ORAL PRESENTATION

(8:35 AM)
STERILE VS CLEAN GLOVES IN MOHS SURGERY RECONSTRUCTION: A LARGE RETROSPECTIVE ANALYSIS
Hott ME, Zloty D
Department of Dermatology and Skin Science, University of British Columbia

Published data suggest a very low rate of surgical infection in Mohs Micrographic Surgery (MMS) regardless whether reconstruction is completed with clean or sterile gloves. However, to date this data is not robust as there are no large studies directly comparing infection rates with clean vs sterile gloves in the reconstruction phase of MMS. In the current study we retrospectively reviewed 4129 consecutively performed MMS procedures in a single academic center. All cases were performed with clean gloves for tumor extirpation. Half the cases were performed with sterile gloves and half with clean gloves for reconstruction. Routine prophylactic antibiotics were not given. Surgical infection rates in the two groups were compared, statistically controlling for age, gender, tumor type, tumor size, surgical site, and repair type (i.e. primary closure, flap, or graft). Initial statistical analysis shows no difference in surgical infection rate between the two groups. This data strongly suggests that clean gloves, with meticulous surgical technique, can be used safely for both tumor extirpation and surgical reconstruction in MMS. A follow up large prospective trial would be of value to confirm the results of this study, and aid in creating a more uniform standard of care among MMS centers.
Category: Early experiments with well defined objectives/hypotheses

(8:46 AM)
EIF5A2, A DOWNSTREAM TARGET OF PI3K/AKT PATHWAY, IS AN ADVERSE PROGNOSTIC MARKER OF MELANOMA PATIENT SURVIVAL BY INCREASING CELL INVASION
Shahram Khosravi, Ronald P.C. Wong[1], Magdalena Martinka[2], and Gang Li[1]
1Department of Dermatology and Skin Science, 2Department of Pathology, Jack Bell Research Centre, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, British Columbia, Canada

Human cutaneous melanoma is a life-threatening skin cancer due to its invasive nature and high metastatic potential, leading to poor prognosis for melanoma patients. However, the mechanisms for melanoma invasion and metastasis are poorly understood. Human eukaryotic translation initiation factor 5A2 (EIF5A2) has been shown to be associated with tumor progression in multiple types of cancers. We examined EIF5A2 expression in 459 melanocytic lesions at different stages using tissue microarray and immunohistochemistry and analyzed the correlations between EIF5A2 expression and clinicopathologic parameters and patient survival. We found that positive EIF5A2 staining was significantly increased in primary melanomas compared to dysplastic nevi (P=0.002), and further increased in metastatic melanomas (P=0.036). EIF5A2 expression was correlated with melanoma thickness (P=0.0004) and was inversely correlated with overall and disease-specific 5-year survival of primary (P=0.008 and 0.007, respectively), especially low-risk (≤2.0mm) melanoma patients (P=0.026 and 0.044, respectively). We also examined the correlation between EIF5A2 and p-Akt protein expression and their role in regulating melanoma cell invasion. Combining the TMA data sets for EIF5A2 and p-Akt, we found that positive EIF5A2 staining directly correlated with strong p-Akt expression (P=0.026). Additionally, overexpression of PTEN or inhibition of p-Akt or ILK significantly reduced EIF5A2 expression. EIF5A2 overexpression also increased melanoma cell invasion and MMP-2 activity. We for the first time showed that the expression of EIF5A2, a downstream target of PI3K/Akt pathway, is significantly increased during melanoma invasion and is inversely correlated with patient survival, suggesting that EIF5A2 may be used as a potential therapeutic target for melanoma.
Category: Early experiments with well defined objectives/hypotheses.

(8:57 AM)
TOWARDS OPTICAL BIOPSIES WITH MULTIPHOTON MICROSCOPY
Anthony Lee [1,2], Hequn Wang [1,3], Zack Frehlick[1], Harvey Lui[1], Shuo Tang [4], David I. McLean[1], Haishan Zeng [1,2]
[1]Laboratory for Advanced Medical Photonics, Integrative Oncology Department - Imaging Unit, British Columbia Cancer Research Centre and Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia & Vancouver Coastal Health Research Institute, Vancouver, BC, Canada [2]Department of Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada
[3]Interdisciplinary Oncology Program, University of British Columbia, Vancouver, BC, Canada
[4]Department of Electrical and Computer Engineering, University of British Columbia, Vancouver, BC, Canada

Standard microscopic examination of the skin involves an invasive biopsy procedure that results in scarring and cosmetic disfigurement. The burden of biopsy is accentuated when examining patients with a large non-homogeneous lesion or a large number of lesions. Furthermore, biopsy cannot be used when one wants to follow the natural evolution of a lesion. Thus, optical techniques that can reduce or eliminate the need for biopsy are in great need. Two techniques that can potentially fill this need are reflectance confocal microscopy (RCM) and multiphoton microscopy (MPM). Both RCM and MPM are capable of providing depth-resolved microscopic images of in vivo tissue with resolution approaching that of histological preparations.Here, we present our development and early results from a multimodal combined RCM/MPM instrument. This instrument is capable of simultaneously acquiring both RCM and MPM video streams without the use of exogenous contrast agents. A single femtosecond laser excitation source is used for all channels ensuring perfect image registration between the MPM and RCM images. Images and videos acquired with the system show that MPM and RCM images provide complementary information in in vivo human skin measurements. We present our current progress and achievements, as well as outline planned improvements and experimental applications for dermatology.
Section: Pilot/Exploratory Experiments

(9:08 AM)
GENOMIC EXPRESSION PROFILE OF ERYTHEMATOTELANGIECTATIC ROSACEA
Katie Beleznay, Ming-Wan Su, Bryce Cowan, and Youwen Zhou
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, British Columbia, Canada

Purpose: Rosacea is a common chronic inflammatory skin condition of the face. Subtype 1 or erythematotelangiectatic rosacea (ETR) is the most common form and presents with facial flushing, erythema and telangiectasias. Understanding the genomic expression profile (GEP) of ETR may provide insight into the pathogenesis of rosacea and lead to improvements in treatment. Methods: 8 subjects with ETR and 8 non-rosacea controls volunteered for this study. Full thickness skin samples were obtained. Messenger RNA was extracted from the tissue, and GEP analysis was done using Agilent 41,000 series of DNA microassays. GeneSpring software was used to analyze and identify genes that had expression levels ≥2 fold higher in ETR compared to normal skin with a p value <0.05. Results: Following analysis, 34 genes were found to be upregulated in ETR skin. Of the 34 upregulated genes, 9 of the genes represented proteases and 7 of the 34 genes were innate immune system regulators. The second set of results came from the part of our study in which we compared the GEP of ETR to atopic dermatitis (AD). Of the 34 genes upregulated in ETR, the majority or 25 genes were also upregulated in AD. Clinical Relevance: Given that this research indicates that proteases and innate immunity are involved in the pathogenesis of rosacea, perhaps innovative therapies that target these pathways can be developed. In addition, further analysis of the molecular expression similarities between ETR and AD may help with our approach to treatment of both conditions.
Category: Early experiments with well defined objectives/hypotheses

(9:19 AM)

MEASUREMENT OF SKIN ROUGHNESS IN-VIVO USING LASER SPECKLE

Gurbir Dhadwal[1], Diana Diao[1], Bernadette Ortiz-Policarpio1, Harvey Lui[1,2,] Liuodmila Tchvialeva[1], David I Mclean[1], Tim K Lee,[1,2,3]

[1.] Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute, Vancouver, Canada V5Z 4E8. [2].Departments of Cancer Control Research and Cancer Imaging, BC Cancer Agency, Vancouver, Canada V5Z 1L3. [3.] School of Computing Science, Simon Fraser University, Burnaby, Canada V5A 1S6

Background: Roughness is a property used for diagnosing many skin conditions, such as skin cancer. We developed a novel device and are conducting a study to measure in-vivo the skin roughness of 25 body sites. Methods: Our study has recruited 40 volunteers (18 males; 22 females; mean age 39.6 +/- 13.7), who have had 25 body sites measured by our portable device. The device is based on the contrast of laser speckle patterns which are light and dark stochastic interference patterns generated when coherent light interacts with a rough surface. Body sites were categorized into minimally, intermittently and maximally sun exposed. ANOVA was used to assess for a significant relationship between skin roughness, body site and sun exposure. Results: Statistical analysis showed a significant relationship between body site and measured Rq roughness. The values of roughness ranged from 12.1u +/- 1.4u for the palm, the smoothest site, to 32.4u +/- 1.1u for the ear lobe, the roughest site. On subgroup analysis, roughness of maximally sun exposed sites (28.0u +/- 0.4u) was found to be significantly higher than the roughness of intermittently (21.4u +/- 0.4u) or minimally (21.2u +/- 0.5u) sun exposed sites. Conclusions: Here we report a data set of in-vivo skin roughness of 25 body sites. We found that the roughness measurements from analysis of laser speckle were consistent with previously published results using other assessment methodologies. Our research will translate into improved patient care by helping define normal skin roughness, to which concerning skin lesions can be compared.

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

(9:30 AM)

STEPWISE MULTIPHOTON EXCITATION FLUORESCENCE SPECTROSCOPY FOR CUTANEOUS MELANIN DETECTION AND EVALUATION

Yunxian Tian [1,2], Jianhua Zhao [1], Harvey Lui [1], Haishan Zeng [1,2]

[1] Laboratory for Advanced Medical Photonics, Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia & Vancouver Coastal Health Research Institute and Imaging Unit - Integrative Oncology Department, British Columbia Cancer Agency Research Centre, Vancouver, B.C., Canada

[2] Department of Physics and Astronomy, University of British Columbia, Vancouver, BC, Canada

Melanin plays an important role in malignant transformation in melanocytes. The mechanism remains a puzzle and it hampers the delineation between "benign" and "malignant" melanomas in vivo. Previous reseach has successfully demonstrated stepwise two-photon excitation fluorescence spectroscopy of pigmented lesions in human skin ex vivo. Another study showed that stepwise three-photon excitation might occur by using less expensive laser source. We are interested in studying the mechanism of melanin structures by both stepwise two-photon and three-photon fluorescence spectroscopy and extending it to in vivo human skin spectroscopy for improving clinical diagnosis. The proposed work is divided into several stages. First build stepwise fluorescence system by using nanosecond laser and CW laser as the excitation source. Measure spectra of synthetic melanin in original powder form and in solvents. Obtain spectra of melanin from different pigmented skin lesions ex vivo. Investigate melanin-based fluorescence spectra in vivo. Compare the two stepwise fluorescence spectroscopy methods and evaluate the feasibility in melanin detection in vivo. We hope Step-wise excitation fluorescence spectroscopy will assist physician to better distinguish malignant melanoma from benign pigmented lesions without removing tissue.

Category: Pilot/exploratory experiments

(11:30 AM)
USE OF A HYDROGEL-COLLAGEN COMPOSITE, IDO EXPRESSING MATRIX IMPROVES ACUTE WOUND HEALING IN A RAT MODEL
R. Hartwell[1], V. Leung[2], A. Hosseini-Tabatabaei[1], T. Curran[1], F. Ko[2], A. Ghahary[1]
1. BCPFF Burn & Wound Healing Research Group, University of British Columbia, Vancouver, BC. 2. AMPEL Dept. Material Engineering, University of British Columbia, Vancouver, BC.

Introduction: chronic wounds and burns account for over two-thirds of the wound care market. Treatments are both costly and challenging for healthcare professionals. For those patients with severe burns or diabetic wounds requiring autologous grafts, donor sites may be limited if not available. In this scenario skin substitutes and acellular scaffolds may be used as coverage. Although these strategies have improved healing outcome in patients they are limited by the length of time it takes to integrate with surrounding tissue, become vascularized, as well as populated by cells. Moving toward a skin substitute that is patient ready we developed an in-situ gelling scaffold that would permit integration with surrounding tissue. Our hypothesis that a composite matrix using both a collagen:Glycosaminoglycan network and a crosslinked PVA-hydrogel would provide an environment that would gel rapidly, increase the matrix strength while mitigating hyperproliferation of fibroblasts. Results: Our results demonstrate that hydrogel collagen composites exhibit faster fibril formation, reduced contracture, reduced cell proliferation, linear cellular organization and unique architecture ($p<0.05$). Mechanical strength is improved ($p<0.05$), yet elasticity is decreased. Gels integrated with the wound bed and promote improved healing; encouraging polarized cellular arrangement and angiogenesis. Conclusions: Our findings suggest that the addition of PVA hydrogels to the crosslinked collagen based systems, enhances both mechanical and gelling properties, in addition to providing an integrative environment that mitigates gel contracture by fibroblasts.Ultimately our novel in-situ gelling composite mark an improvement in the current scaffolds that are used to treat the chronic wounds and burn patients.
Category: Applied/functional experiments

(11:41 AM)
REAL-TIME RAMAN SPECTROSCOPY FOR *IN VIVO* EVALUATION OF SKIN CANCERS
Jianhua Zhao, Haishan Zeng, David I. McLean, and Harvey Lui
Laboratory for Advance Medical Photonics, Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia and Vancouver Coastal Health Research Institute; and Imaging Unit - Integrative Oncology Department, British Columbia Cancer Agency Research Center

Background: Real-time Raman spectroscopy has been explored for *in vivo* skin cancer diagnosis in our group for the past few years. We will present the first large-scale clinical evaluation of Raman spectroscopy for skin cancer diagnosis. **Methods:** An integrated real-time Raman spectroscopic system was constructed, which is composed of a portable hand-probe and dedicated software for data acquisition and processing. Over 1000 lesions have been acquired using the integrated real-time Raman spectrometer system. Multi-variant statistical data analysis including principal component analysis, general discriminant analysis, and partial least squares were used for lesion classification. **Results:** Five hundred and eighteen (518) cases encompassing a spectrum of skin cancers/pre cancers and benign pigmented lesions were prospectively analyzed in this study. The analyses were divided into the following three classifications based on clinical interest: (1) to discriminate skin cancers and precancers from benign skin lesions; (2) to discriminate malignant melanoma from non-melanoma pigmented lesions; and (3) to discriminate malignant melanoma from seborrheic keratosis. The areas under the receiver operating characteristic (ROC) curves and their 95% confidence intervals (CI), were found to be 0.879 (CI: 0.829-0.929), 0.823 (CI: 0.731-0.915) and 0.898 (CI: 0.797-0.999) for the above three analyses, respectively. **Conclusion and Knowledge Translation:** Real-time Raman spectroscopy can distinguish malignant from benign skin lesions with good diagnostic accuracy comparable to clinical examination and other optical-based methods.
Category: This study belongs to knowledge stage III, Applied/Functional Experiments (*in vivo* studies)

(11:52 AM)
SOMATOSTATIN EXPRESSION IN HAIR FOLLICLE OUTER ROOT SHEATHS MAY CONTRIBUTE TO IMMUNE PRIVILEGE

Trisia Breitkopf, Blanche KK Lo, Gigi Leung, Mei Yu, Jerry Shapiro, and Kevin J McElwee
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, BC, Canada

Immune privilege (IP) is believed to exist in the anagen hair follicle (HF). We wanted to further probe IP in human HFs, hoping to elucidate a functional mechanism of IP in HFs. Human HFs were microdissected to isolate the bulb and the remaining dermal sheath and root sheaths for separate investigation relative to dissected interfollicular epidermis. Peripheral blood mononuclear cells (PBMC) from healthy volunteers were cultured with histo-incompatible primary interfollicular epidermal cells or HF bulb or sheath cells from normal tissue. HF bulb and sheath cells induced significantly less IFN-γ secretion (18.4 and 9.8 pg/ml, respectively) from PBMCs than epidermal cells (35.3 pg/ml). We screened expression of 40+ IP-related genes by quantitative RT-PCR in HF bulb and sheath relative to interfollicular epidermal samples. Most notably, somatostatin (SST) was significantly upregulated in the HF. Examining SST further showed strong staining in HF outer root sheaths compared to epidermis. There was also significantly greater SST secretion from HF sheath than epidermal cell culture. PBMCs cultured with allogeneic nonfollicular epidermal cells and SST showed that SST significantly inhibited PBMC IFN-γ secretion, especially at lower concentrations. Using a SST antagonist in PBMC and allogeneic sheath cell co-culture led to higher IFN-γ secretion. Our results reveal a novel finding that SST is expressed in the human HF and that it can have inhibitory effects on PBMC activation. We propose that SST may have an IP role in the HF. This could have implications for new treatments for inflammatory hair loss diseases or for tissue transplantation
Category: Early experiments with well defined objectives/hypotheses

(12:03 PM)
SUBCUTANEOUS PROTEIN ANTIGEN WITH EPICUTANEOUS TOLL-LIKE RECEPTOR 9 AGONIST INDUCES PROTECTIVE IMMUNE RESPONSES AGAINST INFLUENZA A VIRAL INFECTION

Cheng, WK.[1], Plumb, A.[2], Abraham, N.[2], and Dutz, J.P.[1]
[1]Department of Dermatology & Skin Science, Child & Family Research Institute, University of British Columbia, Vancouver, BC, Canada[2.] Department of Microbiology & Immunology, Life Sciences Institute, University of British Columbia, Vancouver, BC, Canada

Humoral and cell-mediated immune responses are critical to combat viral infections. This study presents a novel delivery method of vaccines to enhance both humoral and cell-mediated immune responses by combining protein antigen with a Toll-like receptor 9 agonist (CpG ODN1826) administered through the subcutaneous and epicutaneous route, respectively. Relative total OVA-specific IgG and IgG2c levels in sera determined by ELISA 4 weeks post boosting (prime and boost 3 weeks apart) were significantly higher when CpG adjuvant was administered epicutaneously compared to subcutaneously. Using flow cytometric analysis, significantly higher percent of OVA-specific CD8+ memory T cells were preferentially detected in the lung and bronchoaveolar lavage fluid of mice immunized in combination with CpG adjuvant compared to antigen alone (prime and boost 7 days apart) post intranasal challenge with recombinant influenza A virus expressing the OVA257-264 peptide (PR8-OVA). These data demonstrated prime-boost immunization of protein antigen with CpG adjuvant enhanced rapid and memory specific CD8+ T cell production as well as specific IgG2c antibodies. Furthermore, these responses conferred protection against intranasal challenge with PR8-OVA demonstrated by lower viral titers detected in the lung using plaque assay. Taken together, these results demonstrate that administering a Toll-like receptor 9 agonist epicutaneously as adjuvant augments both arms of protective immune responses. This vaccination regimen has great potential to be implemented in human vaccinations to improve effectiveness of vaccines without reformulation to combat viral infections.
Category: Applied/functional experiments

(12:14 PM)
AN EXPANDED SERIES OF SCREENING ALLERGENS IN ADDITION TO SUPPLEMENTAL ALLERGEN TESTING IMPROVES DETECTION OF OCCUPATIONAL ALLERGIC CONTACT DERMATITIS.

Aaron Wong MD, Dermatology Resident, UBC Department of Dermatology & Skin Science; Sayali Tadwalkar MD CCFP, Family Physician;Gillian de Gannes MD FRCPC FAAD, Clinical Instructor, UBC Department of Dermatology & Skin Science. Director, UBC Contact Dermatitis Clinic

An appropriate number of allergens is important for the diagnosis of occupational allergic contact dermatitis (OACD). This prospective trial of 100 participants compared the use of a 45 allergen series with the North American Contact Dermatitis Group (NACDG) 70 allergen series. The primary outcome was to identify the number of patients with at least one positive patch test reaction in the 70 allergen NACDG screening series allergens that would have been missed with the 45 allergen series. Secondary outcomes included identifying the percentage of participants who reacted to supplemental allergen testing and those with any allergen identified, irrespective of the allergen series. After ethical review board approval, patch testing with the NACDG 70 allergen series and relevant supplement trays was carried out on patients referred for suspected OACD. Patch test results from the 70 allergen series were then compared to the 45 allergen series. Results showed that using the 45 allergen series alone missed 27% of participants compared to the 70 allergen series. Similarly, supplemental allergen testing yielded at least one positive test in 23%. In summary, 50% of those with ACD would have been missed with the 45 allergen series and no supplemental testing. This study represents a prospective trial to demonstrate that an expanded series of screening allergens in addition to supplemental testing improves detection of occupational allergic contact dermatitis.
Early experiments with well defined objectives/hypotheses

(12:25 PM)
PROGNOSTIC SIGNIFICANCE OF FBW7 IN HUMAN MELANOMA AND ITS ROLE IN CELL MIGRATION

Yabin Cheng[1], Guangdi Chen[1], Magdalena Martinka[2] and Gang Li[1]
[1]Department of Dermatology and Skin Science, [2]Department of Pathology, Jack Bell Research Centre, Vancouver Coastal Health Research Institute, University of British Columbia, Vancouver, British Columbia, Canada

The ubiquitin ligase Fbw7 (F-box and WD repeat domain-containing 7) is a tumor suppressor because of its role in ubiquitination and turnover of several well-known onco-proteins. Loss or mutations of Fbw7 has been associated with increased chromosomal instability and deregulation of cell cycle, which implicated in several human cancers. However, whether Fbw7 plays a role in human melanoma development is unclear. Here we show that the Fbw7 is a prognostic marker in melanoma. Using tissue microarray, we examined the expression of Fbw7 in 501 melanocytic lesions at different stages. The results showed that Fbw7 expression is significantly reduced in primary melanoma and metastatic melanoma, compared with normal and dysplastic nevi ($P < 0.05$). We also found significantly lower expression of Fbw7 in advanced melanoma (AJCC stage III-IV) than melanoma at AJCC stage I-II ($P = 0.027$). We also observed a strong correlation between negative Fbw7 expression and a worse 5-year survival in melanoma patients ($P = 0.015$). Using specific primers for Fbw7, we found that isoform α is the most abundant and the mRNA levels of all three isoforms were significantly reduced in 9 melanoma cell lines compared with normal melanocytes. Strikingly, we observed remarkable increase of cell migration and stress fibre formation in Fbw7 knockdown melanoma cells. The increased migration on Fbw7α knockdown depends on the phosphorylation of MAPK/ERK, and is abolished upon selective MEK inhibitor treatment. Our results indicate that Fbw7 regulates cell migration through MAPK/ERK signal pathway, and may serves as a therapeutic target for human melanoma.
Category: Early experiments with well defined objectives/hypotheses

(12:36 PM)

FRONTAL FIBROSING ALOPECIA – A RETROSPECTIVE CLINICAL STUDY OF 62 PATIENTS WITH TREATMENT OUTCOME AND LONG TERM FOLLOW-UP.

Nusrat Banka, MD,[a] Kevin McElwee, PhD,[a] Jerry Shapiro, MD, FRCPC[a].
Department of Dermatology and Skin Sciences, University of British Columbia, Vancouver, Canada[a].

Frontal fibrosing alopecia (FFA) is a distinct form of alopecia, first described by Kossard in 1994.[1] The striking presentation is frontal and temporoparietal recession of the hairline with affected skin appearing pale and lacking follicular ostia. Its etiopathogenesis remains unknown. Objectives: We report clinical findings and treatment outcome of 62 patients with FFA with long term follow up. Methods: A retrospective data analysis was performed on 62 patients with FFA. Data was collected from case notes of patients and involved demographics, clinical presentation and response to various treatment modalities and a follow-up ranging from six months to seven years. Results: Except for one male patient all other patients were female (61 patients). Age of onset of FFA was between 18 and 81 years. Out of 61 female patients, 49 were post menopausal and 12 premenopausal. Clinical examination revealed a band of frontal hairline recession in all patients with loss of eyebrows in 50 patients. A significant reduction in symptoms and stabilization of hairline was achieved with intralesional triamcinolone. Conclusion: FFA is predominantly seen in post menopausal women and rarely in men. FFA possibly shares immune and hormone mediated complex aetiology. Despite the limitations of retrospective study, we conclude early intervention and treatment with intralesional triamcinolone acetonide may halt the progression of FFA.

(1:35 PM)

NOVEL BIOMARKERS FOR CUTANEOUS T CELL LYMPHOMA

Yuanshen Huang[1,2], Yang Wang[1,2], Richard Yu[1,2], Magda Martinka[3], Jan Dutz[1], Ming-wan Su[1,2] and Youwen Zhou[1,2] [1]Department of Dermatology and Skin Science, University of British Columbia;[2]Molecular Medicine Laboratory and Chieng Genomics Center, Vancouver Coastal Health Research Institute [3]Department of Pathology, University of British Columbia

Background and objectives Cutaneous T cell lymphomas (CTCL) are the most common primary lymphomas of the skin, with two major subtypes: Mycosis Fungoides (MF) and Sezery Syndrome (SS). Although multiple cellular abnormalities have been identified, the mechanism responsible for CTCL pathogenesis remains unknown, and there is a lack of specific markers for CTCL. In this study, we aim to investigate potential biomarkers for CTCL. **Method** Transcriptome analysis was performed on early stage MF (N=5) and SS (N=6), compared to chronic dermatitis (N=5) and normal CD4+CD7+ T cells from healthy volunteers (N=9), respectively. Differentially expressed genes with more than two fold changes were further validated by RT-PCR, Western Blotting, and immunohistochemistry in additional samples. Student t tests were performed with significance set at two-sided 5% error level. Bonferroni correction was used in case of multiple testing. **Results** Among the up-regulated genes in early stage MF and SS, an early T cell development regulator gene was the only gene displayed up-regulation in both conditions. Furthermore, the mRNA and protein levels of this gene were significantly higher in CTCL, compared to chronic dermatitis or CD4+CD7+ T cells from healthy volunteers. **Conclusion** A biomarker has been identified that shows strong potential as a specific positive identification marker for CTCL. **Interpretation** Our findings have the potential to improve the diagnosis and staging of CTCL.
Abstract category: a. Pilot/exploratory experiments

(1:46 PM)
RECOVERING INTRINSIC SKIN REFLECTANCE UNDER ARBITRARY ILLUMINATION FROM DERMOSCOPY IMAGES

Maryam Sadeghi[1,2], Tim K. Lee[1,2,3] , David McLean[2,3] , Harvey Lui[2,3], and M. Stella Atkins[1]
[1]School of Computing Science, Simon Fraser University, Burnaby, BC, Canada. [2]Cancer Control Research, BC Cancer Agency, Vancouver, BC, Canada. [3]Department of Dermatology and Skin Science, and Photomedicine Institute, UBC, Vancouver, Canada.

New dermoscopes come with a polarization feature that allows the user to reduce the effect of reflections and glare. However, the built-in white LEDs used for polarization cause a special redial lighting artifact resulting in separate areas of over and under-exposure that must be removed before any image analysis. For example, the consistent lighting is an extremely important feature in segmenting lesions from normal skin. We have proposed a new approach that finds intrinsic images by a fast entropy minimization and subtraction. First, two images with different lightings (polarized and non-polarized) are captured from the same skin surface. Pixels are transformed from 3D RGB triples into a 2D colour space G/R, B/R, and then logarithms are taken. The values across different lightings tend to fall on straight lines in 2D and change of illumination simply amounts to movement along such lines. Therefore, it is straightforward to devise a 1D illumination-invariant image by projecting the 2D chromaticity points into a direction perpendicular to all such lines. We find the projection angle such that minimizes the entropy. This intrinsic images plus a calibration image of the normal skin is used to find the artifact pattern to be subtracted from dermoscopy images to recover the image that portrays only the inherent reflectance properties of skin. The qualitative results of our experiments show that the proposed method can significantly improve the quality of images and our quantitative results show 11.5% improvement in skin lesion segmentation accuracy in illumination corrected data sets. Clinical Significance and KT: Our method is a fully automated method for enhancing dermoscopy images be used in the skin lesion diagnosis.
Category: Early experiments with well defined objectives/hypotheses.

(1:57 PM)
PREVALENCE OF EXPOSURE TO SOLAR ULTRAVIOLET RADIATION (UVR) ON THE JOB IN CANADA

Peters CE, Nicol AM, Demers PA
School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada

Objectives: Over one-third of all newly diagnosed cancers in Canada in 2010 were skin cancer, despite the fact that skin cancer is largely preventable by limiting ultraviolet radiation (UVR) exposure. Outdoor workers are at risk of exposure to UVR, yet the prevalence of exposure in Canada is unknown. The objective of this study was to estimate the number of outdoor workers in Canada. **Methods:** Building on CAREX Canada methods, we used a combination of data in the original Finnish CAREX, an Australian skin cancer prevention workbook, career-selection websites, and published studies to flag jobs at high risk of exposure. We created two categories for moderate exposure, where workers were not likely to spend their whole day outside. Adjustments were made for industry-driven exposure, and prevalence of exposure was assigned for all jobs. Prevalence data were linked to census data to derive the number of workers exposed to solar UVR. **Results:** Over 1.5 million Canadian workers are exposed to solar UV at work, and ~900,000 of these were flagged as 'high exposed' (outdoors ≥75% of the workday). The largest occupational groups were construction labourers, farmers, and landscapers. Proportions of the workforce exposed ranged by province, with 5.3% of workers exposed in Ontario, up to 12% in Prince Edward Island. **Conclusions:** Information on solar UVR exposure prevalence is needed for primary skin cancer prevention for the targeting of high risk groups, priority setting, and better risk assessment. This study showed that solar UVR exposure is occurring on a large scale in Canada.

(2:08 PM)
TWO-PHOTON ABSORPTION FOR HIGHLY TARGETED SKIN EVALUATION AND PHOTOTHERAPY: A PILOT STUDY ON EX VIVO MOUSE SKIN

Hequn (Tracy) Wang, Soodabeh Zandi , Jianhua Zhao, Anthony M.D. Lee, Harvey Lui, David I. McLean, and Haishan Zeng
Laboratory for Advanced Medical Photonics, Photomedicine Institute, Department of Dermatology and Skin Science, University of British Columbia & Vancouver Coastal Health Research Institute and Imaging Unit - Integrative Oncology Department, British Columbia Cancer Agency Research Centre, Vancouver, B.C., Canada V5Z 4E8

Background: Current laser treatment methods may not necessarily be selective at the microscopic level, resulting in non-specific tissue. Two-photon fluorescence (TPF) from endogenous fluorophores, e.g., keratin, nicotinamide adenine dinucleotide phosphate [NAD (P)H], melanin, and elastin; and second harmonic generation (SHG) from collagen allows depth-resolved, *in vivo*, non-invasive imaging of skin with detail approaching that of conventional histology. At higher excitation power, two-photon absorption (TPA) from the skin may provide precise damage to specific skin structures. Our objective is to explore the feasibility of two-photon laser absorption for targeted skin therapy, which may potentially be used to precisely treat dermal tumors, hirsutism, hyperhidrosis, and birthmarks without damaging the skin or causing scarring. **Materials and Methods**: All the treatment was performed using 150 mW of power on the dermis of ex vivo mouse skin. The reflectance confocal (RC) and the combined TPF and SHG (TPF&SHG) imaging channels were used to monitor the two-photon treatment (TPT). The laser wavelength of 785nm and field-of-view (FOV) of 150μm × 150μm were selected for both non-invasive imaging and TPT. The skin was sectioned and stained after each treatment for comparison. **Results:** Localized destruction of dermal fibers was observed without discernible epidermal damage on combined TPF and SHG images. TPF and SHG images correlated well with conventional histologic examination. **Conclusions:** Two-photon-based light absorption provides highly localized intradermal tissue alteration that may prove useful for therapeutic applications.
Category: Pilot/exploratory experiments

(2:19 PM)
IMPAIRED WOUND HEALING IN APOLIPOPROTEIN E DEFICIENT MICE

Paul R. Hiebert[1,2], David J. Granville[1,2]
[1] UBC James Hogg Research Centre at St. Paul's Hospital, [2] Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC, Canada

Apolipoprotein E (ApoE) functions as a key mediator of circulating cholesterol and deficiencies in ApoE can result in hypercholesterolemia. In addition, ApoE is highly expressed in the skin, where it can regulate inflammation through its anti-oxidative and anti-inflammatory properties. Mice deficient in ApoE develop an inflammatory skin phenotype prone to accelerated aging featuring increased thinning, collagen disorganization and susceptibility to injury. We hypothesized that ApoE knockout (ApoE KO) mice will demonstrate increased inflammation in response to injury thereby impairing the wound healing process. Seven week old C57BL/6 wild type mice and ApoE KO mice were given a single 1 cm diameter full thickness skin wound on their mid backs. Wound tissue was harvested at 2, 8 or 16 days post-wounding and analyzed histologically. Wound closure times for all groups of mice were similar, with wounds showing full closure by 16 days. Histological analysis of the newly formed dermis revealed an increase in inflammatory cells in the ApoE KO mice, as well as alterations in collagen structure. While healed tissue from wild type mice demonstrated the formation of new sebatious glands, hair follicles and mature collagen, these were not observed in ApoE KO mice. In conclusion, wound healing in ApoE KO mice is impaired compared to wild type mice, featuring increased inflammation and altered collagen/dermal structure.
Category: Applied/functional experiments

(2:30 PM)

COMBINING MICROPARTICULATE-ENCAPSULATED ANTIGEN WITH TOPICAL CpG ADJUVANT AS A SINGLE-INJECTION IMMUNIZATION STRATEGY

Jacqueline Lai[1], Tullio Esposito[2], Urs Hafeli[2] and Jan Dutz[1]
[1]Department of Dermatology and Skin Science. [2]Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada, V5Z 4H4.

Antigen-presenting cells (APCs) are responsible for presenting foreign antigens to, and activating T cells to fight off an infection. Manipulation of APCs to modulate immune responses to immunization has been a focus in vaccinology. Due to high frequencies of APCs present in the skin, we are interested in using the skin as a site for immunization. Keratinocytes and skin-resident plasmacytoid dendritic cells can be activated via binding of their Toll-like receptor 9 to bacterial DNA. CpG oligodeoxynucleotides (ODN) are synthetic DNA that mimic unmethylated CpG bacterial DNA. Here, we show that mice immunized subcutaneously in a prime-boost regime with polylactide co-glycolide-encapsulated ovalbumin microparticles (PLG-OVA) generate antigen-specific cytotoxic T cells when CpG ODN is used as the adjuvant. Using flow cytometric analysis, 1.5 and 2.1% antigen-specific cells are detected within the $CD8^+$ cytotoxic T cell population in the peripheral blood when CpG ODN is administered subcutaneously or topically respectively ($P < 0.01$ compared to PLG-OVA alone). In addition, 0.7 and 0.5% of $CD8^+$ splenocytes produce interferon-gamma when re-stimulated with the OVA (SIINFEKL) peptide in vitro ($P < 0.001$). Using the release properties of PLG-OVA and repeated topical application of adjuvant, we enhanced the generation of antigen-specific cytotoxic T cells in the peripheral blood (from 0.4 to 0.9%, $P < 0.05$) and OVA-specific antibody production, effectively generating a single-injection vaccine that induces robust CTL and B cell responses. Generating single-injection vaccines will enhance compliance with vaccination in the general population and may also decrease the cost of vaccine administration.
Category: Pilot/exploratory experiments (for study design, hypotheses creation, etc)

(2:41 PM)

SKIN CANCER DETECTION BASED ON POLARIZATION MAPPING OF SPECKLE IMAGES - AN IN-VIVO NONINVASIVE TECHNIQUE

Bahman Sotoodian[1], Lioudmila Tchvialeva[1], Sunil Kalia[1], Gurbir Dhadwal[1] Haishan Zeng[1,2], Harvey Lui[1,2], David I. McLean[1,2], Tim K. Lee[1,2]
[1]Facaulty of Medicine, University of British Columbia, Vancouver. [2]BC Cancer Agency, Vancouver.

Objective: Our study demonstrates that different skin lesions, malignant vs. benign, could be distinguished using a novel in-vivo non-invasive optical method based on polarization mapping of speckle images. Design: We statistically compared the optical measurements for 5 categories of skin lesions: malignant melanoma (MM), seborrheic keratosis (SK), nevus, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). **Material & Methods:** By capturing the speckle images of skin lesions, performing pixel-by-pixel correspondence (registration) using MATLAB, we constructed the degree of linear polarization (DOLP) map associated with each skin lesion. The distribution of the DOLP maps reveals that different tissues respond at different polarization directions. We hypothesized that the distribution of a DOLP map, expressed statistically as mathematic moments, could be used as a diagnostic parameter for skin lesions. We tested our hypothesis in a clinical study conducted at the Skin Care Centre from July 2008 to November 2010. **Results:** We examined 22 MM, 76 SK, 44 nevi, 27 BCC, and 11 SCC skin lesions under two lasers, blue and red. All malignant cases were confirmed by biopsy. The DOLP maps for these skin lesions were constructed. The first 4 mathematical moments were calculated from the DOLP maps. The 3rd and 4th order moments showed significant differences between some of malignant skin lesions from benign ones. **Conclusion:** Our innovative approach towards skin cancer had demonstrated great promise in influencing the diagnosis of Melanoma and other skin lesions. Our method would substantially assist Dermatologists in deciding whether to biopsy the lesions or not.
Category: Early experiments with well defined objectives/hypotheses

(2:52 PM)

PROSPECTIVE QUANTITATIVE DOCUMENTATION OF PRE AND POST-OPERATIVE ANXIETY IN MOHS MICROGRAPHIC SURGERY: PRACTICAL COUNSELLING IMPLICATIONS.

Dr. Irèn Kossintseva and Dr. David Zloty
Department of Dermatology and Skin Science, University of British Columbia, Vancouver, Canada

Pre-operatively, patients undergoing Mohs Micrographic Surgery (MMS) on the face exhibit anxiety about the presence of the cancer. Post-operatively, many patients show even greater anxiety associated with the degree of reconstruction and expected long-term cosmetic outcome. The purpose of this study is to obtain quantitative measurement of pre and post-operative anxiety levels in MMS patients, to document that cosmesis-based anxiety does decrease over time in a predictable manner, and to ascertain parameters that may influence this anxiety. Single-blinded prospective study of patients presenting between November 2010 and September 2011 for MMS on the face. Questionnaire-based assessment of patient demographics and evaluation of their anxiety levels using a Visual Analogue Scale (VAS). Assessment was completed immediately pre-operatively, and postoperatively over a 6 month follow-up course.Data from 174 patients demonstrates that overall the average patient is more anxious about cancer. However, the most anxious patients are worried more about cosmesis; these tend to be younger females. Cosmetic anxiety decreases predictably over time, and returns to baseline at 6 months. Surgical site, type of closure, length or quality of scar, level of education, or presence of mood disorders did not influence the degree of anxiety a patient experiences.Our findings allow for practical quantitative counselling guidelines. They also surprisingly demonstrate that reconstructive option or the presence of a mood disorder did not influence patient anxiety.

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