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Abnormal autophagosome formation increased melanocyte sensitivity to H2O2-induced oxidative stress in vitiligoT Cui, S Li, K Li, Z Jian and C Li *Dermatology, Xijing Hospital, Xi'an, Shannxi, China*

Autophagy is a controlled self-digestion process which can protect cells against oxidative damage. Dysregulated autophagy has been demonstrated to increase melanocyte sensitivity to oxidative stress in vitiligo. However, the exact mechanism is still not clear. This study aimed to determine the implications of autophagy for melanocyte survival in response to oxidative stress. Our results demonstrated that the autophagic flux in PIG1 exposure to H2O2 was significantly enhanced compared with that in PIG3V, which were accompanied by high level of ROS accumulation, membrane potential changes, and increased apoptosis. It indicates that vitiligo melanocytes exhibited hypersensitivity to H2O2-induced oxidative injury due to dysregulated autophagy. To further explore the mechanism, we performed RNA sequencing to compare the RNA expression in PIG1 and PIG3V cells exposed to H2O2, the bioinformatic analysis indicate that autophagosome formation was impaired in vitiligo melanocytes, our in vitro study also showed that inhibition of autolysosome degradation can not lead to autophagosome accumulation in vitiligo melanocytes, confirming that the impairment of autophagosome formation is responsible for the defects of autophagy in vitiligo melanocytes, the further study also showed that overexpression of HSF1, the main transcription factor for Atg5 and Atg12, could reduce H2O2-induced oxidative damage of vitiligo melanocytes. Our data demonstrated that owing to the deficiency of HSF1 expression, the autophagosome formation was blocked, which resulted in autophagy impairment and further increase the sensitivity of vitiligo melanocytes to oxidative stress. Our results indicating that targeting autophagy may be a potential therapy option.



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Racial differences in the health-related quality of life of chronic pruritus patientsK Whang¹, Y Semenov², R Khanna¹, K Williams¹, V Mahadevan¹ and S Kwatra¹ *1 Department of Dermatology, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States and 2 Department of Dermatology, Massachusetts General Hospital, Boston, Massachusetts, United States*

Chronic pruritus is a condition with profound impact on quality of life (QoL), which has been shown to vary with race. The goal of our study was to characterize the racial differences in the health-related QoL of patients diagnosed with chronic pruritus. We administered a cross-sectional survey of 95 patients with chronic pruritus utilizing the Ontario Health Utilities Index Mark 3 (HUI3) questionnaire. We obtained normal population data from healthy US adults (n=4,187) from the 2002-2003 Joint Canada/United States Survey of Health. HUI3 scores, representing overall health performance and health in specific domains, were compared between the groups and stratified by race. Chronic pruritus patients were significantly more likely to be black compared to the general population (OR 6.67, 95% CI [4.26-10.48], p<0.001). Among the subset of chronic pruritus patients diagnosed with prurigo nodularis, black race was associated with decreased overall health performance in multivariate regression adjusting for demographics and itch severity (coefficient -0.49, 95% CI [-0.98 to -0.01]). This association was not observed in other diagnosis classes for chronic pruritus. Black chronic pruritus patients had a significantly higher average quality-adjusted life year (QALY) loss, calculated based on HUI3 scores, than white chronic pruritus patients (7.66 vs. 6.18 years, p=0.003). The QALY loss by black chronic pruritus patients translates to an increased individual lifetime financial burden of \$383,036 compared to \$309,011 for white chronic pruritus patients. This study demonstrates racial differences impacting health-related QoL and economic burden of chronic pruritus. Further research must be performed to study etiologic factors responsible for the observed racial disparities.



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Patient race affects dermatologists' assessments and treatment of psoriasisA Sevagamoorthy, A Bazen, D Shin, FK Barg and J Takeshta *University of Pennsylvania, Philadelphia, Pennsylvania, United States*

Racial disparities in psoriasis treatment have been suggested. Little is known about how physicians' assessments and treatment patterns may contribute to these disparities. We aimed to evaluate whether patient race, gender, or socioeconomic status affect dermatologists' assessment and treatment of psoriasis. We conducted a cross-sectional survey study of a random sample of dermatologists (N=3,352) who are members of the American Academy of Dermatology. Each dermatologist was randomly assigned one of eight identical survey options which differed only by either patient race (white vs black), gender (male vs female), or socio-economic status (high vs low). Each vignette described and visually depicted a 50-year old with severe psoriasis followed by questions assessing the dermatologist's confidence in the diagnosis of psoriasis and their first line treatment recommendation. We performed multivariable logistic regression to evaluate the associations among patient characteristics and the dermatologist's confidence in psoriasis diagnosis and treatment recommendation. In total, 668 dermatologists returned the survey yielding a response rate of 19.9%. Most dermatologists were between the ages of 35 and 54 years (54%), white (74%), and practiced in a single specialty private setting (49%). Dermatologists were less likely to be confident in the diagnosis of psoriasis among black patients compared to white patients (odds ratio [OR] 0.15, 95% confidence interval [CI] 0.08-0.29). Lack of confidence in the diagnosis of psoriasis was also associated with a lower likelihood of recommending appropriate treatment for severe psoriasis with phototherapy, oral systemics or biologics (OR 0.35, 95% CI 0.17-0.71), independent of disease severity assessment and other patient and dermatologist characteristics. Our findings identify differences in the confidence of psoriasis diagnosis among dermatologists by patient race, which likely drive treatment recommendations whereby black patients are more likely to be underdiagnosed and undertreated for their psoriasis.



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Keloids are associated with Th2, JAK3, and CCR9/CCL25 inflammationJ Wu¹, E Del Duca¹, M Espino¹, A Diaz¹, N Zhang¹, A Gontzes¹, Y Estrada¹, JG Krueger², A Pavel¹ and E Guttman-Yassky¹ *1 Dermatology, Icahn School of Medicine at Mount Sinai, New York, New York, United States and 2 Laboratory for Investigative Dermatology, Rockefeller University, New York, New York, United States*

Keloids occur due to disturbed wound healing and abnormal collagen production, often affecting African American (AA) and Asian populations. An increased prevalence of atopic conditions, particularly asthma, has been described in keloid patients. However, its immune pathomechanism has not been studied, inhibiting therapeutic development. To evaluate the inflammatory signature of keloids in skin we obtained lesional and nonlesional biopsies from 3 AA patients with new onset keloids and 5 AA healthy controls. We profiled the cellular and molecular phenotype of keloids using immunohistochemistry, RNA-seq, and RT-PCR. Significant increases in cellular infiltrates were found in keloids including OX40⁺ T-cells and OX40L⁺ dendritic cells, tryptase⁺ mast cells, and periostin⁺ cells. Expressions of CCR9 and its ligand CCL25, that regulate cellular recruitment in early asthma inflammation, were significantly upregulated in keloid lesions (p<0.05). Lesional skin also showed upregulation of immune markers related to Th2 (IL13, IL4R, OX40L, CCL25), Th17 (CCL20, PI3), Th1 (CXCL9/10/11), and JAK3 signaling (p<0.05). T-cell migration (CCR7, CCL19) and cytotoxic (granzyme B) markers were also highly upregulated in keloid lesions (p<0.05). Similar trends of upregulations were found in nonlesional compared to normal skin. Among significantly down-regulated markers in both lesional and nonlesional skin, was the negative regulator IL-37 (p<0.05). We also identified increased fibrosis/bone/cartilage-differentiation products, consistent with prior studies, (p<0.05). Overall, our data show a strong Th2/JAK3 inflammatory milieu, indicating the potential use for Th2 targeting agents in keloids, similar to other atopic indications, such as atopic dermatitis and asthma.



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Doctor-level multi-classification of skin diseases and a dataset for the Yellow RaceX Chen, S Zhao, Y Kuang, M Chen and W Zhu *Department of Dermatology, Xiangya Hospital, Central South University, Changsha, Hunan, China*

Convolutional Neural Networks has superior performance in image recognition. But it relies on a large amount of data. However, there has not been public skin disease dataset for a specific race. This paper builds such a dataset for the yellow race. It includes 108,248 images from 474 different skin diseases, and part of these images are also annotated with location for individual skin lesions. All these annotations are validated by at least 3 dermatologists and matched with corresponding pathology information as golden standard. Moreover, each image in this dataset are matched with clinical history. Based on this dataset, a framework for skin disease diagnosis was proposed. This framework was designed based on the properties of skin lesions, such as scattering and irregular shape. For an input images, this framework first detects individual skin lesions to generate local results, and then these local results combine to come up with the final result which indicate the disease category for the input image. We conducted a competition between our framework and 31 professional dermatologists. And in the competition, some indistinguishable images from six common skin diseases are used as the testing data, including skin benign tumors (Seborrheic Keratosis), skin malignant tumors (Basal Cell Carcinoma), connective tissue disease (Lupus Erythematosus), allergic skin disease (Eczema), and bullous skin disease (Pemphigus), erythematous papule scaly skin disease (Psoriasis). Comparing the performance on the same testing data, our framework achieved average precision of 64.75% (top1) and 84.77% (top3), and for dermatologists there are 62.13% (top1) and 78.15% (top3). Which shows that, in our dataset for the yellow race, the framework proposed in this paper reached the average level of dermatologists. It laid the foundation to the building of intelligent diagnosis and treatment platform for skin diseases.



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Understanding the intersectional stigma of HIV-related dermatologic disorders in KenyaD McMahon¹, L Butler², N Busakhal³, L Chemtai⁴, A Semeere⁵, H Byakwaga⁵, M Laker-Oketta², J Martin⁶, I Bassett⁷ and E Freeman⁷ *1 Harvard Medical School, Boston, Massachusetts, United States, 2 University of Connecticut, Storrs, Connecticut, United States, 3 Moi University, Eldoret, Kenya, 4 AMPATH, Eldoret, Kenya, 5 Infectious Disease Institute, Kampala, Uganda, 6 UCSF, San Francisco, California, United States and 7 Massachusetts General Hospital, Boston, Massachusetts, United States*

Stigma is an independent determinant of health inequities for people with HIV and skin disease, yet few studies have examined how the intersection of these conditions influences overall stigma. This intersectional stigma may be particularly prominent for people with Kaposi's Sarcoma (KS), a common HIV-related dermatologic condition in sub-Saharan Africa. In this study we used qualitative interviews with KS patients in Kenya to assess HIV stigma, dermatologic stigma, and intersectional stigma for both conditions. All patients ≥18 with newly diagnosed Kaposi's sarcoma within the AMPATH clinic network in Western Kenya from 2016-2019 were enrolled in the parent study. Of these, 88 were purposively selected to participate in a semi-structured interview. Coded transcripts were analyzed with framework analysis using the Health Stigma and Discrimination Framework. Our findings highlight six themes demonstrating how the intersection of HIV and dermatologic stigma produce health inequities: (1) Multiplied fears of contagion and (2) Physical disability and disfigurement resulted in (3) Loss of relationships and employment, as well as produced (4) External fears of witchcraft, ultimately leading to (5) Social isolation and (6) Decreased motivation to travel to and engage with the health system. To improve healthcare engagement for people with HIV-related skin disorders, the intersection between dermatologic conditions and HIV should be considered. Potential interventions to reduce stigma include incorporation of dermatologic screening and treatment at existing HIV centers, support groups for patients with shared identities, as well as continued efforts to reduce community-level and structural drivers of stigma.

