ORAL PRESENTATION

(8:40 AM)

Thymocyte Selection-Associated High Mobility Group Box Protein (TOX) Is A Novel Diagnostic and Prognostic Marker for Mycosis Fungoides and Sézary Syndrome

Yuanshen Huang[1], Ivan Litvinov[2], Yang Wang[1], Mingwan Su[1], Jan P. Dutz[1], Denis Sasseville[2], and Youwen Zhou[1]

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This study aims to test the utility of TOX as a diagnostic and prognostic marker for mycosis fungoides (MF) and Sézary syndrome (SS), which currently do not have reliable molecular markers. Skin biopsies were obtained from MF (N=116) and control (benign inflammatory dermatoses (BID) or normal skin (NS), N=36) subjects. Peripheral blood $CD4^+$ T lymphocytes were prepared from SS (N=12) and control (BID or NS, N=27) subjects. TOX mRNA was measured using quantitative polymerase chain reaction. TOX protein was visualized using immunofluorescence (IF) microscopy. Receiver operating characteristic (ROC) was used to evaluate the diagnostic potential of TOX, whereas Kaplan-Meier method was used to test the prognostic utility of TOX. MF skin biopsies expressed 11.3 times more TOX mRNA than non-MF biopsies ($p=0.00001$). Similarly, peripheral blood $CD4^+$ cells in SS patients contained 4.6 times more TOX mRNA than benign $CD4^+$ T cells ($p=0.000008$). In IF analysis, TOX protein was specifically detected in the $CD4^+$ cells in MF biopsies, but not in the $CD4^+$ T cells of non-MF biopsies. Further, in ROC analyses TOX accurately diagnosed MF/SS subjects (specificity 90.5% and 83.3%; sensitivity 75.0% and 85.2%, respectively). Finally, TOX expression positively correlated with risk of disease progression for MF ($p=0.0127$), and disease specific mortality for both MF ($p=0.0175$) and SS ($p=0.039$). In conclusion, TOX is a novel molecular marker for the malignant $CD4^+$ T cells in MF/SS. Not only can it be used to establish MF/SS diagnosis, it can also be used to predict long term clinical outcomes of MF/SS patients.

Category: Early experiments with well defined objectives/hypotheses

(8:51AM)

Efficacy and Safety of Intralesional Triamcinolone Acetonide in Comparison to Diphenylclopropenone in the Treatment of Severe Alopecia Areata: A Prospective Randomized Controlled Trial

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Alopecia areata (AA) is a chronic autoimmune inflammatory disease causing non-scarring hair loss. It affects mostly the scalp; however, any body site can be affected. The lifetime risk of developing the condition is 1.7%. The extent of hair loss ranges from a single patch to a very extensive alopecia involving the entire scalp and body hair. Spontaneous hair regrowth occurs in 50 % of patients within 1 year but relapses are common. Many treatment modalities can be helpful in AA; however, none on them cure the disease. Treatment with intralesional corticosteroids (ILCSs) is considered the first-line therapy in adults with less than 50% scalp involvement. Treatment with contact immunotherapy such as Diphenylcyclopropenone (DPCP) is considered now the first line treatment in patients with severe AA (involving > 50% of the scalp). One study showed that DPCP was not statistically better than ILCSs in

treatment of AA with a size of less than 50 cm^2. However, in cases of AA larger than 50 cm^2 including alopecia totalis and universalis, DPCP proved to be superior to ILCSs. We believe that ILCSs is as effective as DPCP in the treatment of severe AA. Treatment with ILCSs is safe, repeated every 4 weeks in contrast to the weekly treatments of DPCP and doesn't produce itching or allergic contact dermatitis as compared to DPCP and thus it is more tolerable by most patients. Treatment with ILCSs can be associated with higher treatment compliance by patients as compared to the weekly DPCP.

Category: Early experiments with well defined objectives/hypotheses.

(9:02 AM)

Prognostic Significance of KAI1/CD82 in Human Melanoma and its Role in Cell Migration and Invasion

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KAI1 is a member of the transmembrane 4 superfamily and its expression is reduced in many types of cancers, including prostate, breast, ovarian, cervical, and endometrial cancer. However, the role of KAI1 in melanoma pathogenesis is not known. In this study, we investigated the expression level of KAI1 in a large set of melanocytic lesions at different stages. We found that KAI1 expression is drastically reduced in primary melanoma compared to dysplastic nevi (P=1.8×10^{-4}, χ^2 test) and further reduced in metastatic melanoma compared to primary melanoma (P=9.4×10^{-15}, χ^2 test). Furthermore, decreased KAI1 staining is strongly correlated with a worse 5-year patient survival. Multivariate Cox regression analysis showed that KAI1 is also an independent prognostic factor. Moreover, we found that KAI1 significantly inhibited melanoma cell migration through suppression of Rho-associated kinase (ROCK)-mediated formation of stress fiber. Our data also indicated that KAI1 significantly inhibited melanoma cell invasion by reducing the activity of metalloproteinase (MMP)-2. In addition, we found that suppression of melanoma cell migration by KAI1 is mediated by another tumor suppressor ING4. Taken together, our data suggest that KAI1 may be used as a promising prognostic marker and a potential therapeutic target for human melanoma.

(9:13 Am)

Validation of *In-Vivo* Skin Roughness Measured With Laser Speckle

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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 24normal skin sites. The device is based on measuring the contrast of laser speckle patterns, which are light and dark stochastic interference patterns generated when coherent light interacts with a rough surface. Methods/Results: Our study has recruited 72 volunteers (27 males; 45 females; mean age 38+/-14). Body sites were categorized into minimally, intermittently and maximally sun exposed. Repeated Measures

ANOVA with a Greenhouse-Geisser correction was used to assess for a significant relationship between skin roughness and body site. Relative humidity and gender were corrected for as covariates ($p<0.001$; $p=0.013$); age and skin color were not found to be significant during model building ($p>0.05$). There was a statically significant difference in roughness among the skin sites ($p=0.016$).Post-hoc analysis using the Bonferroni correction revealed the skin sites maximally exposed to the sun were significantly more rough than intermittently or minimally sun exposed sites ($p<0.001$). Conclusions: Here we report a data set of in-vivo skin roughness of 24 skin sites. We found that the roughness measurements from analysis of laser speckle were consistent with previously published results using other assessment methodologies and correlate with relative sun exposure to different body sites. 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)

(9:24 AM)

Relationship between Modifiable Lifestyle Factors and Sun Safety Behaviours

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Background: Non-melanoma skin cancer is the most commonly diagnosed skin cancer in fair-skinned individuals. Previous studies have found clustering of lifestyle factors that may increase the risk of certain cancers. More investigation is required to examine how these lifestyle factors may correlate with skin cancer risk. **Purpose:** This study will examine the relationship between modifiable lifestyle factors and sun protection behaviours. **Methods:** Cross-sectional data from the 2007-2010 Canadian Community Health Survey (CCHS) was analyzed (N = 31, 445). The outcome variables included the presence of sunburn, probability of prolonged sun exposure, and frequency of seeking shade, wearing a hat, and wearing sunscreen. The explanatory variables included physical activity level, BMI, alcohol consumption, cigarette consumption, fruit/vegetable consumption, and having a regular family doctor. Using the Statistical Analysis System (SAS) 9.3.1, the final multivariate logistic regression was manually compiled, with variables significant at $p<0.01$ level (Wald chi-square test). **Results:** Higher levels of physical activity were correlated with presence of sunburn and higher sun exposure. Otherwise, other unhealthy behaviour practices were associated with sunburns or infrequent sun protection behaviour, such as alcohol intake, cigarette consumption (either current or former smokers), not having a regular doctor and low levels of fruit and vegetable consumption. **Conclusion:** The correlation between risky lifestyle factors and risky sun protection behavior indicates populations that are at high risk of developing skin cancer and should be targeted in prevention campaigns. Additional studies are required to further explore the relationships between the risk factors and assess possible prevention campaigns.

Category: Exploratory Study

(9:35 AM)

Continuous Versus Interrupted Sutures for Mohs Surgery Repair (CONVIR): A Randomised Prospective Study

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The aim of this study is to compare the cosmetic appearance of scars resulting from facial surgical wounds after Mohs surgery sutured either with continuous or with interrupted percutaneous sutures. One hundred and five patients with facial Mohs surgery defects were randomized. Depending upon randomization, either the superior/medial or inferior/lateral half of the scar was sutured with interrupted stitches. The other half was closed with running continuous stitches. All surgeries were performed by either an experienced dermatologic surgeon or a fellow in training. At 1 week, 8 weeks and 6 months the cosmetic results of each half of the scar was evaluated by the investigators using the 100 point visual analogue scale and two specific scar evaluation scales. The cosmetic appearance of photographs of wounds immediately after suture removal, at two months and 6 months were also assessed by a plastic surgeon and a dermatologist blinded to the technique used. A total of 105 patients participated in the trial over a period of 6 months. The esthetic results obtained by continuous versus interrupted stitches techniques have yet to be analyzed by statistical methods and the results will be available for disclosure at the beginning of the next academic year. This study will be the largest of its kind to compare the cosmetic results of continuous versus interrupted suture. We hope to shed light on this controversial topic as the esthetic appareance of scars is among the most important concerns of patients undergoing Mohs surgery.

Category : Early experiments with well defined objectives/hypotheses

(11:40 AM)

TET1 is Regulated by O-GLCNAC Transferase (OGT) for Target Gene Repressionin Mouse Embryonic Stem Cells

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Abstract: As a member of the Tet (Ten-eleven translocation) family proteins that can convert 5-methylcytosine (5mC) to 5-hydroxyl methylcytosine (5hmC), Tet1 has been implicated in regulating global DNA de-methylation and gene expression. Tet1 is highly expressed in Embryonic Stem (ES) cells and appears to repress developmental genes for maintaining pluripotency. To understand how Tet1 may regulate gene expression, we conducted large-scale immunoprecipitation (IP) followed by mass spectrometry of endogenous Tet1 in mouse ES cells. We found that Tet1 could interact with multiple chromatin regulators, including Sin3A and NuRD complexes. In addition, we showed that Tet1 could also interact with the *O*-GlcNActransferase (Ogt) and be *O*-GlcNAcylated. Depletion of Ogt led to reduced Tet1 and 5hmC levels on Tet1-target genes, while ectopic expression of wild-type but not enzymatically inactive Ogt increased Tet1 levels. The expression of Tet1 protein was also stimulated by PUGNAc, which increased *O*-GlcNAcylation. In addition, high dose glucose increased Tet1 protein levels, which effect could be abolished by the inhibitor of Ogt; alloxan. We found that Tet1 can be *O*-GlcNAcylated at threonine 535 (T535) and the mutants of T535 decreased the *O*-GlcNAcylation and expression of Tet1 protein. Our results suggest that *O*-GlcNAcylation can positively regulate Tet1 protein concentration and indicate that Tet1-mediated 5hmC modification and target repression is controlled by Ogt. The Ogt-Tet1 link should further our understanding of how post-translational modifications are integrated into the regulatory networks of ES cell maintenance. These data could also apply to adult stem cells in hair follicles. Investigation will begin soon.

Category: Early experiments with well defined objectives/hypotheses

(11:51 AM)

Genetically Modified Skin Cell Therapy Prevents Development of Alopecia Areata

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Alopecia areata (AA) is an autoimmune skin disease affecting millions of men, women, and children worldwide. It manifests as a sudden loss of hair without associated visible scarring or inflammation of the skin. The natural history of AA is unpredictable and contributes to the devastating nature of the condition and the serious impact it can have on the quality of life of the patients it affects. No cure currently exists for AA and treatments used to manage it are only minimally effective. Our research group, however, has come up with a genetically modified skin cell therapy that does prevent AA and could be the first therapy of its kind. Although the exact etiology and pathogenesis of AA are not well understood, the histopathological finding of a peri- and intra-follicular infiltration of CD4+ and CD8+ lymphocytes, respectively, targeting anagen stage follicles suggest this to be the potential mechanism involved in the damage of hair follicles seen in AA. Our novel therapy targets these CD4+ and CD8+ lymphocytes. Preliminary results revealed that none of the C3H/HeJ mice (n=3) treated with our therapy developed AA compared to 80% of control animals that developed severe AA within 8-16 weeks after transplantation of an AA affected skin. These results are extremely promising and with a grant from the National Alopecia Areata Foundation, we look to conduct further studies on the use of our novel therapy and hope that it can be the answer in helping cure the millions of people affected by this traumatizing condition.

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

(12:02 PM)

Genetic Epidemiology of Primary Hyperhidrosis

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Background: Primary hyperhidrosis (HH) is common condition and a disabling disorder that interferes with social, psychological, and professional activities. Up to date, comprehensive genetic analysis and the causative genes implicated in HH have not been determined.
Objectives: The degree of genetic contribution, the mode and the penetrance of inheritance for HH are determined. Methods: All consecutive patients presenting to the Vancouver Hospital Hyperhidrosis Clinic (2002-2012) were interviewed about family history, age of onset, and the distribution of the sweating areas. Familial aggregation was estimated by relative risk ratios (λs) compared with the general population. The heritability (h2) in first-degree relatives was estimated by using Falconer's formula. Complex segregation analysis was performed using the SAGE-SEGREG program. Penetrance rate K was evaluated by PENCALC software. Results: Among 577 HH patients analyzed, 39.52% have family history. Compared with sporadic HH cases, the familial HH patients have earlier age of onset (13.17±8.82, p=0.038), wider sweating distribution (P=0.003). In addition, the first degree relatives of HH patients have

14.41 times higher relative risk of developing HH compared with the general population, making the heritability of 0.661. Complex segregation analysis showed that HH is an autosomal dominant disease involving multiple alleles. The penetrance rate (K) was estimated to be 0.906 (95%CI: 0.872-0.934). Conclusion: The results established HH as a highly genetic disease that is likely inherited as an autosomal condition involving multiple genetic alleles. These results have established a solid foundation for further genetic analyses that ultimately may lead to the identification of HH gene mutations.

(12:13 PM)

The Prognostic Value of BRAF Mutation in Melanoma and Colorectal Cancer: A Systematic Review and Meta-Analysis

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Background: Mutation of *BRAF* is a predominant event in cancers with poor prognosis such as melanoma and colorectal cancer. *BRAF* mutation leads to a constitutive activation of mitogen activated protein kinase pathway which is essential for cell proliferation and tumor progression. Despite tremendous efforts made to target BRAF for cancer treatment, the correlation between *BRAF* mutation and patient survival is still a matter of controversy. **Methods/Principal Findings:** Clinical studies on the correlation between *BRAF* mutation and patient survival were retrieved from MEDLINE and EMBASE databases between June 2002 and December 2011. One hundred twenty relevant full text studies were categorized based on study design and cancer type. Publication bias was evaluated for each category and pooled hazard ratio (HR) with 95% confidence interval (CI) was calculated using random or fixed effect meta-analysis based on the percentage of heterogeneity. Twenty six studies on colorectal cancer (11,773 patients) and four studies on melanoma (674 patients) were included in our final meta-analysis. The average prevalence of *BRAF* mutation was 9.6% in colorectal cancer, and 47.8% in melanoma reports. We found that *BRAF* mutation increases the risk of mortality in colorectal cancer patients for more than two folds; HR=2.25 (95% CI, 1.82-2.83). In addition, we revealed that *BRAF* mutation also increases the risk of mortality in melanoma patients by 1.7 folds (95% CI, 1.37-2.12). **Conclusions:** We revealed that *BRAF* mutation is an absolute risk factor for patient survival in colorectal cancer and melanoma.

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

(12:24 PM)

Treatment of Posterior Cheek Enlargement in HIV+ Patients with Botulinum Toxin A.

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Posterior cheek enlargement is very common in a subset of individuals infected with human immunodeficiency virus (HIV). This can lead to significant disfigurement and social stigmatization. Although parotid hypertrophy is a recognized and common complication of HIV, treatment options are limited and ineffective. These include highly active antiretroviral therapy (HAART), steroids, radiation and surgical resection of tissue, which can result in significant morbidity. Botulinum toxin is a highly efficacious, minimally invasive option for reducing the width and improving the shape of the lower face and jawline. Two HIV+ patients with posterior cheek enlargement were successfully treated with

botulinum toxin A with excellent results. The effect was long lasting even at 5-6 months post-injection, and well tolerated, with no side effects reported. Posterior cheek enlargement in HIV+ individuals has not been well characterized anatomically. Both the parotid gland and masseter muscle overlie the mandibular ramus, thus contributing to the lower facial contour. Although parotid enlargement is a common finding in HIV-associated salivary gland disease, masseter muscle enlargement may also contribute. The aesthetic appearance may also be due to apparent muscle enlargement attributable to facial lipoatrophy. A pilot study is going to be undertaken in order to better characterize posterior cheek enlargement in HIV+ patients and explore treatment with botulinum toxin A. This research may eventually lead to a potentially less invasive treatment for posterior cheek enlargement in HIV+ patients, with advantages of a good result that is long lasting with good tolerability and minimal risk to the patient.

Category: Pilot/exploratory experiments

(12:35 PM)

Occupational Exposure to Skin Carcinogens in Canada

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Objective: To estimate the number of Canadian workers who are potentially exposed to skin carcinogens, focusing on identifying occupations with concurrent exposures. **Methods**: Exposures with potential to cause skin cancer were identified using the CAREX Canada database in consultation with the International Agency for Research on Cancer (IARC). Exposure estimates of interest were those where ≥25% of workers were exposed to an identified skin carcinogen, and/or ≥500 workers were exposed in any job (≥5,000 for solar radiation), as well as jobs were workers were potentially exposed to >2 carcinogens. **Results**: Seven agents (solar radiation, artificial radiation, PAHs, creosotes, coal-tars, bitumens, arsenic) were identified as known or suspected skin carcinogens. Exposure prevalence estimates ranged from 4800 exposed workers (creosotes) to 1.5 million workers (solar radiation) in Canada (2006). There were 11 jobs with >2 skin carcinogen exposures where >25% of workers were exposed to each agent (or ≥500 workers were exposed; ≥5,000 for solar radiation). Of note, construction labourers were exposed to 5 of the 7 agents, welders and heavy equipment operators to 4 agents each, and roofers to 3 agents. **Conclusions**: The preceding population based exposure estimates indicate that many Canadian workers are potentially exposed to known or suspected skin carcinogens, and that many have co-exposures. These estimates highlight the need for further research on exposure mechanisms (i.e. skin cancer risk among welders), the skin toxicity of co-exposures, as well as the need for continued public health, clinical, and occupational health policies and programs to reduce/prevent exposures and protect workers.

(1:40 PM)

Hand-Held Optical Confocal Imaging Scanner for Skin Cancer

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Skin cancer is the most common cancer in North America. Severe consequences, including death, could occur if certain skin cancers such as melanoma are not detected early. This project is to design a MEMS (Micro Electro Mechanical System) based, hand-held size, confocal optical scanner for clinical skin imaging *in vivo*. The scanning area will be approximately 300×300μm^2 in the cross-sectional plane of the skin tissue, which is the plane perpendicular to the skin surface. In the first prototype, different tissue layers will be imaged with targeting resolution of 3μm×10μm in the lateral and axial directions, respectively. The mechanical actuations in the lateral and axial directions are achieved by a MEMS mirror and a voice coil, respectively. This optical scanner imaging system will be based on the principle of reflectance confocal microscopy, with potential capability for Raman spectroscopy. Currently, a preliminary scanner has been constructed, with more improvements on image acquisition and signal processing to be finished. By using this hand held skin scanner, dermatologists may be able to reduce the number of unnecessary and repetitive skin biopsies, which will lower the cost of examination, as well as better utilize medical resources in the health care system. This project is a collaboration between UBC MEMS lab, BCCA Cancer Imaging unit, and VGH Skin Care Centre.

Category: Early experiments with well defined objectives/hypotheses

(1:51 PM)

D-Dimer Levels as a Marker of Vasculopathy: Case Report of Polyarteritis Nodosa and Case Series

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Biochemical markers of disease allow clinicians to monitor disease severity, progression and response to treatment. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are commonly used biochemical markers of inflammatory disease. D-dimers are small protein fragments generated by fibrinolysis of a thrombus or blood clot. D-dimer assays are often used as aids in the diagnosis venous thrombosis. Damage to blood vessel walls leads to activation of the coagulation cascade, thrombus formation and D-dimer release into the blood stream. D-dimer levels may be elevated in forms of vasculitis including Henoch-Schonlein purpura (HSP), Kawasaki disease and Churg-Strauss syndrome. Here we report a 51 year old female patient who presented with recurrent leg ulcers and livedoid pattern erythema. Initial investigations revealed an elevated D-dimer that correlated with clinical manifestations of disease and led clinicians to suspect a primary thrombotic disorder. The patient was treated with anticoagulation but demonstrated minimal clinical improvement and persistent elevation of D-dimer levels. She was eventually diagnosed with polyarteritis nodosa (PAN) and treated with immunosuppressants. As clinical manifestations resolved, D-dimer levels decreased. We present results of D-Dimer analysis in a variety of inflammatory conditions including HSP, leukocytoclastic vasculitis, Behcet's syndrome, lupus, Still's disease, graft versus host disease (GVHD), urticarial vasculitis and pyoderma gangrenosum (n = 16). Our findings suggest that measuring D-dimer levels may be useful as a clinical marker of vasculopathy in autoimmune and autoinflammatory disease. We show here the use of D-dimer measurements as a marker of vasculocentric/vasculopathic inflammation and reveal the possibility that vascular enodothelial damage may be ongoing in many inflammatory conditions.

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

(2:02 PM)

UV Canada II: Time2burn Alert for Skin Cancer Prevention by Phone

Maryam Sadeghi[1,2,3], Tim K. Lee[1,2,3] , David McLean[3] , Harvey Lui[2,3], and M. Stella Atkins[1]
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Overexposure to the sun's ultraviolet (UV) rays causes skin damage that can lead to skin cancer, including melanoma. The UV Index, a simple measure of the intensity of the sun's UV radiation, is a useful tool to alert people to the need for sun protection. The objective of this project was to provide an easy tool that helps Canadians receive daily notifications about the UV hazards in users' location and the time to prevent skin cancer. The app UV Canada employs state-of-the-art human-computer interaction techniques to provide the public with educational material about the risks of sunburn in various locations and activities, the appropriate type and effectiveness of sunscreen, and tips on how to avoid sunburn. The new version, UV Canada II, offers a new alert system called "Time2Burn" to let users set personalized alert settings to allow them to enjoy the sun while reducing their cancer risk, based on the users' choice of environment, their skin type (acquired by a quiz approved by dermatologists), the SPF of their sunscreen, and UV index data from Environment Canada. The data is contributed by the weather office of the government of Canada. This app has been featured in Global National TV and casted over Canada. The application has been downloaded over 35000 times, over 9 million user locations are recorded, and 11 million user requests have been processed so far. We have also extended this service for users of other mobile devices with Android OS and US cities to be released for summer 2013.

Category: Early experiments with well defined objectives/hypotheses.

(2:13 PM)

Analysis for the Potential of Skin-Localized Tregs in Systemic Sclerosis to Transdifferentiate to Cytokine Producing Cells

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T regulatory cells (Tregs) are critical for maintaining self-tolerance. They express constitutively high levels FOXP3 but typically do not express inflammatory cytokines. Recently Tregs have been observed producing inflammatory cytokines in autoimmune diseases, such as multiple sclerosis, implying that Treg plasticity may underlie the breakdown of tolerance in autoimmunity. There is accumulating evidence that deficiencies or dysfunction in Tregs underlie the pathogenesis of a number of inflammatory skin diseases such as scleroderma (SSc), however these studies have not evaluated the potential of plasticity. **In this work,** skin biopsies from SSc patients and healthy donors were minced, placed on Stamatrix®, and after a 3 week culture analyzed by intracellular cytokine staining, in-vitro co-culture with fibroblasts, and pyrosequencing. Blood was analyzed in parallel. We found no difference in the number of FOXP3+ T cells in patients compared with healthy controls, but interestingly, found that a significant proportion of FOXP3+ T cells in SSc skin produce IL-4 and IL-13. Importantly, these cells cannot be found in patient blood but initial data shows FOXP3+ cells in patient blood express the skin homing marker CLA. Work is ongoing to analyse these FOXP3+ cells at the epigenetic level to confirm that they are bona fide Tregs. Preliminary data suggests that healthy donor Tregs are resistant to Th2

polarization in vitro unless co-cultured with SSc fibroblasts. Overall, this research highlights the importance of examining tissue-localized cells and suggests a potential mechanism underlying chronic skin inflammation, which may generate new therapeutic targets to improve patient outcomes.

Category: Early experiments with well defined objectives/hypotheses.

(2:24 PM)

Why are Skin Creases Visible? A Morphologic and Optical Analysis of Palm Crease Pigmentation Using Different Imaging Methods

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Background: Amongst different individuals, there appears to be greater inter-individual differences in color of palm creases as compared to overall palm color. The specific morphologic basis for the darker color of palm creases is unknown. The objective of this study is to determine the origin of palm crease pigmentation. **Methods:** The palm creases of patients with vitiligo involving the hand were assessed, using digital photography, dermoscopy, Wood's light, and near infrared (NIR) imaging. Reflectance confocal microscopy (RCM) and two punch biopsies were performed in one patient. **Results:** Four patients with vitiligo involving the palm were evaluated, and the findings were similar in all patients. Digital photography and dermoscopy showed complete loss of crease pigmentation within depigmented patches. Wood's light examination demonstrated prominent accentuation of the color of the unaffected creases compared to the surrounding normal non-crease skin. In the affected creases, there was a complete loss of pigmentation under Wood's light. A bright linear white signal was detected within normal creases and absent in the contiguous affected creases on NIR imaging. Thea RCM showed brighter signals within keratinocytes in the normal crease when compared to both the normal surrounding non-crease skin and vitiligo-involved crease. Histology revealed increased epidermal melanin within the normal crease with no increase in melanocyte density as compared to normal non-crease skin. **Conclusion:** The preliminary results of this study show evidence of increased melanin in the palm crease which is probably responsible for its darker color. However, there does not seem to be an increase in the number of melanocytes within crease skin.

Category: Pilot/exploratory experiments

(2:30 PM)

C-Terminal Tensin-Like Protein (Cten) Is A Novel Oncogene and Prognostic Marker for Primary Melanoma Patients

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C-terminal tensin-like protein (Cten) is a focal adhesion protein originally identified as a tumor suppressor in prostate cancer. It has since been found to function as an oncogene in numerous other cancers, but the role of Cten in melanoma progression is still unknown. Using tissue microarrays containing 562 melanocytic lesions, we evaluated Cten expression by immunohistochemistry. Strong Cten expression was detected in 7%, 24%, 41%, and 46% of normal nevi, dysplastic nevi, primary melanoma, and metastatic melanoma samples, respectively, and Cten expression was found to be significantly higher in dysplastic nevi compared to normal nevi ($P = 0.046$) and in primary melanoma compared to dysplastic nevi ($P = 0.003$). Strong Cten expression was significantly associated with a worse 5-year overall ($P = 0.008$) and disease-specific survival ($P = 0.004$) for primary melanoma patients, and multivariate Cox regression analysis confirmed that Cten expression is an independent prognostic marker for these patients ($P = 0.038$ for overall survival; $P = 0.021$ for disease-specific survival). Moreover, we found that Cten knockdown resulted in a significant decrease in melanoma cell proliferation *in vitro*. Cten is believed to function by interacting with the *bona fide* tumor suppressor Deleted in Liver Cancer-1 (DLC1), causing auto-inhibition of its RhoGAP activity. Lastly, we here show that strong DLC1 protein expression is associated with a better 5-year survival of melanoma patients, regardless of the status of Cten, supporting that theory. Altogether, these results support the use of Cten as a prognostic marker and potential therapeutic target in melanoma.

Category: Early experiments with well defined objectives/hypotheses