



Relationship Between Sun Exposure and Molecular Markers of Facial Skin Aging—The Multi-Decade & Ethnicity Study

Poster #3739

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*This work has been funded by Procter & Gamble
Dr. Kimball is a consultant and investigator to P&G*

Introduction

We have reported previously that youthful facial skin appearance is associated with altered expression of approximately 2100 epidermal genes related to cellular functions including DNA repair/replication, cell survival, cell response to oxidative stress, energy metabolism, and barrier. These findings were based on a study, The Multi-Decade & Ethnicity (MDE) Study, of female volunteers spanning in age from 20 to mid-70s, with the goal of defining molecular pathways associated with aging of skin and the relationship to facial appearance. We now have evaluated if youthful appearance can be associated with lifestyle choices.



Methods

- Skin samples were obtained from both photoexposed (face, outer forearm) and photoprotected (buttocks) body sites of Caucasian (Fitzpatrick I-III with majority Northern European ancestry confirmed by genotyping) with approximately 25 volunteers in each age decile. The degree of photoaging was confirmed by histological assessment of elastosis (Fig. 1).
- Facial skin appearance was evaluated based on consumer assessment of youthfulness in pair-wise comparisons of subject facial images, as compared to the chronological age of the subjects.
- RNA was isolated from either full-thickness or laser capture microdissected skin biopsies; the analysis reported here focused on two skin sites – face and dorsal forearm. Transcriptomics profiling was conducted using Affymetrix HG-U219 gene arrays.
- The study participants also completed a questionnaire that included lifestyle habits, practices and attitudes.



Results

- Skin from the two photoexposed body sites evaluated (face, arm) showed evidence of solar elastosis in women ≥ 40 years old, thus confirming the lifetime sun exposure for these body sites (Fig. 1). However elastosis was not apparent in photoprotected buttocks skin (Fig. 1).
- Across the women participating in the MDE Study, the apparent age of the women based on their facial skin appearance correlated with their actual chronological age, however some women looked younger or older than their actual age (Fig. 2).
- Women with older appearing facial skin reported that they had above average lifetime sun exposure, reflecting attitudes of “I love the sun” and “I really don’t pay much attention to the sun” (Fig. 3). These women had marked signs of facial skin aging such as lines, wrinkles and hyperpigmentation (Fig. 4). The high degree of lifetime sun exposure paralleled elevated levels of expression of a molecular marker of cellular senescence, CDKN2A; women with above average lifetime sun exposure had significantly higher CDKN2A expression in photoexposed body sites (Figs. 3 and 4).
- In contrast, women with younger appearing facial skin reported they had lower lifetime sun exposure (Fig. 3), reflected by an attitude of “I try to stay out of the sun as much as possible and if I must be out in the sun, I wear some kind of protection (clothes, hats, sunscreen).” Women with average or below lifetime sun exposure also had significantly lower levels of CDKN2A expression (Figs. 3 and 4).
- We report separately (AAD 2016, Poster #3445) that CDKN2A is greatly increased in expression in skin from sun-exposed body sites in both Caucasian and African-American women and to a far lesser extent in skin from a sun-protected body site (buttocks).
- In addition to sun exposure, other lifestyle choices evaluated in this study did not show a statistical correlation with youthfulness of facial skin appearance, including water consumption, sleep and exercise (data not shown).



Figure 1. Age-Associated Increase in Dermal Elastosis

Elastosis was apparent in skin from photoexposed body sites (face, dorsal forearm) commencing in the 40s, but was absent in photoprotected buttocks skin.

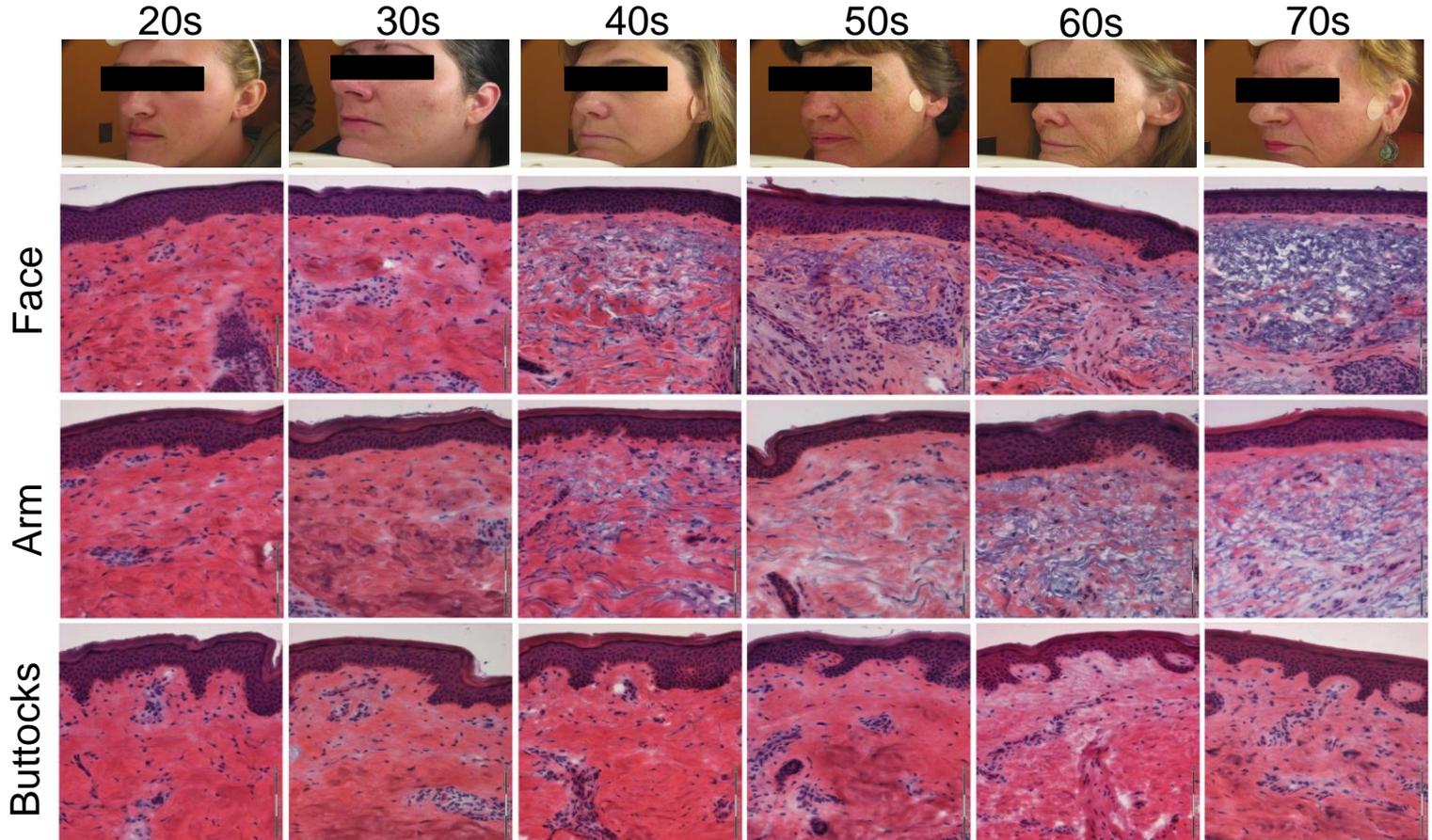


Figure 2. Comparison of Facial Skin Appearance Age to Actual Age

- The chronological age of each subject (x-axis) was compared to the visual age score (y-axis) for Caucasian (blue symbols) and African-American (red symbols) subjects.
- There was a strong (> 0.9 rank-correlation) linkage of apparent age score to chronological age across the subjects.
- Within each decade of chronological age, there was a range of apparent age from slower to faster agers. For example, one 44 year old subjects' facial skin appeared more youthful (lower inset image – slow ager) than another 44 year old subject (upper inset image – fast ager).

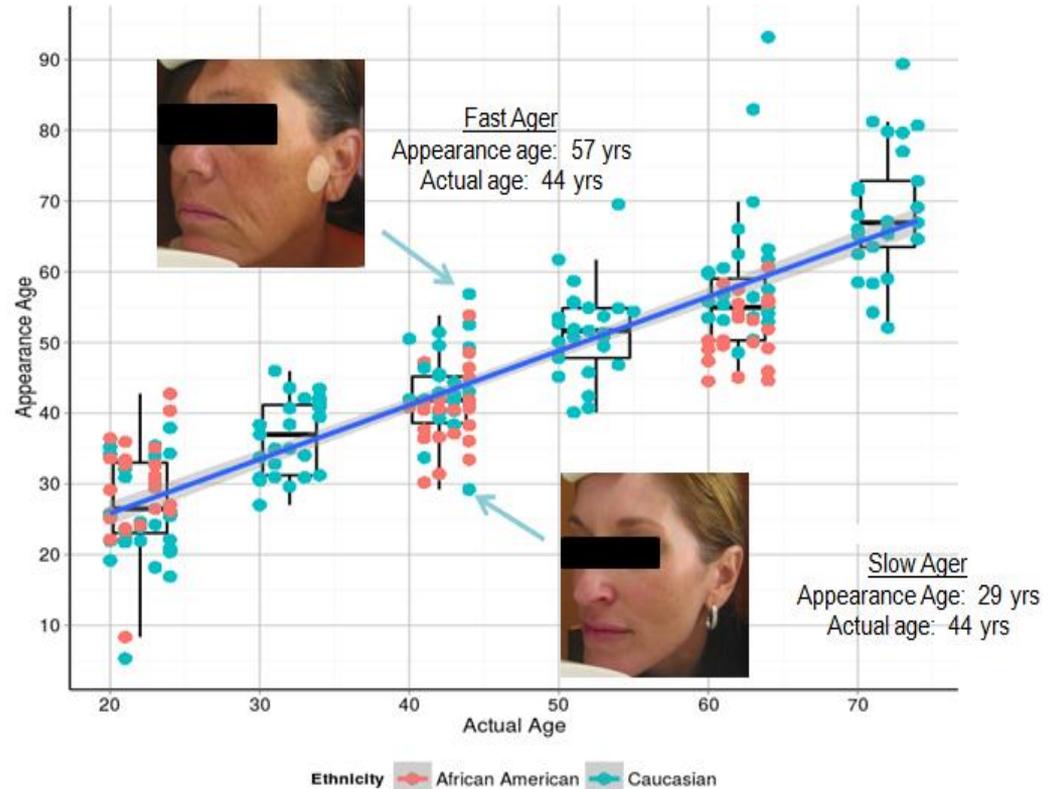


Figure 3. Relationship of Appearance Age & Cellular Senescence to Sun Exposure

- Women who indicated that they had an above average lifetime sun exposure also had older appearing facial skin than women with lower lifetime sun exposure (left).
- In parallel, CDKN2A expression, a marker of cellular senescence, was higher in the skin of women with above average lifetime sun exposure, in two sun-exposed body sites: facial epidermis (middle) and arm skin (right).

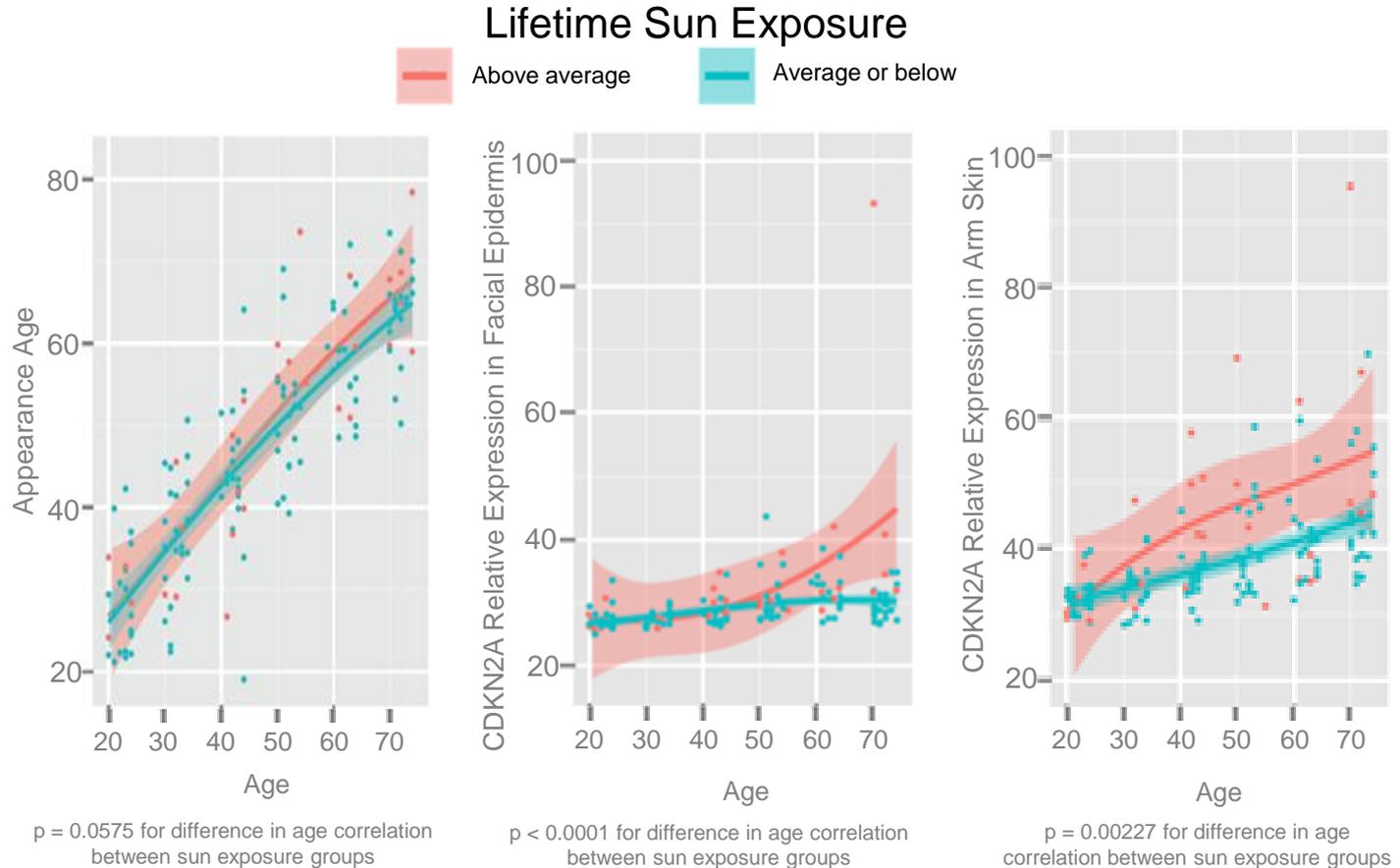
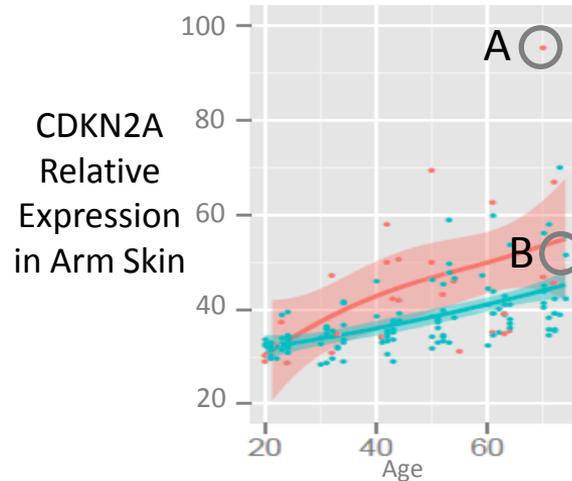
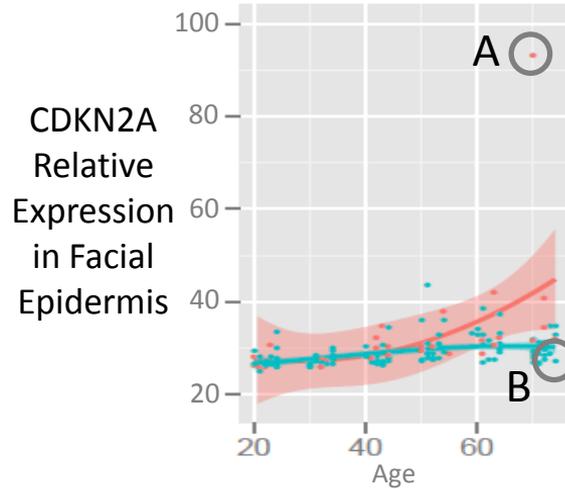
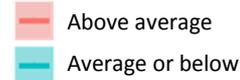


Figure 4. Appearance, Senescence & Sun Exposure

- Images indicate examples of women in their 70s, with Older (A) and Younger (B) appearing skin. The older appearance in A was driven by a higher degree of lines, wrinkles and pigmentation.
- CDKN2A expression was approximately 3-fold higher in the facial epidermis (top graph) of the woman with older appearing skin (A), as compared to the woman with younger appearing skin (B).
- CDKN2A elevated in another sun-exposed skin site – the dorsal arm (bottom graph) – approximately twice the level in woman A as compared to woman B.

Lifetime Sun Exposure



Conclusion

The results confirm that sun exposure is a major factor contributing to molecular changes associated with aged skin appearance. This finding supports that sun protection is a lifestyle choice that could contribute to achieving and maintaining exceptionally youthful appearing skin.



Acknowledgements

Harvard Medical School & Massachusetts General Hospital

- Elvida Arias
- Monica Enamandram
- Neil Houston
- Tyler Petersen

Procter & Gamble

- Chelsea Combs
- Michelle Hare
- Raghu Kainkaryam
- Yogita Mantri
- Daniel Schnell
- Dionne Swift
- Jay Tiesman
- Jun Xu



Thank you

