27 Caucasian, 5 Asian, and 3 East Indian. 28 cases of FFA started after menopause. Minimum age of onset was 18 years, maximum was 73. Some loss of the eyebrows was found in 26 patients. Lack of axillary hair was evident in 6 patients and pubic total hair loss in 4 patients while 11 patients had thinning of both. Autoimmune diseases were manifested by 17 patients, particularly hypothyroidism (14 patients), Symptoms like itching, burning, pain, perifollicular erythema, perifollicular keratosis, and atrophy, were found in all patients. Hair loss rates were variable ranging between 0.1 mm to 1.9 mm per month. 18 patients remain stable with the same frontotemporal measurements. The pathogenesis of FFA remains unknown. Theories involve a T- cell mediated inflammatory reaction and androgen involvement. The condition is a clinicopathologic variant of lichen planopilaris, gold and mercury may also have a role in the pathogenesis.

POSTER #11

EPIDEMIOLOGY OF FOLLICULITITS DECALVANS AND KERATOSIS FOLLICULARIS SPINULOSA DECALVANS IN BRITISH COLUMBIA

Nina Otberg, Jerry Shapiro
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada

Folliculitis decalvans (FD) is a rare inflammatory scalp disorder, classified as primary neutrophilic cicatricial alopecia that predominantly occurs in middle-aged adults. The hallmark of FD is the development of scarred areas and follicular pustules on the scalp. Keratosis follicularis spinulosa decalvans (KFSD) or Siemens-1 syndrome is a rare X-linked disease of unknown etiology affecting the skin and the eye. KSFD is characterized by diffuse keratosis pilaris with a scarring alopecia of the scalp and associated photophobia, facial erythema, and palmoplantar keratoderma. Although initially described as a sex-linked disorder, several different inheritance patterns have been observed. The cicatrical alopecia in KSFD shows clinical and histological similarities to FD. The incidence of these two forms of cicatricial alopecia is unknown. The goal of this research project is to determine the prevalence and incidence of folliculitis decalvans and keratosis follicularis spinulosa decalvans in British Columbia. A province wide survey amongst dermatologists and pathologists will be arranged. The physicians will be asked to report all FD and KSFD cases to the Department of Dermatology and Skin Science, UBC. The study will help to get a better understanding of the epidemiology of these rare disfiguring scalp diseases.

POSTER #12

PRETIBIAL ANGIOPLASIA: A NOVEL ENTITY ENCOMPASSING THE CLINICAL FEATURES OF NECROBIOSIS LIPOIDICA AND THE HISTOPATHOLOGY OF VENOUS INSUFFICIENCY

Nisha Mistry[1], H Chih-ho Hong[1], Richard I Crawford[1,2]
[1]Department of Dermatology and Skin Science, University of British Columbia;
[2]Department of Pathology and Laboratory Medicine, University of British Columbia

BACKGROUND: Necrobiosis lipoidica is a condition of unknown pathogenesis, which presents most commonly as waxy yellow-brown plaques on the shins. Venous insufficiency occurs in a similar distribution; however it has distinct clinical and pathologic features. We present here a series of eight patients, who clinically were suspected to have necrobiosis lipoidica, however on pathology showed features of venous insufficiency. METHODS; Between 1997 and 2008 eight patients were identified at St. Paul's Hospital, Vancouver to have had a clinical diagnosis of necrobiosis lipoidica and histopathologic features of venous insufficiency. The charts and pathology reports

of these patients were reviewed. Clinical information was extracted on demographic data, disease states, morphologic and histopathologic features. RESULTS: The patient ages at time of biopsy ranged from 39 to 73 years. Only one of the eight patients was female. Members of the group did have clinical diagnoses of diabetes, renal failure, venous disease or arterial disease. Most patients had lesions on both anterior shins. The clinical diagnosis was generally deemed to be necrobiosis lipoidica; other differentials included morphea and Kaposi's sarcoma; in no cases did the lesions have a clinical resemblance to venous insufficiency. All patients had features on pathology of venous insufficiency and no features of necrobiosis lipoidica. CONCLUSION: We put forth that this combination of clinical features of necrobiosis lipoidica and histopathological features of venous insufficiency represents a novel entity for which we propose the name pretibial angioplasia.

POSTER #13

WITH A CLINICAL SUSPICION OF BULLOUS PEMPHIGOID, IS A SKIN BIOPSY FOR DIRECT IMMUNOFLUORESCENCE MORE LIKELY TO BE POSITIVE FROM LESIONAL OR PERILESIONAL SKIN?

Chris Sladden[1], Richard I. Crawford[1,2]
[1]Dept. of Dermatology and Skin Science, UBC. [2]Dept. of Pathology and Laboratory Medicine, UBC.

A skin biopsy for direct immunofluorescence (DIF) may show differing sensitivity depending on whether it is taken from lesional or perilesional skin, and this difference depends upon the specific disease being biopsied. As of yet, there is no scientific information to indicate whether lesional or perilesional biopsies are more sensitive in the DIF diagnosis of bullous pemphigoid (BP). The main objective of this study was to assess the likelihood of a biopsy being diagnostic when taken from lesional versus perilesional skin when there is a clinical suspicion of BP. Methods: This retrospective study reviewed all 1423 DIF biopsies processed at St. Paul's Hospital, Vancouver from the period 1998 to 2008, including 260 specimens with a clinical suspicion of BP. Each BP specimen was designated as either lesional, perilesional or indeterminate. The biopsy results were recorded as diagnostic of bullous pemphigoid, non-diagnostic, non-specific or supportive of another diagnosis. Results: Of the 56 lesional biopsies, 28 (50%) showed a positive result, while 10 of 45 (22%) perilesional biopsies and 19 of 159 (12%) indeterminate biopsies showed a positive result. Discussion: With a clinical suspicion of BP there was more likelihood of a positive result if the biopsy was taken from clinically or histologically lesional skin. We would suggest that the highest yield on DIF biopsies for BP would come from an intact lesional sample, or alternatively from a sample close enough to the lesion to contain histologically identifiable lesional skin.

POSTER #14

DEVELOPMENT OF A SYPHILIS VACCINE

Tatyana Hamilton[1], Caroline Cameron[2].
[1] PGY-2 Dermatology resident, UBC. [2] Department of Biochemistry and Microbiology, University of Victoria.

Background and significance: Syphilis, caused by the spirochete bacterium Treponema pallidum subsp. Pallidum, is a chronic bacterial infection that remains a global health concern. Ten years ago, the worldwide burden of syphilis was estimated at 12 million new infectious cases per year, with an overall prevalence of at least 25 million. Within the United States and Canada, the rates of primary and secondary syphilis have been steadily increasing. A 56% increase in total cases was seen between 2005 and 2006 in British Columbia, which paralleled the rate of new HIV infections. Worldwide, 1.5 million infants are affected by congenital syphilis each year. Thus, in 2005, the World health Organization made elimination of congenital syphilis a top priority. Study rationale: The syphilis vaccine project will be conducted in three stages: 1) Large-scale protein expression and selection of antigen cocktail formulations for testing will be carried out drawing on extensive expertise of Dr. Cameron and her research team with structure-functional analysis of treponemal outer membrane proteins. 2) Evaluation of vaccine efficacy against infection in male and female rabbits. 3) Phase 1 clinical trials. Clinical Significance and Knowledge Translation: Vaccines are universally acknowledged to be the most cost effective of all healthcare technologies. The goal of this project is the translation of the results of animal trials to the initiation of clinical trials with human volunteers, something not previously achieved in the history of syphilis.

POSTER #15

SURVEY OF RECENT CANADIAN DERMATOLOGY GRADUATES

Stephanie J. Côté and Richard I. Crawford
University of British Columbia, Vancouver, Canada

Background: Despite workforce shortages, there are relatively few dermatologists trained every year in Canada. A Canadian dermatology workforce survey conducted in 2001 confirmed this reality and provided information about the demographics, workload, and future career plans of dermatologists in this country. An appraisal of dermatology residency training in 2004 provided data to assist dermatology programs with the improvement of their curricula. No prior studies have evaluated how recent dermatology graduates perceive their residency to have prepared them for their careers, nor has any previous study examined the demographics and practice components of this group. Hypotheses: 1) Current residency programs provide a broad-based training curriculum; and 2) Components of recent graduates' current practices differ from what

they had perceived during residency that these would subsequently be. Objectives: 1) To identify the basic demographics and practice components of recently graduated Canadian dermatology residents; 2) To characterize additional formal and informal training completed after residency; 3) To assess their perceived adequacy of residency training in preparing them for their current endeavors; 4) To provide suggestions for improvement in residency training programs; and 5) To help evaluate whether areas of need are being filled in Canada. Methods: Anonymous survey of Canadian dermatology graduates from the classes of 2001-2006. Results: Will be presented

POSTER #16

COMPARATIVE ADRENAL SUPPRESSION OF INHALED CORTICOSTEROIDS IN ASTHMATIC HIV PATIENTS ON RITONAVIR

Mohammed AlJasser, R. Robert Schellenberg
St. Paul's Hospital, Department of Medicine, University of British Columbia

Background: Ritonavir is a protease inhibitor that has a potent inhibitory effect on cytochrome p450 (CYP) 3A4. Fluticasone, a potent ICS, is also metabolized by CYP which can result in high serum levels in patients using ritonavir. There are reports of iatrogenic Cushing syndrome and adrenal insufficiency in HIV patients using inhaled fluticasone and ritonavir concurrently. No published data exist for other ICS in patients taking ritonavir. Objectives: To compare the effects of various ICS on adrenal function in asthmatic HIV patients on ritonavir. Methods: HIV patients on ritonavir with stable asthma on a fixed dose of ICS will be recruited. Exclusion criteria will include patients on other CYP inhibitors, use of systemic steroids during the past 3 months, use of cutaneous or intranasal steroids during the past 1 month, and patients with other causes of Cushing syndrome. Patients (20 per treatment arm) will be randomized to take equivalent doses of either inhaled fluticasone, ciclesonide, or budesonide for a duration of 2 weeks. Early morning serum cortisol and 24-hour urinary cortisol, at baseline and at the end of the 2 week treatment period, will be measured and differences between treatments analysed by ANOVA. Results (anticipated): Due to differences in systemic bioavailability, protein binding and affinities for the glucocorticoid receptor, we anticipate differing degrees of adrenal suppression with the different ICS. Conclusion: Determination of which ICS, when combined with ritonavir, has the least adrenal suppression would optimize management of asthmatic HIV patients using ritonavir.

POSTER #17

CLINICAL TRIALS AT THE UBC DEPARTMENT OF DERMATOLOGY AND SKIN SCIENCE: 2008 IN REVIEW

Rayone Christante, Sherry Phillips, Anna Daly, Jennifer Briggs, Stuart Maddin.
Clinical Trials Unit, UBC Department of Dermatology and Skin Science, The Skin Care Centre.

Building upon the expertise of the members of the Department of Dermatology and Skin Science at UBC, the Clinical Trials Unit at the Skin Care Centre has been investigating novel therapeutics for a wide range of dermatological conditions for over 40 years. A review of the activity of the Clinical Trials Unit over the past year was conducted. From January to December 2008, over 138 subjects participated in 15 Phase II, III & IV trials. The indications included moderate to severe plaque psoriasis, facial psoriasis, and field actinic keratoses (Aks), superficial basal cell carcinomas (sBCCs), and Bowen's disease. Therapeutics studied included topical agents, oral therapies, IV infusion therapies, and intramuscular and subcutaneous injection therapies. Recruitment targets were met or exceeded in approximately 65% of the trials. Clinical Significance and Knowledge Translation: Trials performed in the Unit provide investigators and faculty with the opportunity to become familiar with new treatment agents, and provides patients with access to the latest developments in dermatologic therapies at no cost. A variety of pharmaceutical sponsors, faculty members and clinic staff have partnered with the Clinical Trials Unit to make each of these studies possible.

POSTER #18

PATIENT PROFILE AND CLINICAL IMPACT OF PRIMARY FOCAL HYPERHIDROSIS VARY ACCORDING TO ANATOMICAL LOCATIONS

Christina Han, Lin Gao, Youwen Zhou
Hyperhidrosis Clinic, The Skin Care Center, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada

Objective: Few studies have compared hyperhidrosis affecting different anatomic sites. This study aims to characterize the patient profiles and quality of life impact of hyperhidrosis involving various anatomic locations. Design: Survey of clinical features and quality of life impact. Setting: A specialty clinic in an academic center. Participants: One hundred sixty-two consecutive patients with primary focal hyperhidrosis who filled out the questionnaires completely. Intervention(s): Two questionnaires are filled by each patient. One is on the clinical features including gender, age of onset, anatomical locations, and family history. The other is a generic, health- related quality of life (QOL) survey, SF-12v2 (QualityMetric). Main Outcome Measure(s): For each anatomical group (axillary, palmoplantar, and facial), the following are calculated: age of onset, gender, family history, SF-12v2 QOL scores. Results: Compared with axillary hyperhidrosis, palmoplantar hyperhidrosis has an earlier age of onset (10.9 years versus 13.8 years, $p<0.01$), a lower female to male gender ratio (0.67, versus 2.45, $p<0.05$), less family members with hyperhidrosis (14% versus 32%, $p<0.05$), and a lower mental component score on the SF-12v2 survey (47.39 versus 51.69, $p<0.05$). This score is much lower than that of the general population, and similar to that found in many common chronic diseases including dermatitis, chronic heart disease, cancer, and arthritis. Conclusions: Significant differences exist in the clinical profiles and quality of life impact of primary

focal hyperhidrosis according to the anatomical locations involved. Specifically, further research and better treatments are needed for palmoplantar hyperhidrosis.

POSTER #19

A NOVEL SUBCUTANEIOUS FLORESCENT IMAGING IN ANGULAR DOMAIN

Fartash Vasefi[1, 2], Bozena Kaminska[1], Glenn H. Chapman[1], Jeffrey J.L. Carson[2, 3]
[1]The School of Engineering Science, Simon Fraser University, Burnaby, BC, Canada
[2]Imaging Program, Lawson Health Research Institute, London, ON, Canada
[3]Medical Biophysics, University of Western Ontario, London, ON, Canada

We describe a novel florescent imaging methodology applicable for detecting fluorescent photons embedded below skin. This method exploits the collimation detection capabilities of an angular filter device to extract photons emitted by a fluorophore embedded under the skin within the tissue. A femto-second pulsed laser source is used to excite the fluorophore within the medium. The photons emitted by the fluorophore that are not greatly scattered pass through the angular filter array and are detected by the ultra fast gate-intensified CCD camera (PicoStar, la Vision). Scattered photons are rejected by the filter and do not pass through to the camera. We fabricated angular filter arrays using silicon bulk micromachining, an array with the optimum size of 80 μm square-shaped micro-tunnels 1.5 cm in length accepted photons with trajectories below 0.5 degree off the axis of the micro-tunnels. This small acceptance angle rejects most of the scattered light exiting the tissue. The performance of the angular filters does not depend greatly on coherence or the wavelength of light. For the proof of concept, the experiments have been conducted to localized IRDye® BoneTag™ optical Probe in mouse in vitro. NIR fluorescence detection improves depth of penetration due to low tissue autofluorescence, translating to low background interference enabling to detect optical probes under the skin. The imaging spatial resolution has been analyzed and compared with X-ray CT images. This method may become a practical tool in skin cancer diagnosis and screening procedures in the future.

POSTER #20

INTEGRIN-LINKED KINASE (ILK) REGULATES THE EXPRESSION OF INTERLEUKIN-6 AND VASCULAR ENDOTHELIAL GROWTH FACTOR IN MELANOMA CELLS

Aijaz A. Wani, Gang Li,
Department of Dermatology and Skin Science, Jack Bell Research Centre, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, British Columbia, Canada

Integrin-linked kinase (ILK) is a highly conserved serine-threonine protein kinase that regulates cell-ECM interactions, cytoskeletal organization, and cell signaling.

Overexpression of ILK in epithelial cells leads to anchorage independent growth with increased cell cycle progression. Previously, we have shown that ILK upregulation strongly correlates with melanoma progression, invasion and inversely correlates with 5-year survival of melanoma patients. However, the molecular mechanism by which ILK enhances melanoma angiogenesis is currently unknown. In the present study, we found that angiogenic molecules such as interleukin-6 (IL-6) and vascular endothelial growth factor (VEGF) are the downstream transcriptional targets of ILK in melanoma cells. ILK overexpression increased IL-6 and VEGF expression, whereas silencing of ILK by shRNA suppressed IL-6 and VEGF expression at both transcriptional and translational levels. Furthermore, overexpression of NF-κB p65 protein significantly increased IL-6 and VEGF mRNA and protein levels (p<0.05). Whereas, shRNA mediated inhibition of NF-κB p65 expression resulted in a significant decrease in IL-6 mRNA transcripts (p<0.05). The results suggest that ILK mediates melanoma angiogenesis by upregulating IL-6 and VEGF probably through NF-κB pathway. Clinical Significance and knowledge transfer: The results from this study will help us to better understand the role of ILK in melanoma angiogenesis and to design novel therapies against melanoma.

POSTER #21

FIELD CELLULAR DEFECTS IN VITILIGO VULGARIS

Wei S, Su M, Wang Y, Zhang Y, Lui H, and Zhou Y
Chieng Genomics Centre, Predictive Medicine and Therapeutics, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada

Vitiligo is the most common depigmenting disorder, with a prevalence of ranges from 0.1–4 % in worldwide. It can cause severe distress and disfigurement in the affected individuals. The pathogenesis is unclear. In order to provide additional clues to vitiligo pathogenesis, we had performed large scale gene expression analyses on the lesional skin in vitiligo, and discovered that a group of membrane bound proteins previously unknown to melanocyte structure or function were specifically and consistently decreased in vitiligo-affected skin biopsies. Cellular localization using immunohistochemistry stains as well as immunofluorescence has determined that these molecules were normally present in dermal, non-melanocytic cells, where as these cells were absent in vitiligo lesions, parallel to the demise of melanocytes. Therefore, we propose that the death of melanocytes is one manifestation of a global cellular defects present in vitiligo. Significance: This project may help clarify the pathogenesis of vitiligo vulgaris, and point to new approaches for developing therapies for vitiligo in the future.

POSTER #22

ECTODYSPLASIN RECEPTOR EDAR IS HIGHLY EXPRESSED IN NODULAR BASAL CELLL CARCINOMAS

Mei Yu, Sam Ma, David Zloty, Bryce Cowan, Jerry Shapiro, and Kevin J. McElwee
Department of Dermatology and Skin Science, University of British Columbia, Canada

In the hair follicle skin appendage, the Sonic hedgehog (Shh), Wnt, and Eda pathways play primary roles in development and growth. Studies with mice either lacking the functional proteins of Eda pathway or overexpressing the ligand or receptor suggest that Eda signaling has multiple roles in ectodermal organ development regulating their initiation, morphogesis, and differentiation. Basal cell carcinomas (BCCs) can be regarded as aberrant skin appendages where Shh and Wnt have been shown to have primary roles. Pervious microarray analysis of BCCs also suggested an active Eda pathway. We further investigated components of Eda signaling in nodular BCCs versus normal skin epithelium and hair follicles. Quantitative PCR (qPCR) of nodular BCCs (n=8), normal skin epithelium (n=8), and microdissected hair follicles (n=8, ten hair follicles per donor sample) revealed possible increased EDA and significantly increased EDAR (43-fold increase in BCCs over hair follicles). In contrast, XEDAR (0.17-fold), and TRAF6 (0.27-fold) exhibited statistically significant suppression in BCCs as compared to hair follicles. Immunohistology revealed distribution of Eda, Edar, and Xedar in BCC keratinocytes consistent with cell membrane expression and with strongest expression in those cells at the periphery of tumor cell nests. In contrast, positive expression in hair follicles was evenly distributed in the non-bulbar outer root sheath. This preliminary investigation suggests that, in addition to Shh, and Wnt signaling, other hair follicle appendage signaling pathways, including Eda, may be active in BCC growth. The potential role of Eda pathway in BCCs may correlate with its ability to regulate ectodermal organ development.

POSTER #23

IDO MAY CONFER IMMUNE PRIVELEGE TO BASAL CELL CARINOMAS

Blanche K.K. Lo [1], Navkiran Sidhu [1], David Zloty [1], Reza B. Jalili [2], A. Ghahary [2], Bryce Cowan [1], Jerry Shapiro [1], and Kevin J. McElwee [1]
[1] Department of Dermatology and Skin Science, University of British Columbia, Canada
[2] Department of Surgery, University of British Columbia, Canada

Basal cell carcinoma (BCC) is the most prevalent malignancy found in the Caucasian population. It has been suggested that immunoprotection may be involved in BCC tumorigenesis; however, the nature of putative immunoprotective mechanisms has yet to be established. In this study, we profiled the expression of genes associated with immune privilege (IP) in BCCs by real-time RT-PCR using human nodular BCC samples (n=10) as compared to non-lesional skin epithelium control tissue (n=10). BCC samples

exhibited significant upregulation in 9 of 19 immunoregulatory genes including IDO (1.96-fold). Immunohistochemistry (IHC) and Western blot confirmed the IDO protein was present in relatively high concentrations in nodular BCCs. IDO was mainly localized in the tumor nests while a weak, non-specific staining was distributed in the stromal region of the BCC biopsies. There was some immuno-labeling in the normal skin biopsies, especially in hair follicle outer root sheath and sebaceous glands. IDO proteins were present in the non-follicular epithelium of both BCCs and control tissues. IDO in BCCs had a 30kDa molecular weight which was smaller than recombinant IDO (42kDa). In conclusion, the data suggest BCCs may employ IP mechanisms to avoid targeting by the host immune system. Of several differentially expressed IP genes, IDO may be a key factor. The BCC cells synthesize and release a truncated IDO protein. Further functional assays of the BCC-derived IDO will be needed to determine its immunosuppressive potency. The results may ultimately shed light on the impact of IDO and other IP genes on BCC growth.

POSTER #24

A CLINICAL TRIAL ON THE REDUCTION OF BACTERIA (INCLUDING MRSA) IN MRSA POSITIVE WOUNDS

Anna Hinek[1], Brian Kunimoto[1], Chris Miller[2], Anthony Papp[3]
[1]Department of Dermatology, University of British Columbia, Vancouver, British Columbia, Canada. [2]Faculty of Experimental Medicine, University of British Columbia, Vancouver, British Columbia, Canada. [3]Division of Plastic Surgery, University of British Columbia, Vancouver, British Columbia, Canada

Background: Chronic wounds colonised with bacteria, especially if the colonising organisms are organized into a biofilm are known to heal at a slower rate. Over the years the use of antibiotics in the treatment of such wounds contributed to the emergence of resistant organisms such as methicillin resistant *Staphylococcus aureus (*MRSA). Nitric oxide (NO) has been shown to be bactericidal towards various organisms. Previous *in vitro* and *in vivo* animal models have shown antibacterial effects of direct application of 200 ppm gaseous nitric oxide (gNO) on common bacterial strains contributing to wound infections, as well as significant biofilm reduction and promotion of wound healing in a single human subject. **Objectives**: The purpose of this study is to investigate the efficacy of topically applied gNO for a significant reduction of bacterial burden, including MRSA, in chronic wounds. **Methods**: gNO at 10,000 ppm will be applied to MRSA-colonized wounds for 30 minutes for 3 consecutive days using a specialized delivery apparatus. Efficacy will be evaluated by measuring the number of subjects in whom a minimum of 3-Log reduction of total bacteria, including MRSA, has been confirmed through comparison of punch biopsy cultures of their wounds. The lesions will be sampled upon enrolment into the trial and the log reduction will be calculated by comparing the sample results from day 1 and day 3 of the trial.

POSTER #25

TREATMENT OF NOTALGIA PARESTHETICA WITH BOTULINUM TOXIN TYPE A

Tarek Afifi[1], Shane Silver[2]
[1]University of British Columbia, Department of Dermatology. [2]University of Manitoba, Department of Internal Medicine

Background: Notalgia paresthetica (NP) presents with unilateral pruritus involving the midscapular border, classically in a dermatome innervated by thoracic spinal nerves T2 to T6. Associated symptoms may include hyperesthesia, burning, or paresthesia. Although benign, the burdensome symptoms and unremitting course lead to significant morbidity. To date, there have been no adequately studied, non-invasive therapies showing lasting efficacy. Evidence suggests a neuropathic etiology involving thoracic and/or cervical spinal nerves. Itch likely results from mechanical irritation of C-fibers that activate neurons in the dorsal horn. Botulinum toxin (BT), well known for its effects on acetylcholine, has also been shown to affect three nociceptive neurotransmitters: substance P, calcitonin gene related peptide, and glutamate. This ability to interfere with nociceptor release and signaling suggests potential utility for sensory, in addition to motor, neuropathies. Indeed, many neuropathic pain syndromes have been treated w BT, including post-herpetic neuralgia and, more recently, two patients with NP. Objective: To evaluate the efficacy of BT-A in the treatment of NP. Methods: This study, currently underway, is a randomized single-blinded hemi-crossover trial. Subjects with NP are being treated with either placebo (saline injections) or BT-A. Measures of pruritus and quality of life are being recorded at baseline and every 3 months for the duration of follow-up. Subjects in the placebo arm will cross into the treatment arm at 6 months. Subjects will be followed for one year from the time of BT treatment. The rationale for and status of the study will be presented.