

2016 Oral Abstracts

A 13-YEAR RETROSPECTIVE STUDY OF BASAL CELL CARCINOMA IN A CANADIAN POPULATION: A COMPARISON BETWEEN ANATOMICAL LOCATION AND HISTOPATHOLOGIC SUBTYPES

Rivers JK MD FRCPC, FAAD¹, Mistry BD BHS (Hons)², Hung T MD, FRCPC³, Vostretsova K MD², Mistry N MD, FRCPC, FAAD⁴

¹The Department of Dermatology and Skin Science, University of British Columbia and Pacific Dermaesthetics, Vancouver, British Columbia. ²Faculty of Medicine, University of British Columbia, Vancouver, British Columbia. ³DynalifeDx, University of Alberta, Departments of Pathology and Dermatology, University of Alberta, Edmonton, Alberta. ⁴Department of Medicine (Dermatology), University of Toronto, Toronto, Ontario

Although basal cell carcinoma (BCC) is the most common type of skin cancer, there are no Canadian studies to document the histological variants of this tumor and their relationship with age, gender and body site. We investigated the relationship between the different BCC histopathologic subtypes and anatomic distribution of the BCC in a Canadian population. Between 1993 and 2005, the charts of all patients diagnosed with BCC in a single private dermatology practice in Vancouver, Canada, were retrospectively reviewed. Only the first two histologically confirmed tumors were collected from each patient. From a total of 418 patients with 1005 tumors, 557 qualifying BCCs were identified; 418 were a first BCC diagnosis. Overall, nodular BCCs accounted for 58% of all tumors and 66% were situated on the head/neck (OR=3.0, 95% CI=2.1-4.3, p<0.0001) and in older people (OR=1.6, 95% CI=1.1-2.1, p=0.02). Superficial BCCs were often localized to the trunk (OR=3.2, 95% CI=2.1-4.9, p<0.0001) and almost half were evident in those between the ages of 40-59 years (OR=1.8, 95% CI=1.2-2.7, p=0.004). Infiltrative and mixed BCCs appeared predominantly on the head and neck (OR=2.9, 95% CI=1.6-5.2, p<0.0001). Nodular (OR=3.1, 95% CI=2.1-4.5, p<0.0001) and mixed BCCs (OR=6.3, 95% CI=1.5-26.9, p=0.004) were more common in men. Infiltrative (OR=2.4, 95% CI=1.5-4.1, p=0.0003) and superficial BCCs were more common in women (OR=3.7, 95% CI=2.5-5.7,

p<0.0001). Our results show a preference of at least some BCC subtypes for certain anatomical locations and gender. This suggests possible differences in the pathogenesis of this malignancy.

Category: Early experiments with well-defined objectives/hypotheses

ANTI-STOKES FLUORESCENCE SPECTROSCOPY AND IMAGING FOR CUTANEOUS PORPHYRIN DETECTION

Yunxian Tian^{1,2,3}, Jianhua Zhao^{1,2}, Zhenguo Wu^{1,2}, Mohammed Al Jasser¹, Harvey Lui^{1,2}, David I. McLean¹, Haishan Zeng^{1,2,3}

¹Photomedicine Institute - Department of Dermatology and Skin Science, University of British Columbia & Vancouver Coastal Health Research Institute, Vancouver, Canada. ²Imaging Unit - Integrative Oncology Department, BC Cancer Agency Research Centre, Vancouver, Canada. ³Department of Physics and Astronomy, University of British Columbia, Vancouver, Canada

Porphyrins produced by *Propionibacterium acnes* represent the principal fluorophore associated with acne, and appear as orange-red luminescence under the Wood's lamp. Assessment of acne based on Wood's lamp (UV) or visible (VIS) light illumination is limited by photon penetration depth and has limited sensitivity for earlier stage lesions. Two-photon excitation fluorescence detection has better imaging depth, but requires expensive femtosecond (fs) laser excitation. Anti-Stokes fluorescence as a new technology could be generated by low cost, continuous-wave laser source. Different from two-photon fluorescence realized by ultra short laser pulse excitation, anti-Stokes fluorescence allows us to focus at specific molecules since most other molecules failed to fulfill the excitation conditions. We applied this technology to a complex biological system - facial sebum. Anti-Stokes fluorescence under NIR CW excitation is more sensitive and specific for porphyrins than UV- or visible light-excited regular (Stokes) fluorescence and fs laser-excited multi-photon fluorescence. This approach also has higher image contrast compared to NIR fs laser-based multi-photon fluorescence imaging. The anti-

Stokes fluorescence of porphyrins within sebum could potentially be applied to detecting and targeting acne lesions for treatment via fluorescence image guidance.

Category: pilot/exploratory experiments

AMELANOTIC LENTIGO MALIGNA MELANOMA OF THE HEAD AND NECK: MOHS MICROGRAPHIC SURGERY AS THE DEFINITIVE TREATMENT OF A CLINICALLY INVISIBLE TUMOR

Ponzo MG¹ and Kossintseva I¹

¹Department of Dermatology and Skin Sciences, University of British Columbia, Vancouver, British Columbia, Canada

Background: Diagnosis of amelanotic lentigo maligna melanoma (ALMM) is delayed owing to the lack of pigmentation and disease is often advanced at presentation. Excision with appropriate margins is the treatment standard, however, clinical estimation of the border can result in positive margins post-excision, necessitating further surgery. ALMM of the head and neck pose additional challenges because closure of defects is performed with flaps. If margins are subsequently found to be positive, deciphering the location of tumor involvement is nearly impossible. **Objectives:** We describe two cases treated by Mohs micrographic surgery (MMS) that would not have been cleared by wide local excision alone and review the literature regarding the presentations and treatment challenges of ALMM. **Methods:** Both patients presented with histologic diagnoses of melanoma, one with a barely perceptible biopsy scar on the left eyelid/infra-orbital cheek (Breslow 1.8mm), and the second with a nodule on the right helix (Breslow 10mm). Due to the location, aggressive histology, amelanotic appearance and no apparent surrounding skin surface changes, MMS was elected to maximize margin control.

Results: After standard margins were taken, both cases revealed remaining invasive and *in situ* tumor component that required further surgery to achieve clear margins. Final anatomical defect sizes in each case were far larger than anticipated. **Conclusions:** Because of clinician's

inability to judge the surface spread of this clinically invisible tumor, MMS allows for immediate histologic feedback on tumor margins, and thus offers the most definitive treatment. Subsequent reconstruction with flaps can proceed without apprehension.

Category: Early experiments with well-defined objectives/hypotheses

EXTENSIVE DERMATOPHYTOSIS: A CLUE TO ADULT ONSET PRIMARY IMMUNODEFICIENCY

Rayan Alkhodair¹, Jan Dutz²

1- King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

2- University of British Columbia, Vancouver, BC, Canada

Primary immunodeficiencies may present in adulthood with atypical autoimmunity, cytopenias and infections. Often, there are clues to the diagnosis in cutaneous manifestations. Good syndrome (GS) was first described by Dr. Robert Good in 1954 and is an example of an as of yet poorly characterized immunodeficiency. To date, less than 200 cases of GS have been reported in the literature. The clinical features of this syndrome include thymoma, immunodeficiency and hypogammaglobulinemia. Patients are at increased risk of death secondary to infections, autoimmunity and hematologic complications. With regards to the autoimmune presentations, pure red blood cell aplasia and myasthenia gravis were the most prevalent, followed by oral lichen planus, aplastic anemia, macrocytic anemia, autoimmune hemolytic anemia, monoclonal gammopathy, diabetes mellitus, polyarthropathy, and myelodysplastic syndrome. More recent case reports have described associations of GS with polymyositis and autoimmune retinopathy. Management consists of thymectomy, intravenous immunoglobulins, treatment of associated infections and autoimmune disorders. Recent data suggests that mortality and morbidity related to autoimmunity and infections is greater than in common variable immunodeficiency.

We describe two cases of Good Syndrome diagnosed with an atypical cutaneous presentation of extensive dermatophytosis. The first patient had a history of excised thymoma and both patients had myasthenia gravis. Further investigations confirmed the diagnosis. We propose that generalized dermatophytosis may be a clue to a primary immunodeficiency such as Good Syndrome. Awareness of generalized dermatophytosis as a clue to immunodeficiency may lead to earlier recognition and possibly decreased mortality and morbidity in GS and similar conditions.

Category: Case-series

AUTOFLUORESCENCE BIOMARKERS OF VITILIGO REVEALED BY EXCITATION-EMISSION MATRIX SPECTROSCOPY

Jianhua Zhao^{1,2}, Vincent Richer¹, Mohammed AlJasser¹, Soodabeh Zandi¹, Nikiforos Kollias¹, Sunil Kalia¹, Haishan Zeng^{1,2}, Harvey Lui^{1,2}

¹ Photomedicine Institute - Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute, Vancouver, Canada. ² Imaging Unit - Integrative Oncology Department, British Columbia Cancer Agency Research Center, Vancouver, Canada

Background: Fluorescence signals depend on excitation light intensity, fluorophore absorption, and the efficiency with which the absorbed photons are converted to fluorescence emission. The appearance and optical features of vitiligo have heretofore been explained primarily on the basis of reduced epidermal pigmentation, resulting in characteristic white patches on the skin.

Objective: The objective of this study is to explore the fluorescence properties of vitiligo using fluorescence excitation-emission matrix (EEM) spectroscopy. **Patient and Method:** Thirty five (35) volunteers with vitiligo were measured using a double-grating spectrofluorometer with excitation and emission wavelengths of 260-450 nm and 300-700 nm respectively. **Results:** As expected the most pronounced difference between the spectra obtained from vitiligo lesions

versus normal skin was that the overall fluorescence emission was much higher in vitiligo; these differences increased at shorter wavelengths, thus matching the spectral absorption of epidermal melanin. When comparing the fluorescence excitation spectra from vitiligo to normal skin we also detected three distinct spectral bands centered at 280, 310, and 335 nm. These three excitation signals may possibly be due to inflammation, reactive oxygen species, and collagen or keratin cross links respectively. **Conclusions:** These autofluorescence peaks may serve as biomarkers of vitiligo for diagnosis or monitoring of vitiligo therapy. Furthermore their presence indicates that there are more optical differences between vitiligo and normal skin than can be accounted for by melanin alone.

Category: Pilot/exploratory experiments

THE USE OF MINOCYCLINE IN PROMOTING SECONDARY INTENTION HEALING OF DEFECTS FOLLOWING MOHS MICRORAPHIC SURGERY

Daram Singh¹ and Iren Kossintseva¹

¹Dermatologic Surgery Centre, Department of Dermatology and Skin Sciences, University of British Columbia, Vancouver, Canada.

Background: Tetracyclines are reported to increase collagen content and reduce connective tissue degeneration through their inhibitory effects on collagenolytic matrix metalloproteinases (MMPs), whilst also having anabolic potential in periosteal fibroblasts. **Objectives:** While there is a paucity of literature on the use of tetracyclines in Mohs Micrographic Surgery (MMS) surgical defects allowed to heal by secondary intention, the tetracycline antibiotic minocycline has been reported in the dental literature for its matrix stimulatory effects on connective tissue and bone. Furthermore, through its inhibition of MMP's, immunomodulatory and anti-inflammatory effects, it has also proven beneficial in the healing of chronic venous ulcers. Our aim is to bridge and bring this knowledge into the post-operative practice of Mohs surgeons. **Methods:** We report a series of surgical defects following MMS, which were allowed to heal by

secondary intention. **Results:** The granulation of surgical wounds was significantly hastened by postoperative course of oral minocycline 100mg daily. These defects included areas of exposed bone where periosteum was stripped as part of the tumour removal. Lacking periosteum normally impedes granulation process. **Conclusions:** Given its reported beneficial effects on the healing milieu, minocycline represents a therapeutic consideration as adjuvant therapy for wounds allowed to heal by secondary intention or in those wounds responding poorly to basic wound care. Our post-operative implementation of minocycline as an aid to secondary intention healing demonstrates successful and fast granulation of surgical defects over exposed bone.

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

GAINING LARGE COVERAGE WITH SMALL ISLAND PEDICLE FLAPS IN TIGHT COSMETIC SUBUNITS: TAKING ADVANTAGE OF ROTATION AND Pincer PRINCIPLES

Michael Samyca¹, Irènn Kossintseva¹

¹Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada

Background: Island pedicle flaps (IPFs) are widely used as “V to Y” advancements in reconstructive surgery due to their versatility, tissue efficiency and excellent clinical outcomes. While IPF rotations and ‘pincer flap’ modifications have been sparsely described, these are grossly underused in IPF practice. Objective: We sought to demonstrate that principles of both rotating IPFs and pincer technique can be used alone or together in a variety of situations, including for defects traditionally considered too large for classic IPF design. Methods: Our technique is described and a number of cases are presented with photographs. Results: Modifications to the flap are simple to perform. Reconstruction using these flaps bears minimal complications and delivers good cosmetic results. A greater curvature of rotation allows greater

length of coverage. Leading with the superior tip of the triangle or creating a pincer flap lengthens coverage even further. Conclusions: Reconstruction of large defects in small cosmetic subunits of the face such as the nasal ala can be performed using principles of both rotating IPFs and 'pincer flap' technique. Degree of rotation is directly related to length of coverage. Using these techniques, larger defects that previously would have been reconstructed using flaps that cross cosmetic boundaries can now be reconstructed within the cosmetic unit, thus improving aesthetic outcomes.

Category: Early experiments with well-defined objectives/hypotheses

Autoimmune Gigantomastia is Associated with Local Type-1 Interferon and Rank Ligand Expression

Misha Zarbafian¹, Mehran Ghoreishi², and Jan P. Dutz².

¹Faculty of Medicine, University of British Columbia, Vancouver, Canada, ²Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada.

Background/Purpose: Gigantomastia is characterized by rapid onset of massive breast hypertrophy. Gigantomastia has been associated with autoimmune diseases including rheumatoid arthritis, systemic lupus erythematosus (SLE), and psoriasis, although the mechanism remains unclear. Progesterone receptor (PR) signaling induces breast glandular cell proliferation, and the tumour necrosis factor family member RANKL is required for PR-induced mammary gland development and proliferation. We sought to determine whether local inflammation, specifically type-1 interferon-related protein expression in breast tissue, correlates with RANKL expression and the development of breast hypertrophy in autoimmunity. **Methods:** We examined seven cases of autoimmune-associated gigantomastia. Paraffin-embedded formalin-fixed breast tissue samples were studied for human myxovirus resistance protein 1 (MxA, a type-1 interferon dependent antigen), RANKL and PR expression by immunohistochemistry. **Results:** Six out of seven cases demonstrated expression of RANKL

in mammary gland epithelial cells and ducts. Cases with RANKL expression also demonstrated glandular, endothelial, and inflammatory infiltrate-associated MxA expression. PR expression was identified in all samples. Normal breast tissue expressed PR, but not MxA or RANKL. There was a positive correlation between the intensity of MxA and RANKL expression. Topical toll-like receptor 7 agonist is a potent inducer of interferon- α , and induced RANKL expression in mice. **Conclusion:** Dysregulated expression of type-1 interferon-related proteins is sufficient for the development of systemic and localized autoimmunity. Local expression of type-1 interferon-related proteins within breast tissue may be associated with RANKL expression and the development of gigantomastia. These observations suggest that denosumab, a RANKL inhibitor, may be therapeutically useful in the treatment of autoimmune-associated gigantomastia.

Category: (3) Applied/functional experiments (animal models of disease and in vivo studies, etc)

PATIENT KNOWLEDGE AND SATISFACTION AT THE "SCREEN" (SKIN CANCER POST- TRANSPLANT) CLINIC

Baldwin, Sarah¹ and Au, Sheila²

¹Medical student, University of British Columbia, Faculty of Medicine, Vancouver, Canada.

²Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada and Division of Dermatology, Department of Medicine, St. Paul's Hospital and Providence Health Care, Vancouver, Canada.

Background: We sought to determine skin cancer risk awareness and knowledge in post-transplant patients prior to and following attendance at the SCREEN (Skin Cancer Post-Transplant) clinic at St. Paul's Hospital in Vancouver B.C. Patient satisfaction was also measured with a Likert Scale score after clinic attendance to help determine quality of care.

Methods: Separate questionnaires were mailed to 2 different populations - 583 pre-SCREEN (hadn't attended the clinic) patients and 240 post-SCREEN (had attended the clinic) patients. 221 (38%) pre-SCREEN and 81 (34%) post-SCREEN anonymous questionnaires were returned.

Data was analyzed using the statistical program "R"; McNemar's chi-squared test was used to evaluate statistical significance. **Results:** Seventy-seven percent of pre-SCREEN patients knew of their increased risk of skin cancer, while 80% felt they had inadequate access to a dermatologist for screening. Regarding the SCREEN Clinic, the majority of patients assigned the rating "good" or "excellent" to the categories of accessibility (66%), quality of care (77%), procedures (86%), and interaction with the dermatologist (80%) and program assistant (84%). Eighty-six percent felt the clinic enhanced their care, and 96% thought it should continue to operate. There was a statistically significant difference ($p < 0.05$) before and after clinic attendance in patient knowledge and risk avoidance. **Conclusion:** Post-SCREEN patients demonstrate statistically significant differences in key areas relating to prevention and knowledge about skin cancer, and show high levels of satisfaction in areas of accessibility, quality of care, procedures, and staff interactions.

Category: Pilot/exploratory experiments

The potential use of detergent free decellularized dermal matrix transplantation on full thickness skin wounds in mouse model

Ali Farrokhi, Mohammadreza Pakyari, Layla Nabai, Ryan Hartwell, Reza Jalili, Aziz Ghahary.

Professional Firefighters' Burn & Wound Healing Research Laboratory, Department of Surgery, International Collaboration on Repair Discoveries (ICORD), University of British Columbia, Vancouver, Canada.

Introduction: Acute and chronic wounds affect millions of people around the world. Covering the skin defects is essential for wound healing. Among current strategies for skin coverage, extracellular matrix-based biomaterials such as acellular dermal matrix (ADM) have many inherent advantages over synthetic polymer materials. These scaffolds have a high mechanical strength and retained biological activity. **Objectives:** The primary objective of this study was to

develop a detergent-free decellularization method for preparing ADM that efficiently removes cells and maintains the mechanical and structural integrity of the tissue. To have more clinically relevant data and provide head-to-head comparison of different ADMs, as a secondary objective we evaluated the outcome of using these ADMs for transplantation in full thickness skin wounds in a mouse model. **Methods:** Three decellularization methods were employed: ionic and non-ionic detergent-based methods and detergent free method. Scaffold variants were evaluated for mechanical and biological characteristics as well as transplantation on full thickness wounds in a mouse model. **Results:** All three methods produced dermal matrix with no detectable cell remnants and could support fibroblast cell growth and infiltration. Although they had the same amount of collagen in compare to normal skin, only in the detergent free method there was no change in glycosaminoglycans (GAGs) content, Elastin integrity and mechanical strength of scaffold. Three weeks after transplantation, the results showed reepithelialization, angiogenesis and migration of host cell into scaffolds with no immunogenic reaction in all ADM types tested.

Conclusion: Our results emphasize on advantages of detergent free method for decellularization of skin and suggest considering both *in vitro* and *in vivo* outcomes for evaluating the ADM quality.

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

COULD MELASMA BE A VASCULAR DISORDER? AN OPTICAL APPROACH

Pegah Kharazmi¹

quality of life. Melasma is believed to be a pigmentary disorder; however unique morphology of melasma and the relationship between human melanocytes activity and angiogenic factors leads to the hypothesis that abnormal cutaneous blood vessels are involved in the pathogenesis of melasma. In this study, we use a non-invasive optical method and image analysis to investigate the vascular component of melasma lesions. For this purpose, we acquire dermoscopy images of melasma patients recruited in Vancouver Skin Care Centre. Using our previously developed technique to study skin vascularization, we decompose the melasma lesion into melanin and hemoglobin channels by performing independent component analysis on the RGB image of the lesion. By clustering each of the channels, we then extract melanin maps and hemoglobin maps to outline the locations and quantify the degree of pigmentation and vascularization. Subsequently, we co-register the pigment and blood maps in order to study the patterns of melasma and find a correlation between the severity of the disease and the presence of vascular component. Our objective is to obtain a better understanding of the pathogenesis of melasma which would lead to better therapeutic solutions.

Category: Early experiments with well-defined objectives/hypotheses

DOES THE VISIBILITY OF SUNSCREENS ON THE SKIN CHANGE OVER TIME FOLLOWING APPLICATION?

Diana Diao¹, Vincent Richer², Pegah Kharazmi^{3,4}, Sunil Kalia¹, Tim Lee^{1,3}, Harvey Lui^{1,3}

¹Department of Dermatology and Skin Science, Vancouver General Hospital, University of British Columbia & Photomedicine Institute, Vancouver Coastal Health Research Institute. ²Department of Medicine, Dermatology Division, Centre Hospitalier de l'Université de Montréal, Québec, Canada. ³Departments of Cancer Control Research Program and Integrative Oncology – Imaging Unit, British Columbia Cancer Agency, Vancouver, Canada. ⁴Biomedical Engineering, University of British Columbia

Background: The visibility of sunscreens on the skin after application often influences adherence. Standardized digital photography and computer analysis has previously been used to objectively assess the visual appearance of different sunscreen products on the skin. Within 30 minutes after application to the skin, sunscreens may appear less visible. This phenomenon has not been studied previously; demonstrating time-dependent visibility changes may influence sunscreen-use behavior. **Objective:** To measure sunscreen visibility on the skin as a function of time for 30 minutes following application. **Methods:** In this pilot study, three different sunscreens were applied at timed intervals (0, 1, 5, 10, and 30 minutes) to the backs of three subjects at 2mg/cm². Standardized photographs were taken at baseline and at 30 minutes using a digital SLR camera. L*a*b color values were extracted from images of sunscreen and control areas (without sunscreen). Differences in visible color as measured by the ΔE between sunscreen and control sites were calculated. **Results:** All sunscreens applied were visible for all time points up to 30 minutes when compared to control areas without sunscreen (ΔE range 3.0 to 18.8). ΔE was dependent on the type of sunscreen (physical vs. chemical), which was consistent with our previous study. However, ΔE changes with respect to time were not significantly different from ΔE variations in control areas without sunscreen. **Conclusion:** Time-dependent visibility changes following sunscreen application could not be demonstrated using our current photographic method; refinement of this technique as well as consideration of other techniques will be necessary.

Category: Pilot/exploratory experiments for study design

SUM-12 AS A PRO-METASTATIC FACTOR IN MELANOMA

Xue Zhang¹, Mingwan Su^{1,2}, Yabin Cheng¹, Laura Graziano¹, Gang Wang³, Yu Lei¹, Magdalena Martinka³, Youwen Zhou^{1,2}.

¹Molecular Medicine Lab, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada. ²Vancouver Coastal Health Research Institute, Vancouver, Canada. ³Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, Canada.

Melanoma is the malignancy originated from melanocytes; if detected early, melanoma has a high 5-year survival rate of between 90 and 99%, but this rate drops dramatically to between 10% and 15% once it has metastasized. Using high-throughput methods screening for genes highly enriched in melanoma tissues, we have identified SUM-12 (coded name) as one of the most significantly up-regulated genes in melanoma biopsies compared to normal nevi and skin tissues. In addition, other members of SUM-12 gene have been shown to be involved in regulating cellular extracellular matrix and promoting cancer metastasis. Since among this gene family, SUM-12 is the only one to be significant up-regulated, we hypothesize that SUM-12's aberrant up-regulation is contributed to progression and mortality caused by melanoma. To test the hypothesis, we have performed real-time PCR and Western blot, which detected a significantly higher expression both on mRNA and on protein levels. Additionally, Tissue Microarray with 427 biopsies showed the presence of SUM-12 in melanoma patients is significantly associated with more advanced melanoma stages and worse survival outcomes. Furthermore, functional studies on proliferation, migration, and apoptosis of melanoma cell lines will be conducted. This study will unravel SUM-12 expression patterns and functional effects in melanoma progression. If the important roles of SUM-12 are confirmed in melanoma, this protein will be potentially a useful biomarker for prognostication and a target for developing novel melanoma therapies.

Category: Early experiments with well-defined objectives/hypotheses

SELECTIVE BLOOD VESSEL CLOSURE VIA NONLINEAR ABSORPTION OF AN ULTRAFAST FEMTOSECOND LASER

Yimei Huang^{1,2}, Harvey Lui^{1,2}, Jianhua Zhao^{1,2}, David I. McLean¹, Haishan Zeng^{1,2}

¹Photomedicine Institute - Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute, Vancouver, BC, Canada

²Imaging Unit - Integrative Oncology Department, British Columbia Cancer Agency Research

Center, Vancouver, BC, Canada.

Background: Abnormal blood vessels can appear on the skin from a variety of different pathological processes including developmental anomalies (port wine stain), inflammation (rosacea), and photodamage (actinic telangiectasia). At the present time, these vessels are typically treated with pulsed lasers via a linear light absorption process, but this therapy is associated with some limitations. Non-linear photon absorption using ultrafast lasers is inherently more precise than using conventional pulsed vascular lasers, and offers an alternative approach for achieving selective photothermolysis of pathologic cutaneous vasculature. **Methods:** An ultrafast femtosecond (10^{-15} second), near infrared (830 nm) laser will be used to achieve nonlinear photon absorption that is deep and precise. Mouse ear blood vessels are used in this study as a model for targeting cutaneous blood vessels. A multimodal optical system has been developed to perform the treatment under imaging guidance with reflectance confocal and multiphoton fluorescence microscopy for real-time monitoring of blood vessel closure. **Results and Conclusions:** The results showed that targeted blood vessel closure was achieved, suggesting that femtosecond laser therapy has the potential to provide individualized therapy and obtain better improvement to the vascular skin lesions.

Category: Pilot/exploratory experiments

TOX PLAYS AN ONCOGENIC ROLE IN CUTANEOUS T CELL LYMPHOMA THROUGH INHIBITING TUMOR SUPPRESSORS CDKN1B AND CDKN1C

Yuanshen Huang^{1,3}, Ming-Wan Su^{1,2}, Xiaoyan Jiang³, and Youwen Zhou^{1,2}

¹Molecular Medicine Laboratory, Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada; ²Chieng Genomics Center, Vancouver Coastal Health Research Institute, Vancouver, BC, Canada; ³Terry Fox Laboratory, BC Cancer Agency, Vancouver, BC, Canada

TOX is a critical thymocyte development regulator, which is lowly expressed upon T cell maturation. Previously we found that TOX is aberrantly expressed in cutaneous T-cell lymphoma (CTCL), and contributes to the malignant behaviours of CTCL cells in that TOX suppression induces apoptosis and cell cycle arrest. However, it remains unknown how TOX mechanistically controls the CTCL biology. The objective of this study is to identify potential TOX downstream molecules in CTCL. Given that TOX inhibition leads to marked cell cycle arrest in multiple CTCL cell lines, a list of critical cell cycle regulators were evaluated, among which CDKN1B and CDKN1C expression were found to be up-regulated upon TOX inhibition. Western blotting confirmed the increase of p27 (encoded by CDKN1B) and p57 (encoded by CDKN1C) protein levels in TOX-suppressed cells. Intriguingly, CDKN1B and CDKN1C have been shown to play dual roles in cell cycle regulation and apoptosis. To examine if the increased CDKN1B and CDKN1C are responsible for the growth inhibitory effect, a second gene knockdown for either CDKN1B or CDKN1C was performed in TOX-suppressed CTCL cells, which partially reversed the growth inhibition by TOX suppression. Furthermore, transcriptome analysis between TOX-suppressed cells and control cells uncovered additional genes involved in mediating TOX's effects in CTCL. Collectively, we provide evidence that TOX represses the expression of CDKN1B and CDKN1C in CTCL cells, therefore resulting in uncontrolled cell cycle progression and apoptosis resistance in CTCL. Therapeutic approaches targeting TOX and/or CDKN1B/CDKN1C may be useful in treating CTCL.

Category: Early experiments with well-defined objectives/hypotheses

Anxiety and Depression in Patients with Hyperhidrosis: Prevalence and Predisposing Factors

Rayeheh Bahar¹, Yudan Liu², Arlie Phillips¹, Rachel Yuanshen Huang¹, Mingwan Su¹, Sunil Kalia¹, Sen Yang³, Xuejun Zhang³, Pingyu Zhou², Youwen Zhou¹

¹Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada; ²Shanghai Skin Hospital, Tongji University, Shanghai, China; ³Department of Dermatology, Anhui Medical University, Hefei, Anhui, China.

Background: There are conflicting data about the correlation of hyperhidrosis and stress

symptoms. **Objective:** We sought to compare the prevalence of anxiety and depression in hyperhidrosis and non-hyperhidrosis patients. **Subjects and Methods:** We examined 2017 consecutive dermatology outpatients from Vancouver, Canada and Shanghai, China, using GAD-7 and PHQ-9 scales for anxiety and depression assessments. Multivariate logistic regression analysis was also performed to evaluate the effects of demographic variables. **Results:** The prevalence of anxiety and depression was 21.3% and 27.2% in hyperhidrosis patients, respectively, and 7.5% and 9.7% in patients without hyperhidrosis, respectively (P-value<0.001). There were positive correlations between hyperhidrosis severity and the prevalence of anxiety and depression. **Limitation:** The data from the questionnaires relied on the accuracy of patients' self-reports. **Conclusion:** Both single-variant and multivariate analyses showed that anxiety and depression were more prevalent in patients with, than without, hyperhidrosis. There might be a need for parallel treatment for anxiety and depression in patients with hyperhidrosis in order to alleviate the sweating.

Category: Early experiments with well-defined objectives/hypotheses

DISTRIBUTION AND CLEARANCE OF 5-AMINOLEVULINIC ACID-INDUCED PROTOPORPHYRIN IX FLUORESCENCE IN SKIN TISSUE

Wenbo Wang^{1,2,3}, Nikiforos Kollias¹, Sunil Kalia¹, Harvey Lui¹, Haishan Zeng^{1,2}

¹Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada. ²BC Cancer Agency Research Centre, Vancouver, Canada. ³Biomedical Engineering, University of British Columbia, Vancouver, Canada.

Background: The use of 5-aminolevulinic acid (ALA)-induced protoporphyrin IX (PpIX) has been established for fluorescence visualization and photodynamic therapy (PDT) of skin lesions such as basal cell carcinoma and actinic keratosis. However, the mechanism of PpIX distribution and clearance after administration of ALA in skin is incompletely understood. Previous studies mainly focused on using ultraviolet excitation for PpIX detection with fluorescence

spectroscopy. Though more effective for PpIX visualization, UV light has a superficial penetration depth, limiting the ability to investigate distribution of induced PpIX in deeper layers. Within the visible range, the excitation of PpIX peaks at 545, 575, and 632 nm. **Methods:** In this experiment, a high-speed excitation emission matrix (EEM) fluorescence spectrometer with excitation light in the visible range (550–750 nm) was used to study the dynamics of ALA-induced PpIX in murine skin. PpIX was induced in mouse skin by topical or systemic application of ALA. Over a period of 24 to 48 hours, spatially resolved relative PpIX distribution in terms of EEM peak intensity as a function of radial distance from application sites were measured. **Conclusions:** The time dependent variation of relative PpIX concentration at different distances from the topical application site provides valuable information to help guide topical application of ALA for more efficient photodynamic therapy of skin lesions.

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

Hair Distribution Width: A novel technique for evaluation of pattern hair loss and its automation using a smartphone

Ali Majdzadeh¹, Leopoldo Duailibe Nogueira Santos¹, Thomas Chu¹, Mohammed AlJasser^{1,2}, Hengameh Mirzaalian³, Jerry Shapiro^{1,4,5}, Ghassan Hamarneh³, Harvey Lui^{1,4}, Tim K. Lee^{1,3,4,6}

¹Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC Canada. ²Division of Dermatology, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. ³Medical Image Analysis Lab, School of Computing Science, Simon Fraser University, Burnaby, BC Canada. ⁴Vancouver Coastal Health Research Institute, Vancouver, BC Canada. ⁵The Ronald O. Perelman Department of Dermatology, NYU Langone Medical Center, NY, USA. ⁶Cancer Control Research Program, BC Cancer Agency, Vancouver, BC Canada

Although Pattern Hair Loss (PHL) is relatively simple to diagnose, its progression and response to treatment can be challenging to monitor quantitatively. Caliber variation (CV), the

percentage of total hair shafts that are vellus (diameter < 0.03 mm) in a selected region, is characteristic of PHL when it exceeds 20%, but fails to reflect miniaturization of non-vellus follicles and further caliber changes in vellus hair. This is one of the few quantitative metrics available to dermatologists through dermatoscopy for monitoring PHL non-invasively. In analogy to Red-cell-Distribution-Width (RDW) in hematology which is used to assess variation in red blood cell size, we propose an innovative metric called Hair-Distribution-Width (HDW) which reflects the standard deviation of the calibers of hair shafts in a selected region and can discern subtle progression in follicle miniaturization, and thus in PHL. We aim to assess and compare the accuracies of HDW and CV in diagnosing PHL. A smartphone-based dermatoscope transmits dermatoscopy images to a computer for automated caliber, HDW, and CV measurement. The hair-bearing scalps of fifty patients were imaged to compare the accuracy of utilizing HDW and CV in PHL detection. When used in conjunction with CV, HDW is capable of diagnosing PHL more accurately than when these metrics are used independently. HDW assessment is a clinically-feasible technique which can facilitate the monitoring and diagnosis of PHL with increased accuracy in a clinical setting, and can be expedited using automated smartphone-based caliber measurement.

Category: Applied/functional experiments