11:35 AM

GRANZYME B CONTRIBUTES TO THE DISEASE SEVERITY OF RADIATION DERMATITIS

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Rationale: Radiation dermatitis (RD) is characterized by skin damage that occurs in up to 95% of patients receiving radiation therapy for cancer treatment. The efficacies of current treatments vary and RD symptoms can impede radiation treatments. Granzyme B (GzmB) is a serine protease expressed and secreted by diverse immune and non-immune cell populations into the extracellular matrix. GzmB is elevated in the skin of patients with atopic dermatitis, cleaves cell-cell junction protein E-cadherin, and mediates barrier dysfunction and dermatitis severity in vivo.

Hypothesis: GzmB contributes to increased severity of RD through cleavage of cell-cell junction protein E-cadherin, resulting in impaired epidermal barrier function.

Results: Elevated GzmB and reduced E-cadherin were observed using immunohistochemistry in skin tissues obtained from patients with RD compared to healthy controls. In an established murine model of RD comparing GzmB knockout (GzmB-KO) to wild type (WT) mice, GzmB-KO mice exhibited a significant decrease in overall RD severity score compared to WT mice at day 4 ($p=0.03$), day 6 ($p=0.02$), day 8 ($p \leq 0.001$), day 10 ($p=0.01$), and day 12 ($p=0.01$) post-radiation. Significant reductions in erythema, scaling, and area of crusted wounds were also observed in GzmB-KO mice between days 4 and 12. Future studies will examine the efficacy of a topical GzmB inhibitor in reducing GzmB proteolytic activity and RD severity.

Significance: GzmB contributes to severity of RD and may be a novel therapeutic target.

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

11:43 AM

VIABILITY AND COSMESIS OF RIGHT ANGLE AND VERTICAL PARAMEDIAN FOREHEAD FLAPS ARE EQUIVALENT: A RETROSPECTIVE QUANTITATIVE STUDY

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Background: Paramedian forehead flaps (PMFF) are commonly used for reconstruction of nasal defects. The classic PMFF is vertically oriented, while the modified PMFF is designed with a 90-degree angle. No study has compared outcomes between these PMFF designs.

Objectives: To compare and quantify viability and cosmesis of 90-degree and vertical PMFF.

Methods: Retrospective chart review of 70 consecutive patients with a vertical or 90-degree PMFF design for nasal repairs following Mohs micrographic surgery (MMS). Cosmetic outcome was assessed on a 10 cm, 100-point, visual analog scale (VAS) by an independent observer using standardized 3-month post-operative photographs. Flap viability was assessed using standardized 3-week post-operative photographs. Descriptive statistics, t-test and Mann Whitney test were used for statistical analysis.

Results: Forty-eight patients were repaired with a vertical PMFF and 22 using the 90-degree PMFF. Mean defect area of vertical and 90-degree designs was equivalent (7.7 ± 4.0cm^2 vs 8.1 ± 4.0cm^2, p=0.70). There was no significant difference in cosmetic outcome (75.9 ± 9.4 vs 72.9 ± 6.8, p=0.19), or flap viability (3.8% ± 11.6 vs 2.6% ± 7.9, p=0.67) between vertical and 90-degree designs.

Conclusions: Vertical and 90-degree PMFF designs for nasal repairs following MMS are equivalent in terms of cosmesis, flap viability, and rates of complications.

Category: Early experiments with well-defined objectives/hypotheses

11:51 AM

GRANZYME K CONTRIBUTES TO IMPAIRED CUTANEOUS INFLAMMATION AND EPIDERMAL PROLIFERATION IN PSORIASIS

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Background: Psoriasis is characterized by skin inflammation and epidermal proliferation forming thick, scaly plaques. Current therapies are not ideal and often present with side effects. Hence, a deeper understanding of the pathological mechanisms of psoriasis are necessary. Granzyme K (GzmK) is a serine protease recently elucidated as a mediator of inflammation. Here, we show the role of GzmK in cutaneous inflammation and epidermal proliferation following induction of psoriasis.

Hypothesis: GzmK contributes to the onset and progression of psoriasis through the augmentation of inflammation and/or epidermal proliferation.

Methods: GzmK levels were evaluated histologically in skin biopsies with and without psoriasis. The role of GzmK was investigated in a murine model of psoriasis, comparing GzmK knockout (K-KO) to wild-type (WT) mice. Psoriasis severity (erythema, squamae) was assessed macroscopically. Skin tissue extract were examined for pro-inflammatory markers and epidermal thickness via histology, ELISA and qPCR. To elucidate a mechanistic role, human keratinocytes were cultured with GzmK for assessment of epidermal proliferation and to define the GzmK degradome as it pertains to the epidermis.

Results: GzmK positive cells were elevated 40-fold (p=0.045) in lesional psoriasis skin compared to healthy skin. K-KO mice exhibited an average 60% decrease in plaque severity compared to WT mice. Pro-inflammatory cytokines IL-17 and IL-23 were reduced 46% (p=0.044) and 48% (p<0.001) in K-KO mice, respectively. K-KO mice also exhibited a 30% decrease (p=0.014) in epidermal thickness compared to WT mice. In vitro, GzmK induced keratinocyte proliferation.

Conclusions: Inhibition of GzmK may represent a novel therapeutic approach for treating psoriasis.

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

11:59 AM

Light and Laser-based Treatments for Hidradenitis Suppurativa: A Systematic Review

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Introduction: Hidradenitis suppurativa (HS) is a chronic folliculitis characterized by painful, recurrent lesions occurring mainly in intertriginous areas. HS is primarily managed by modifying lifestyle risk factors, medical, and procedural therapy. The aim of this systematic review was to critically assess HS treated with light or laser-based therapies and characterize their relative effectiveness.

Methods: Cochrane, MEDLINE, and Embase were searched for articles describing laser and light-based treatments for HS.

Results: Data from 41 studies representing 668 patients were extracted and analyzed The most commonly used treatments were carbon dioxide (CO_2) laser (59%, n=396/668), photodynamic therapy (PDT) (25%, n=167/668), and Nd:YAG laser (14%, n=92/668). Among those with reported treatment outcomes, CO_2 laser was effective in 79% (n=311/396) of patients, PDT in 71% (n=118/167), and Nd:YAG laser in 86% (n=30/35). Adverse events were reported in 26% (n=103/393) of patients treated with CO_2 laser, 15% (n=8/53) Nd:YAG, and 36% (n=23/64) PDT. Lasers used for surgery were more effective compared to lasers used for field treatment, showing overall response rates of 80% (n=344/431) and 71% (n=84/118), respectively. However, lasers used for surgery showed higher adverse event rates (25%, n=105/424) compared to laser field treatment (18%, n=24/134). Limitations included a lack of comparative randomized clinical trials, treatment being offered at different HS stages, and the use of different outcome measures.

Conclusions: Our results suggest that light and laser-based treatments are effective in treating HS patients. Larger comparative studies with standardized outcome assessments are needed to compare the efficacy of these devices to medical therapy.

Category: Early experiments with well-defined objectives/hypotheses

12:07 PM

IS THE CANCER REGISTRY COMPLETE FOR ALL SKIN CANCER CASES? A COMPARISON OF THE BRITISH COLUMBIA CANCER REGISTRY TO HEALTH ADMINISTRATIVE CLAIMS-BASED ALGORITHMS FOR ASCERTAINING KERATINOCYTE CARCINOMA

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Keratinocyte carcinomas (KCs) are the most common human malignancy in North America, with 1 in 7 individuals being affected in British Columbia (BC). However, these incident cases are diagnosed and treated in diverse settings and may not be sent for histopathological verification. Thus, KCs are often excluded from cancer registries which limit healthcare burden assessments. A systematic review of the scientific and grey literature suggests there is a lack of completeness in KC case records in cancer registries. The BC Cancer Registry claims to have officially coded and recorded all pathologically confirmed KC cases between 1970 and 1994 and then again in 2003. Therefore, we aimed to compare methods of KC ascertainment using previously validated health insurance claims-based algorithms to the BC Cancer Registry data, and to verify the completeness of the BC Cancer Registry for KC cases in the study period of the years January 1, 1992 to December 31, 1993, and January 1, 2002 to December 31, 2003. We currently have access to KC data within the Medical Services Plan (MSP) and the BC Cancer Registry databases through Population Data BC. Factoring in a margin of error for each ascertainment method, the ascertainment performance (sensitivity, specificity, positive predictive value, negative predictive value) and the percentage of ascertained KC cases will be assessed. We hypothesize that the BC Cancer Registry has an incomplete record of KCs, and that health insurance claims will be a reasonable alternative ascertaining KCs for epidemiological purposes.

Category: Early experiments with well-defined objectives/hypotheses

12:15 PM

SAFETY AND EFFICACY OF ONCE- VERSUS TWICE-WEEKLY ULTRAVIOLET PHOTOTHERAPY REGIMENS IN PATIENTS WITH PSORIASIS AND ECZEMA

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Background: During the COVID-19 pandemic, public health directives necessitated that our patients were restricted to reduced once- or twice-weekly phototherapy treatment regimens over 10-week cycles with higher incremental dosing.

Objectives: Safety and efficacy assessment of once- versus twice-weekly ultraviolet phototherapy regimens for psoriasis and eczema patients.

Methods: Psoriasis (n=492) and eczema (n=271) patients treated at the VGH Phototherapy Clinic between June 2020-August 2021 were assessed. Disease severity was assessed using two previously validated outcome parameters: (1) investigator global assessment times body surface area (IGA*x*BSA), and (2) Dermatology Life Quality Index (DLQI).

Results: Over 30 weeks, erythema higher than grade 1 occurred in 14% and 18% of psoriasis treatments, and 13% and 19% of eczema treatments for once- versus twice-weekly treatment groups. Overall, at 20 weeks, there was significant improvement in disease severity with 66% and 57% median IGAxBSA improvement from baseline ($p<0.001$, Wilcoxon matched-pairs signed-rank test). 39% and 57% of psoriasis patients, and 43% and 44% of eczema patients treated once- versus twice-weekly achieved 50% reduction in IGA*x*BSA, while 12% and 31% of psoriasis patients, and 19% and 13% of eczema patients treated once- versus twice-weekly achieved a 75% IGAxBSA response. Patients with both psoriasis and eczema achieved significant improvement in median DLQI after 10 weeks ($p<0.001$, Wilcoxon matched-pairs signed-rank test).

Conclusions: Reduced treatment frequencies utilizing higher incremental dosing improved disease severity and DLQI measurements. Twice- versus once-weekly treatment showed greater efficacy with slightly higher erythema rates. Differences in efficacy between frequency regimens were less pronounced in eczema patients.

Category: Early experiments with well-defined objectives/hypotheses

12:23 PM

SKIN CANCER DETECTION BY RAMAN SPECTROSCOPY AND DEEP NEURAL NETWORKS: PRELIMINARY RESULTS

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Background: Deep neural networks has been investigated to generate dermatologist-level classification for skin cancer diagnosis based on clinical images. Raman spectroscopy has been used for *in vivo* skin cancer detection with high sensitivity and specificity. The objective of this study is to explore skin cancer detection by combining deep neural networks and Raman spectroscopy.

Patients and Methods: *In vivo* Raman spectra of 340 cancerous and precancerous lesions including malignant melanoma, basal cell carcinoma, squamous cell carcinoma and actinic keratosis and 391 benign lesions including melanocytic nevi and seborrheic keratosis were analyzed in this study. The stratified samples were divided randomly into training (70%), validation (10%) and test set (20%). One-dimensional convolutional neural networks (1D-CNN) were developed for spectral analysis. Data augmentation was implemented with artificially added noise, spectral shift and spectral combination. Area under the receiver operating characteristic curve (ROC AUC) was used as a measure of the diagnostic performance. Multivariate statistical analyses, including logistic regression (LR), support vector machine (SVM), principal component and linear discriminant analysis (PC-LDA) and partial least squares for discriminant analysis (PLS-DA) were also evaluated for comparison purpose.

Results: Using the original training dataset, the ROC AUC of 1D-CNN (0.894±0.027) for the test set is slightly better than SVM (0.830±0.033), PC-LDA (0.884±0.025) and PLS-DA (0.884±0.029). After augmentation of the training dataset, 1D-CNN (0.887±0.025) produced similar diagnostic results with LR (0.886±0.025), SVM (0.885±0.024), PC-LDA (0.881±0.026) and PLS-DA (0.887±0.027).

Conclusions: Convolutional neural networks combining Raman spectroscopy produced equivalent or better performance for skin cancer detection than conventional multivariate statistical analyses.

Category: Applied/functional experiments (in vivo studies)

12:31 PM

BARRIERS TO HEALTHCARE ACCESS FOR PATIENTS WITH PSORIASIS

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Barriers to healthcare access (BtHA) are factors that hinder a patient's access to treatment. Previous studies have shown that a substantial number of patients express dissatisfaction with their treatment and healthcare access, but little research has been done to characterize the types of BtHA experienced by psoriasis patients. We conducted a systematic review to examine the BtHA identified in the psoriasis literature. We categorized our findings as systemic, sociocultural, provider or individual barriers. Individual barriers appeared most often, followed by systemic, provider and sociocultural barriers, respectively. For individual barriers, themes of non-adherence, patient knowledge gaps, opinions about treatment side effects and dissatisfaction with their efficacy were found. Common systemic barriers included therapy costs and geography. Provider level barriers included a lack of culturally competent care, wait times, short appointment durations and and unwillingness to make referrals. Sociocultural barriers included reliance on traditional medications, language and limited levels of therapy knowledge or exposure for certain ethnic groups. Our findings are mostly consistent with the barriers identified in broader healthcare disparity literature, but certain knowledge gaps were noted. Firstly, fewer sociocultural barriers were identified in psoriasis literature compared to general disparity literature. Studies have suggested that psychological factors, prior negative healthcare experience and comorbidities could act as BtHA, but none were found in our review. Future research in this area is important for psoriasis given its psychological and physiological comorbidities. Further investigation into the different BtHA that may be specifically relevant to psoriasis patients and interventions to overcome those barriers is needed.

Category: pilot/exploratory experiments (systematic review)

12:39 PM

NEW APPROACHES TO OLD PROBLEMS - TREATMENT OF LENTIGINES: A SYSTEMATIC REVIEW

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Background: Lentigines are common, benign areas of skin pigmentation characterized by macular, uniform hyperpigmentation, often located on sun exposed areas of the skin, such as the dorsum of the hands, face, and arms. Treatments consist of topical and physical therapies, including chemical peels, lasers, intense pulsed light, and cryotherapy. A direct comparison of treatment methods and their efficacy is lacking.

Objectives*:* To compare treatment efficacy and adverse events for different treatment modalities for lentigines.

Methods*:* We performed a systematic review by searching Cochrane, MEDLINE and Embase. Title, abstract, full text screening, and data extraction were done in duplicate by three reviewers using Covidence. Treatment outcomes were scored as complete response, partial response, and no response.

Results*:* Forty-eight articles met the inclusion criteria, representing a total of 1763 patients. Overall, combination-based treatments showed the greatest frequency of cases with complete response (65%, n=299/458), followed by laser-based treatments (43%, n=398/910), topical retinoids (21%, n=12/57), cryotherapy (15%, n=25/169), and peels (6%, n=8/125). Adverse events occurred most commonly while using topical retinoids (82%, n=23/28), followed by combination-based treatments (44%, n=206/466), cryotherapy (33%, n=47/144), laser-based treatments (37%, n=310/846), and peels (19%, n=21/110).

Conclusions: Our results suggest that combination-based treatments and laser-based treatments were the most efficacious treatment modalities. Although cryotherapy was previously considered first-line, our results show that it has substantially lower pooled response rates compared to other treatment modalities.

Category: Early experiments with well-defined objectives/hypotheses

12:47 PM

CUTANEOUS CpG ADJUVANT CONDITIONING TO ENHANCE VACCINE RESPONSES

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Adjuvant activity of the Toll receptor 9 agonist CpG 1826 was compared when given subcutaneously (s.c.) together with ovalbumin (s.c. [CpG + Ova]), or when given by either s.c. or intradermally (i.d.) routes two days prior to s.c. ovalbumin. Frequencies of $CD8^+$ effector (T_{EFF}) and central memory (T_{CM}) T cells along with total IgG, IgG2c, and IgG1 titres were measured to ascertain how timing and location of CpG conditioning influenced vaccination outcome. Prior treatment with CpG enhanced T_{EFF}, T_{CM}, as well as total IgG responses. T_{EFF} and T_{CM} responses were greatest when CpG was given intradermally and prior to s.c. ovalbumin, conditions that eliminated the fraction of T_{CM} 'non-responders' observed after s.c.[CpG + Ova] vaccination. IgG responses were polarized toward IgG2c after early s.c. CpG but toward IgG1 after early i.d. CpG. Separating CpG adjuvant and antigen application in time and space can improve vaccination outcome.

Category: Applied/functional experiments (animal models, in vivo studies)