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Topical DNA Repair enzyme reversal of UVB-induced gene expression changes



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Background: The ability to detect and treat DNA damage remains a clinical challenge. The purpose of this study is to determine gene expression changes induced by UVB light and assess the effect of topical DNA repair enzymes in reversing these changes.

Methods: Noninvasive adhesive patch skin biopsies were performed on the right and left postauricular areas of 48 subjects before and 24 hours after UVB exposure using an excimer laser (300 mJ). Subjects then applied DNA repair enzymes (T4N5 endonuclease or photolyase) to the right postauricular area only daily for 2 weeks. Subjects returned 2 weeks later for repeat biopsies. RNA was isolated and assessed by reverse transcriptase followed by quantitative PCR to assess gene expression changes.

Results: 7/18 assessed genes demonstrated significant down-regulation (vitamin A, programmed cell death protein, small proline rich protein) or up-regulation (interleukin families 1/2) 24 hours following UVB exposure. T4N5 significantly reversed UVB-induced down-regulation of small proline rich protein and cystatin gene families. Photolyase significantly reversed UVB-induced down-regulation of cystatin gene families.

Conclusions: These results suggest that UVB exposure causes acute changes in gene expression and that DNA repair enzymes demonstrate efficacy in reversing these changes. Topical T4N5 and photolyase can increase cystatin gene expression following UVB-induced down-regulation after only 2 weeks of application. Cystatins have been reported to be diminished or lost in both basal and squamous cell carcinomas and these findings suggest that topical DNA repair enzymes may hold the ability to repair UV-induced genetic changes and protect against future skin cancer development.

Commercial disclosure: None identified.

17080

Real-world treatment patterns and health care utilization in patients with prurigo nodularis



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Background: Prurigo nodularis (PN) is a chronic dermatosis characterized by pruritic, hyperkeratotic nodules. With no FDA-approved therapies or standardized guidelines, little is known about management of PN. Herein we describe treatment patterns and health care utilization in PN in a large ambulatory cohort.

Methods: IBM's MarketScan Commercial Claims Database was queried using ICD-10 diagnosis codes for adults age 18-64 years with PN and patients without PN: age- and sex-matched controls, atopic dermatitis (AD), and psoriasis, from October 2015 to December 2016. Treatments were identified using National Drug Codes and Current Procedures Terminology codes. Generalized linear models (log link, gamma distribution) and negative binomial regression were used to calculate relative cost and incidence rate ratios, adjusting for age and sex.

Results: The majority of patients with PN received corticosteroids: intralesional (36.4%), topical (26.1%), and systemic (19.0%). Among itch-modulating medications, gabapentin (6.5%) was used most frequently. Compared with AD and psoriasis, PN patients were less likely to receive phototherapy ($P < .05$). Mean total health care spending per PN patient was \$8334 (USD), which was increased compared with matched controls. Most PN patients were seen by dermatology (85.9%) and were more likely to see psychiatry compared with all other groups ($P < .001$). Compared with AD and psoriasis, PN was less likely to see internal/family medicine ($P < .001$).

Conclusions: Corticosteroids were the most common treatment in PN, with fewer patients receiving itch-modulating neurologic agents. PN patients incurred higher health care costs than controls and were less likely to be followed by primary care than AD or psoriasis.

Commercial disclosure: None identified.

17063

Skin tone preferences and their influence on skin care behaviors



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Background: Knowledge regarding a difference between actual and ideal skin tone in minority populations and whether this preference influences skincare behaviors is limited.

Methods: Subjects included ≥ 18 -year-old self-identified members of minority populations (African American, Asian, Hispanic/Latino, Native American/Alaskan Native, and mixed race) who could complete an online, English survey. Participants were recruited via ResearchMatch, CT.gov, and flyers on a university campus. A voluntary 31-question survey was given via REDCap. Demographics, actual versus ideal skin tone, medical history, skin care knowledge, attitudes, and behaviors were collected.

Results: 548 subjects completed the survey. A mean difference was calculated between actual and ideal skin tones for the entire population. This was repeated with the 5 racial/ethnic groups (African American, $n = 248$ [45.3%], Asian, $n = 89$ [16.2%], Hispanic/Latino, $n = 111$ [20.3%], Native American/Alaskan Native, $n = 12$ [2.2%], mixed race, $n = 88$ [16.1%]). The Hispanic/Latino group had a statistically significant mean difference, preferring tanner skin ($P < .01$). No other mean difference was statistically significant. Within the Hispanic/Latino group, 98/111 (88.2%) indicated that they sometimes or rarely/never worry about getting skin cancer and 47/111 (42.3%) have engaged in outdoor tanning in the last year. In comparison, only 15.5% of the African-American population tan outside ($P < .0001$), while 23.6% of the Asian population tan outside ($P = .006$).

Conclusions: The rising incidence of melanoma and nonmelanoma skin cancers in the Hispanic/Latino population makes it important to further explore this difference between actual and ideal skin tone and its relationship to tanning behaviors.

Commercial disclosure: None identified.

17083

Identification of psoriasis-protective IL-17D variant associated with increased IL-17D and FAM19A5 expression in psoriatic skin



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Psoriasis is a chronic inflammatory skin disease with an estimated heritability of 80%. Susceptibility loci identified by genome-wide association studies only account for a small fraction of this heritability. Conversely, gene expression analyses have identified thousands of differentially expressed genes in psoriasis but only a small fraction are likely involved in psoriasis pathophysiology. Of these, IL-17A is highly up-regulated in psoriatic skin and appears to be a driver of disease. In contrast, IL-17D is highly expressed in normal skin but down-regulated in psoriatic plaques. We therefore sought to analyze psoriasis RNA-Seq datasets to identify IL-17D variants and the effect these have on psoriasis susceptibility and/or if they alter the psoriasis transcriptome. This led to the identification of an IL-17D-associated allele (rs9509353) that was protective against psoriasis (OR = 0.20, P value = $5.9E-07$). Psoriasis patients with this SNP had increased expression of IL-17D, to a level similar to that seen in healthy skin. Lesional skin from these patients also had increased expression of FAM19A5, a chemokine-like protein also normally down-regulated in psoriasis. Correlative analysis supported a dependent relationship between IL-17D and FAM19A5 ($r = 0.64$, $P = 3.2E-13$). Furthermore, a nonlinear dimensionality reduction strategy used to construct a 2D image of the psoriasis transcriptome illustrated the close spatial relationship between IL-17D and FAM19A5, which mapped together and away from the proinflammatory cytokine cluster comprised of IL-17A, IL-23A, IL-36, and IL-1B. Combined, these results highlight a putative regulatory role for IL-17D and FAM19A5 in psoriasis.

Commercial disclosure: None identified.