

## **POSTER #1**

### **REAL-TIME RAMAN SPECTROSCOPY FOR NONINVASIVE SKIN CANCER DETECTION**

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Background: Raman spectroscopy is a non-invasive optical technique, which has the capability in determining the molecular structure and conformation of biochemical constituents. Recently we developed a rapid real-time Raman spectrometer system, paving the way for clinical application of Raman spectroscopy. Hypothesis: The morphological structure and the bio-molecular constituents have been altered in the cancerous skin and these changes can be detected by Raman spectroscopy. Methods and Patients: The real-time Raman system was used for clinical measurements. The cancerous lesion and its surrounding normal skin were measured for paired analysis. 310 spectral pairs were evaluated including 37 melanomas, 24 basal cell carcinomas (BCC), and 49 squamous cell carcinomas (SCC), 24 actinic keratoses, 53 seborrheic keratoses, 32 atypical nevi, 22 compound nevi, 25 intradermal nevi, 23 junctional nevi, 10 nevi of Ota, and 11 blue nevi. Statistical methods including principal component analysis (PCA), and partial least square (PLS) regression have been used for diagnosis. Results and Conclusion: Cancerous and normal skin have distinctive spectral features. On average, melanoma and SCC have higher fluorescence intensity, while BCC has lower fluorescence intensity than normal skin. However, normal skin has stronger Raman peak intensity (at  $1445\text{cm}^{-1}$ ) than melanoma, BCC and SCC. Statistical analysis demonstrated that skin cancers can be very well discriminated from benign skin lesions (sensitivity= 91%, specificity = 75%) and malignant melanoma from pigmented lesions (sensitivity = 97%, specificity = 78%). The results demonstrated that real-time bedside Raman spectroscopy is both technically feasible and promising for non-invasive skin cancer diagnosis.

## **POSTER #2**

### **CLINICAL TRIALS AT THE UBC DEPARTMENT OF DERMATOLOGY AND SKIN SCIENCE: 2007 IN REVIEW**

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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 nearly 40 years. A review of the activity of the Clinical Trials Unit over the past year was conducted. Extension studies and studies prematurely terminated by the study sponsor were not included in the analysis. From January to December 2007, over 154 subjects participated in 9 Phase II, III & IV trials. The indications included moderate to severe plaque psoriasis, scalp psoriasis, and field AK, sBCC, and Bowen's disease. Therapeutics studied included topical agents and intramuscular and subcutaneous injection therapies. Recruitment targets were met or exceeded in more than 75% of the trials. 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 #3**

#### **COOPERATION OF TUMOR SUPPRESSOR ING1B AND SWI/SNF CHROMATIN REMODELING COMPLEX IN NUCLEOTIDE EXCISION REPAIR**

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Skin cancer melanoma is a life-threatening disease, for its ability to metastasize rapidly and its resistance to radiotherapy and chemotherapy. Ultraviolet (UV) radiation is the major environmental factor for development of melanoma. UV-damaged DNA is repaired by the nucleotide excision repair (NER) pathway, which involves up to thirty polypeptides. For this number of repair factors to gain access to the lesion sites, chromatin's compact structure needs to be relaxed. It is proposed that the relaxation process, or chromatin remodeling, precedes NER in order to provide favorable environment for recruitment of repair factors. However, the role of chromatin remodeling in NER is not fully understood. Chromatin remodeling is allowed through histone post-translational modifications and/or through SWI/SNF ATP-dependent chromatin remodeling complex. We have previously showed that tumor suppressor ING1b enhances NER by increasing histone H4 acetylation and chromatin relaxation, and by recruiting lesion recognition protein, XPA, to lesion sites. We recently found that ING1b interacts with SNF5, core subunit of the SWI/SNF complex, by immunoprecipitation in melanoma cell line MMRU and 293 cells. To further study the cooperation of SWI/SNF complex with ING1b in NER, we established stable 293-cell line with SNF5 knockdown. We found that UV-induced chromatin relaxation was abrogated in cells with SNF5 knockdown using Micrococcal nuclease digestion assay. Our data show that ING1b may cooperate with SWI/SNF complex as chromatin remodeling factors in NER. This sheds light on the molecular mechanisms of how UV-damaged DNA is repaired which may enable us to design effective strategies for skin cancer prevention.

### **POSTER #4**

#### **ING4 INHIBITS CELL MIGRATION AND CELL INVASION IN HUMAN MELANOMA**

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Melanoma is the most lethal form of skin cancer with a high mortality rate due to rapid metastasis, and the incidence of melanoma drastically increased over the past decades. Currently, there is no effective treatment for metastatic melanoma. ING4, a member of Inhibitor of Growth tumor suppressor family, has been shown to diminish colony-forming efficiency, induce p53-dependent apoptosis and arrest cell cycle at G2/M phase. Our previous study demonstrated that ING4 expression was significantly decreased in malignant melanoma biopsies compared with benign nevi, and reduced ING4 expression is closely correlated with tumor thickness and poor 5-year survival of primary melanoma patients. However, the underlying mechanism of ING4 regulating melanoma progression is not completely understood. In this study, we further elucidate the role of ING4 in human melanoma cell migration and cell invasion. We found that overexpression of ING4 suppressed melanoma cell migration by 63% when compared with the empty vector control ( $P = 0.0005$ , t-test). Overexpression of ING4 also inhibits RhoA activity and Rock-mediated formation of stress fiber ( $P = 0.0002$ , t-test) in melanoma cells. Moreover, our data showed that overexpression of ING4 inhibits

melanoma cell invasion by 46% through Boyden chamber assay when compared with vector control ( $P = 0.005$ , t-test). Furthermore, ING4-overexpressing melanoma cell showed significantly decreased MMP-2 and MMP-9 activity by 25% and 61% compared with vector control ( $P = 0.01$  and  $0.008$ , respectively). Taken together, our data indicated that ING4 inhibits melanoma cell migration and cell invasion and thus is an important regulator in the progression of human cutaneous melanoma.

## **POSTER #5**

### **BILATERAL NEUTROPHILIC DERMATOSIS OF THE HANDS ASSOCIATED WITH SMALL CELL CARCINOMA OF THE LUNG**

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Pyoderma gangrenosum is an uncommon inflammatory and ulcerative dermatosis, within the spectrum of the neutrophilic dermatoses. It usually presents as painful pustules or bullae which rapidly enlarge, producing central necrotic ulcers with overhanging, undermined violaceous borders. The etiology is unknown but there is an association with systemic disease in about 50% of cases. Most commonly, this is inflammatory bowel disease, but other related conditions include rheumatoid arthritis, leukemia, myeloma, myelodysplasia, hepatitis and, occasionally, solid tumors. The diagnosis is based clinically, with the exclusion of other causes of similar-appearing skin disease, along with supportive histologic findings. Neutrophilic dermatosis of the hands is a recently described clinical entity, comprising Sweet syndrome, pyoderma gangrenosum, and pustular (neutrophilic) vasculitis when they involve the hands. It is rare, with less than 100 published cases. It is often associated with systemic disease, including internal malignancy. Skin involvement may be the primary event with subsequent investigations revealing the underlying condition. There are two published reports of neutrophilic dermatosis of the hands occurring with lung cancer, one anaplastic carcinoma and one squamous cell carcinoma, and one published case of Sweet syndrome associated with adenocarcinoma of the lung. We report the first case, to our knowledge, of bilateral neutrophilic dermatosis of the hands in a patient with known small cell carcinoma of the lung.

## **POSTER #6**

### **EXPRESSION OF INTEGRIN $\alpha V\beta 6$ AND TGF- $\beta$ IN SCAR-FREE VS. SCAR-FORMING WOUND HEALING**

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Objectives: Integrin  $\alpha V\beta 6$  is mostly absent from adult epithelia but its expression is induced in wound healing, cancer and certain fibrotic disorders. In the present study, we investigated the potential for  $\alpha V\beta 6$ -mediated activation of fibrogenic TGF- $\beta 1$  and anti-fibrogenic TGF- $\beta 3$  during wound healing by studying the spatio-temporal co-localization of  $\alpha V\beta 6$  integrin with the molecules involved in TGF- $\beta$  activation in human gingival wounds. In addition, we compared the expression and localization of  $\alpha V\beta 6$  integrin along with its ligands, TGF- $\beta 1$  and TGF- $\beta 3$ , in scar-free gingival versus scar-forming skin

wounds in red Duroc pigs. Methods: Full-thickness excisional wounds were created in the gingiva of human volunteers, and in the gingiva and skin of red Duroc pigs. Wound healing rate was clinically and histologically assessed at different time points up to 60 days after wounding. Immunohistochemical analysis and real-time PCR were used to assess the localization and expression of  $\beta 6$  integrin, TGF- $\beta 1$  and TGF- $\beta 3$ . Results: The  $\alpha v\beta 6$  integrin was found to colocalize with both TGF- $\beta 1$  and TGF- $\beta 3$  in the wound epithelium of human gingiva. Analysis of the pig wounds showed that basal keratinocytes of the clinically healed gingival wounds continued to express  $\alpha v\beta 6$  integrin and TGF- $\beta 3$  while their expression was negligible in scar-forming skin wounds. Conclusion: The spatio-temporal colocalization of  $\alpha v\beta 6$  with TGF- $\beta 1$  and TGF- $\beta 3$  in human gingival wounds demonstrates a potential mechanism to regulate the activity of TGF- $\beta$  isoforms by  $\alpha v\beta 6$  integrin during wound healing. Prolonged expression of  $\alpha v\beta 6$  integrin and anti-fibrogenic TGF- $\beta 3$  in the gingival wound epithelium may be important in protection of gingiva from scar formation.

## POSTER #7

### COMPARISON OF SUN PROTECTION BEHAVIOURS AMONG METROPOLITAN AND NON-METROPOLITAN HEALTH REGIONS

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Because skin cancer is highly associated with ultraviolet radiation, public education programs have aimed to reduce skin cancer through decreasing sunlight exposure. In the present study, the sunburn rates and sun protection behaviours were compared between metropolitan and non-metropolitan Canadian health regions in Alberta and Prince Edward Island. The Canadian Community Health Survey Cycle 3.1 (2006) had 13574 individuals that responded to the sun exposure module. The primary and secondary outcomes were the presence of sunburn and sun protection behaviors respectively. These variables were compared between health regions that differed by their metropolitan status. Simple logistic regression analysis was performed and those variables that were statistically significant were offered to multiple logistic regression analysis. The sunburn prevalence within the preceding twelve months was significantly higher in the non-metropolitan (37.67%) compared to the metropolitan health region (32.38%) yielding a crude odds ratio of 1.20 (95% CI:1.11-1.31). In addition, respondents from the non-metropolitan health region spend a greater amount of time in the sun from 11am to 4pm (1.15,95% CI:1.05-1.26), and applied sunscreen to their face less frequently (1.39,95% CI:1.27-1.53). They were less likely to wear hats seldomly (0.87,95% CI:0.79-0.95). In a representative Canadian population, the sampled non-metropolitan health regions had higher rates of sunburns compared to metropolitan health regions. This effect was independent of age, sex, marital status, education, having a regular doctor and ethnicity. This discrepancy in outcomes and behaviours according to population size, if confirmed in larger scale studies, would be important factors to consider in optimizing the effectiveness of public education and primary prevention.

## POSTER #8

### **A UNIFIED APPROACH TO HUMAN MALIGNANCY**

Dr. G. O. Telford, Private Practice

There has been a dramatic increase in the frequency of cutaneous and systemic malignancies since WW2. A major behavioral change popularized by Coco Channel in the 1940's has been one of our love affair with the sun and outdoor lifestyles. Epidemiological studies have failed to identify the major causative factors of this epidemic with the exception of a cause and effect relationship between sun exposure and Squamous Cell Carcinoma. Streiland documented that 40% of normal people developed immunosuppression on exposure to Ultra Violet (UV) light. This reaction pattern labeled sun induced immunosuppression occurred in 95% of patients with multiple skin cancers and 100% of melanoma patients. The immunosuppression is systemic as well. Others have documented unique immunosuppression associated with exposure to UV A. A major role of the immune system is immune surveillance, i.e. to detect and destroy non self (malignant cells). Lack of recognition of malignant transformation may induce immune tolerance. Hypothesis. A major behavioral change "our love affair with the sun" is the causative agent in the dramatic rise in frequency of cutaneous and systemic malignancies. Epidemiological studies have failed to document this association due a lack of segregation of study groups based on the individual's reaction pattern to UV. This hypotheses could be tested by comparing the frequency of sun induced immunosuppression in an identified group ie patients with a diagnosis of breast cancer in remission. A frequency of 40% or lower would suggest no causative association, a frequency much higher ie melanoma at 100% would suggest a cause and effect relationship. This paper is submitted to stimulate academic discussion and to seek feedback on details of study design.

## POSTER #9

### **EXTRACELLULAR STRATIFIN ACTS AS AN ANTIFIBROGENIC FACTOR IN MODULATION OF EXTRACELLULAR MATRIX PROTEINS IN DERMAL FIBROBLASTS**

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Epidermal-mesenchymal communication plays a key role in regulation of extracellular matrix (ECM) during wound healing. Previously, we have demonstrated that keratinocyte-releasable stratifin stimulates matrix metalloproteinase-1 (MMP-1) expression in fibroblasts. Current study investigates the regulatory role of stratifin in the expression of ECM proteins using a pathway-specific microarray. We also studied the interactions at the cell surface to identify a receptor for stratifin. ECM gene expression profile in fibroblasts co-cultured with keratinocytes or treated with stratifin revealed significant increase in gene expression of MMP-1, stromelysin-1 (MMP-3), stromelysin-2 (MMP-10), collagenase-2 (MMP-8), and MT5-MMP. RT-PCR and Western blot were used to validate microarray results. To characterize interaction of stratifin with cell surface protein(s), a Receptor Binding Assay was performed by competing <sup>125</sup>I-stratifin with excess unlabelled protein. The results revealed a classical ligand-receptor binding curve with excess unlabelled stratifin competing with the bound <sup>125</sup>I-stratifin. This result was further supported by Cell Binding Assay where bound biotin-stratifin was detected by immunofluorescence at the cell surface of fibroblasts. Furthermore, we were able to

isolate stratifin in the plasma membrane fraction of cells incubated with exogenous biotin-stratifin. In conclusion, our results demonstrate that keratinocyte-releasable stratifin acts as a potent antifibrogenic factor by upregulating key MMPs in dermal fibroblasts and this induction appears to be initiated by interaction of exogenous stratifin with a specific cell surface protein.

## **POSTER #10**

### **ANALYSIS OF DEGREE OF LINEAR POLARISATION OF BACKSCATTERED LIGHT FROM POLARISED LASER LIGHT INCIDENT ON IN VIVO HUMAN SKIN**

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Background: Unscattered or weakly scattered light maintains its original polarization stage, whereas multiple-scattered light is randomly polarized. Therefore, the degree of linear polarization (DOLP) of backscattered light varies inversely with the average penetration depth, and relates to the optical, biochemical and morphological properties of skin. In particular, loss of collagen elasticity, and increasing melanin and blood concentrations have all been shown to increase DOLP. Objective: The aim of this pilot study is to explore and understand the depolarization behaviour on human skin. Methods: Polarized red and blue laser light were used to illuminate in-vivo the forearms of 4 human volunteers. Parallel and perpendicularly polarized images were captured with a CCD. The mean intensities of the images were then used to calculate the DOLP. Results: Backscattered red laser light was found to have a decreased DOLP relative to blue laser light because red light penetrates skin more deeply. Further, the DOLP for the female subject under blue laser illumination was found to be larger than the DOLP for the male subjects. This gender difference could be explained by previous published results showing that females have less collagen in their skin than males. Conclusion: We successfully measured the DOLP in-vivo on human volunteers. The differences in DOLP observed with incident wavelength and gender agreed with published data and could be explained by the biochemical and biophysical properties of skin, specifically the birefringent quality of collagen and the absorptive properties of the components of skin.

## **POSTER #11**

### **SKIN IMAGE ENHANCEMENT: COLOUR CALIBRATION**

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Colour calibration is crucial when it comes to medical applications, where the colour of the imaged objects is used for diagnosis. Images captured via most imaging devices are partially distorted in terms of their *colour* as well as *size* of the objects (e.g. skin lesions) in the image. Colour, in particular, would appear slightly differently under different illuminations. It is of high importance to ensure that colours presented in the captured image truly reflect the actual colours of the lesions. Colour distortion happens due to an undesired effect of the illumination. Therefore, we need to eliminate this effect to be able to retrieve the true surface reflectance (colour) of the lesions. One way to achieve this is to model the illumination change via a linear transformation model. In this model, we capture image of the skin lesion under a standard illumination (D65) and also under

another illumination (eg. office/laboratory light). We would then measure the sensor responses, i.e. Red-Green-Blue (RGB) of each pixel, from these two images, and perform a linear computation to come up with a 'transformation matrix'. This matrix models the change in illumination, and can be used to predict and generate the true colour of skin lesions under any illumination.

## **POSTER #12**

### **COMBINATION OF METHOTREXATE AND PREDNISONE IN THE TREATMENT OF CHRONIC SEVERE ALOPECIA AREATA OF THE SCALP: SAFETY AND THERAPEUTIC EFFICACY – PROJECT PROPOSAL**

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Alopecia areata (AA) is an autoimmune condition of great cosmetic concern and unpredictable, relapsing course. It is hypothesized to be an autoimmune disease mediated by lymphocytes directed at hair follicles. The purpose of this study is to examine prospectively the safety and efficacy of the combination of methotrexate and prednisone in the treatment of patients with chronic severe AA of the scalp. Common features between psoriasis and AA, including immunologic and therapeutic aspects, suggests that methotrexate, which has been shown to be a safe and statistically significant beneficial therapeutic modality for the treatment of psoriasis and other autoimmune disorders, may have therapeutic value in AA. Based on the impressive therapeutic responses seen in those with psoriasis treated with methotrexate, a similarly beneficial outcome is tentatively anticipated with treatment of those with AA. The methotrexate effect usually starts within six to eight weeks, during this period; the systemic corticosteroid can induce remission rapidly. The systemic corticosteroid will be tapered down as soon as the methotrexate starts to work. This is an open, single-center, investigator-initiated study. A total of 10 eligible patients will be enrolled in the study and they will receive daily oral administration of 40 mg of prednisone in tapering dose of 5 mg each week over a total period of 8 weeks and weekly oral administration of 25 mg of methotrexate for 24 weeks, to be followed by a 12-week post-treatment period after which the safety, efficacy, and durability of effect in treatment responders will be assessed.

## **POSTER #13**

### **THE ETIOPATHOLOGIC ROLES OF CXCR3/LIGANDS IN THE TUMORIGENESIS OF BASAL CELL CARCINOMAS**

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

Basal cell carcinoma (BCC) is initiated due to genetic mutations of the Sonic Hedgehog (Shh) pathway. Our previous research of immunoregulatory genes in BCCs indicated that expression of mRNA for the IFN- $\gamma$  induced chemokines CXCL11, 10, 9 and their receptor CXCR3 were significantly increased as compared to non-lesional skin epithelium. In this study, we examined the biochemical expression of CXCL11, 10, 9 and CXCR3 by immunohistochemistry (IHC) in normal skin and BCC tissues. Subsequently, we conducted a functional assay of the chemokines using HaCaT immortalized human keratinocyte cultures, IFN $\gamma$  treatment, and CXCL11 peptide supplementation. The IHC

results demonstrated that CXCR3 and its ligands were localized in the keratinocytes of the tumor masses in BCC biopsies. The addition of IFN $\gamma$  to HaCaT cell cultures did not result in significant cell proliferation; however, expression of the Shh pathway downstream targets STAT1, NF- $\kappa$ B1, Gli1, and Gli2 were upregulated in the cultured cells. The addition of CXCL11 peptide to HaCaT cell cultures led to significant increased cell proliferation associated with significant upregulation of mRNA for STAT1 and NF- $\kappa$ B1 in the cells. In conclusion, CXCL11, 10 and 9 may be significantly involved in the regulation of BCC keratinocyte growth. Such outcomes may ultimately provide an insight into novel strategies for BCC regression by suppressing the CXCR3/ligand pathway.

## **POSTER #14**

### **BASAL CELL CARCINOMA GENE EXPRESSION PROFILES RESEMBLE HAIR FOLLICLES BUT WITH SIGNIFICANT DIFFERENCES IN SPECIFIC PATHWAY ACTIVATION**

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Hair follicles (HF) and BCCs can be regarded as ordered and disordered skin appendages respectively and may utilize similar molecular mechanisms of growth. We wanted to examine the similarities and differences in gene expression patterns between BCCs and HF to define common growth mechanisms and gene expression patterns that distinguish an ordered skin appendage from a disordered skin growth. Nodular BCCs, non-follicular skin epithelium and the lower one third of the HF were obtained. Microarray analysis was performed and selected genes were validated using qPCR and histochemistry staining. Two differentially expressed gene sets were identified by significance analysis of microarray in BCC and HF verses skin epithelium respectively. Subsequently, multiple signaling pathway analyses were conducted. The results indicated that Notch, hedgehog, and WNT signaling pathways were involved in regulating formation of both HF and BCCs. However, Notch signaling, including tumor suppressor genes Notch 1,2, Jagged ligands 1,2, signaling inhibitor NUMB, downstream components Lunatic Fringe and Deltex proteins 1,2 and Notch target genes HES1, RBPSUHL, hairless protein and HES7, all showed selective differential activation in BCCs compared to HF. Our data provides compelling evidence that "tumorigenic" growth signaling pathways are commonly expressed in both HF epithelial progenitor regions and BCCs. However, the Notch signaling pathway was highly suppressed in BCCs as compared to HF. These results suggested differential expression of the Notch signaling pathway might play a crucial role in disordered BCC growth. The components of the pathway may be potential new targets in the development of new therapeutic approaches to BCCs.



## POSTER #15

### **REDUCED SCAR FORMATION IN ORAL MUCOSA COMPARED TO SKIN**

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Scar formation in skin can have devastating consequences causing discomfort and functional and esthetic concerns. Interestingly, wound healing in oral mucosa appears to proceed faster than in skin and results in less scar formation but there is little systematic data confirming this. In the present study, we hypothesized that oral mucosa is resistant to scar formation in red Duroc pigs that are prone to hypertrophic-like scar formation in skin. Our long-term goal is to find out the biological mechanisms that lead to better wound healing in oral mucosa and use this information to prevent scar formation in skin. Identical, full-thickness, excisional wounds were made in the gingiva of hard palate and dorsal skin of red Duroc pigs. Standardized images were obtained at different stages of healing to quantify wound contraction rate. Biopsies were collected for histological quantification of key wound healing cell populations by immunostaining and image analysis. Clinical and histological scar formation was quantified using scar assessment scales. Gingival wounds displayed significantly less clinical and histological scar formation than skin and this was associated with significantly reduced inflammatory reaction at the late stage of wound healing. The number of myofibroblasts remained significantly elevated in gingiva as compared to skin 60 days after wounding. Despite of presence of more myofibroblasts, gingival wounds showed significantly less contraction than skin wounds. The findings suggest that scar formation is a complex process and likely depends not only on the number of myofibroblasts but also on their environment regulating their function.

## POSTER #16

### **INCIDENCE AND CLINICAL OUTCOMES OF X-LINKED ICHTHYOSIS IDENTIFIED BY PRENATAL MATERNAL SERUM SCREENING FOR DOWN SYNDROME**

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Between August 2002 and August 2007, Maternal Serum Screening (MSS) was performed on approximately 90000 pregnancies in the province of British Columbia to screen for Down syndrome, trisomy 18, open spina bifida, Smith-Lemli-Opitz Syndrome (SLOS) and other fetal conditions. MSS analyzes levels of maternal serum AFP, uE3 and hCG. Pregnant patients who screen above the cut-off for SLOS, which is based on an algorithm developed by Palomaki et al, were referred to medical genetics for assessment. Patients with a male fetus and maternal serum estriol levels of 0.2 MoM or less were offered investigations for X-linked ichthyosis. Our study proposes to search the Medical Genetics Program Database to identify all cases referred to the program between August 2002 and August 2007 because of a positive screen for SLOS. All cases will be reviewed to ascertain the cases with a final diagnosis of X-linked ichthyosis. We will then review the clinical outcomes of these births, via in office clinical assessment, Infant's Dermatitis Quality of Life Index (IDQLI) scoring, and parents' predicted Children's Dermatology Life Quality Index (CDLQI) surveys. This study aims to aid in the prenatal counseling of mothers who test positive for X-linked ichthyosis in

pregnancy. The ascertainment of patients through maternal serum screening for Down syndrome should provide an unbiased collection of patients for this study.

#### **POSTER #17**

##### **DECORIN ENDOCYTOSIS IS REGULATED BY EGFR, IGF1R AND LRP-1 AND REQUIRES DECORIN-INDUCED FORMATION OF REACTIVE OXYGEN SPECIES IN HUMAN FIBROBLASTS**

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Decorin is a small leucine-rich proteoglycan that is abundantly expressed by fibroblasts during wound healing while its reduced abundance in the extracellular matrix (ECM) appears to promote fibrosis and growth of transformed cells. Decorin regulates several key processes in tissues, including collagen fibrillogenesis and bioavailability of transforming growth factor-beta. In certain cells, it also interacts with cell surface receptors and elicits signaling pathways that regulate cell growth and gene expression. However, these functions appear cell-type specific. In the present study, we hypothesized that in fibroblasts, decorin interacts with multiple cell surface receptors to regulate cell signaling and decorin turnover. Primary human gingival fibroblasts were treated with decorin, and its binding to distinct cell surface receptors and its effect on intracellular signaling and endocytosis were analyzed using various cell culture and molecular biology techniques and utilizing specific pharmacological inhibitors, function blocking antibodies and RNA interference. Decorin associated with epidermal growth factor receptor (EGFR), insulin-like growth factor-1 receptor (IGF1R) and LDL receptor-related protein-1 (LRP-1) on fibroblast cell surface and induced rapid tyrosine phosphorylation on these receptors followed by downstream activation of mTOR and p70S6K and NAD(P)H and mitochondrial electron transport-dependent formation of reactive oxygen species (ROS). Decorin-induced ROS formation was critical for decorin endocytosis by the clathrin-mediated pathway and its endosomal degradation and recycling. Thus, decorin signaling through EGFR, IGF1R and LRP-1 and subsequent induction of ROS formation are critical for decorin endocytosis in fibroblasts and provide a mechanism by which these cells may regulate decorin abundance in the ECM. Supported by CIHR.

#### **POSTER #18**

##### **QUANTITATIVE ANALYSIS OF SKIN MOLECULES USING RAPID NEAR-INFRARED RAMAN SPECTROSCOPY**

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Background: Raman spectroscopy is a non-invasive optical technique that is very sensitive to the structure and conformation of biochemical constituents. It has been successfully used to study dysplasia and cancer in a variety of human tissues including skin. Because skin is the largest organ in humans, it is very important to study the variability of Raman spectra for different body sites. In this presentation we report our

quantitative analysis of normal skin Raman spectra of twenty-five body sites. Methods and Patients: An integrated real-time Raman system was used to measure the Raman spectra of normal skin in vivo. Thirty healthy volunteers were enrolled in this study. Twenty five body sites of each volunteer were measured including: forehead, nose, cheek, earlobe, shoulder, neck, flexor and extensor arm, volar and extensor forearm, palm, hand, dorsum and palmar phalanx, nail plate, upper, middle and lower back, chest, upper and middle abdomen, anterior shin, anterior and posterior thigh, and posterior leg. Partial least square (PLS) analysis was used to quantify the skin molecules from the in vivo Raman spectra. Results: We find that the absolute Raman intensity differs from person to person and from body site to body site. However the normalized Raman spectra show minimal variation for the same body site. Human skin molecules can be modeled and quantified from in vivo Raman spectra using PLS. It is particularly interesting to find that the distribution of skin molecules is clustered for the same body site.