

INTRODUCTION

For decades, Olay has been a pioneer in skin biology research and product innovation, delivering customized beauty solutions. On a journey to understanding everything about women's skin, Olay has developed and refined methods to gain a holistic understanding of skin and aging. Through this approach, Olay aims to provide truly personalized technologies and product regimens that can help women achieve ageless beauty across all stages of life.

Olay has been conducting research and gathering data since the 1990s that has informed its largest-ever ongoing research program, the Multi-Decade and Ethnicity (MDE) study, to advance skin science. The MDE study, which was initiated in 2012, marries genotypic and phenotypic science, and examines women in nearly every decade of life - from their 20s to their 70s - and across ethnicities - including Caucasian, African, Hispanic and Asian - to decode and understand skin's biology and the aging process.¹ Initial results are being presented at the World Congress of Dermatology on June 8-13, 2015 in Vancouver.

As part of this investigational effort, P&G scientists have turned to gene expression profiling to identify key factors in the skin aging process.² The field of genomics has offered insights into skin issues such as pigmentation problems by finding hundreds of proteins involved that could provide a link to hyperpigmentation abnormalities. Identifying triggers like these is helping focus laboratory efforts on the development of new compounds.³ Researchers are also exploring new techniques to further evaluate the perception of the aging human face and recently discovered that the state of the stratum corneum impacts the underlying skin function and the appearance of skin tone.⁴



STUDY DESIGN

Using a holistic Systems Biology approach, which examines genomic, proteomic and metabolomic endpoints, Olay is able to model, predict and manage skin's behavior and appearance to map a multi-dimensional profile of the skin aging process. The MDE study is being led by Dr. Alexa Kimball, Professor of Dermatology, Harvard Medical School /Massachusetts General Hospital. Researchers have been collecting face, forearm (sun exposed) and buttocks (sun protected) skin samples, tape strip skin samples, oral swabs and blood as well as medical history and questionnaires. Initial findings and learnings have been generated from the first group of study participants ~25 women/group across 20s-70s life stages.⁵ Specifically, 231 women from Caucasian and African descent were studied. The MDE study results represent Caucasian women from each decade,⁶ while data from African-descended women are from the 20s, 40s, and 60s.⁷ The MDE study is continuing to collect and analyze samples from Asian and Hispanic women to broaden the application of the study's findings.

COLLABORATORS

Furthermore, to augment the MDE study's results, Olay collaborated with the following organizations to examine additional endpoints:

- ✓ Overall study design: Global Olay Alliance Dermatologists
- ✓ Personal genetics/DNA: 23andMe
- ✓ Metabolites: Metabolon
- ✓ Microbiome: Research and Testing Laboratory
- ✓ Proteins: Institute for Systems Biology and Yale University
- ✓ RNA sequencing: Expression Analysis and BGI Americas
- ✓ Statistics: Mayo Clinic
- ✓ Facial imaging: Canfield
- ✓ Next generation skin models: Durham University

With this robust study cohort and collaboration with outside institutions, Olay is positioned to identify and develop new technologies resulting in superior products.

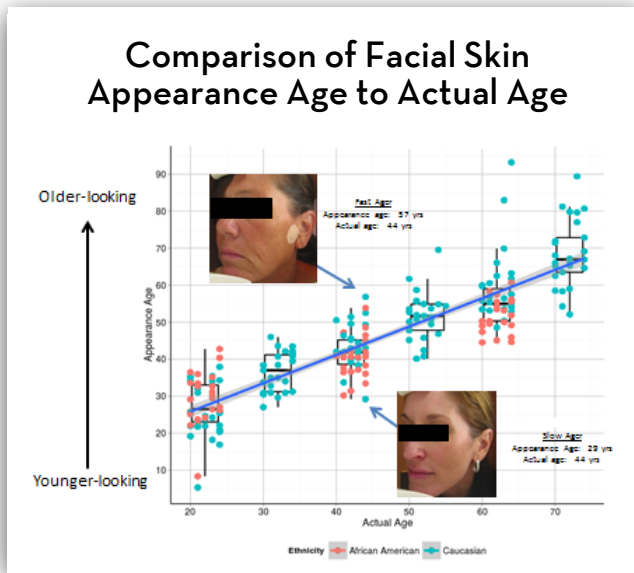
RESULTS

Key Takeaways:

From the initial findings, there are two key takeaways that will help determine what's possible when it comes to cosmetic skin care and looking ageless. First, there are similarities among women who have not undergone cosmetic procedures but still appear to be "ageless."⁶ Second, while it is intuitive that different changes in our skin occur as we age, there is now scientific proof, based on analyses of genes expressed among a subset of Caucasian women, there are distinct gene expression tipping points that occur in each decade as we age.⁵

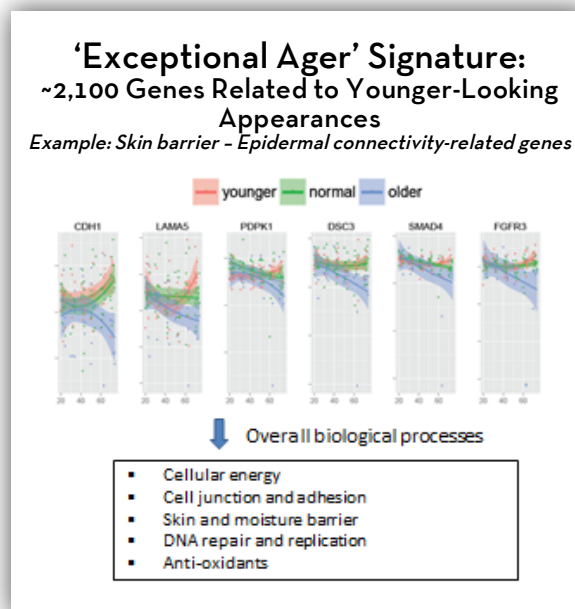
“Exceptional Skin Agers” Have A Unique Skin Fingerprint:

Olay found that there was a cohort of women who looked dramatically younger than their chronological age and classified these women as “exceptional skin agers.” A unique gene expression fingerprint of several hundred genes was identified through advanced bioinformatics methods. Although we all have these genes in our skin, how strongly these genes are expressed is distinct in “exceptional skin agers.”⁶



These genes may hold the key to successful aging, and decoding which pathways they affect can enable Olay researchers to help more women achieve skin that looks like the exception, not the rule at any stage of life.

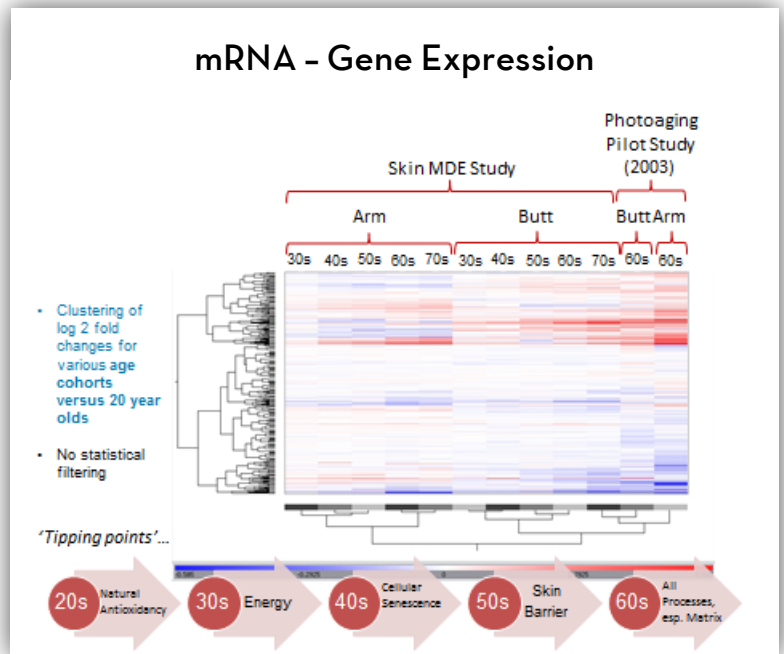
We dug deeper to find out what made these women different at the molecular level. Women with an “exceptional skin ager” profile demonstrated stronger expression profiles of the genes associated with key biochemical pathways involved in cellular energy, cell junction and adhesion, skin and moisture barrier, DNA repair and replication, and anti-oxidants. All of these are involved in biological processes that help maintain younger-looking and healthy skin.⁸



Distinct Gene Expression Tipping Points Strongly Correlate with Changes in Skin During Aging Process:

Olay scientists collected arm and buttock skin samples from a subset of Caucasian women and examined gene expression changes relative to samples from women in their 20s.⁷ The graph below demonstrates gene expression changes in different decades and different skin regions, with each row indicating a specific gene. Additionally, red indicates that the gene expression is increased, while blue demonstrates that the gene expression is decreased.

Bioinformatics cluster analysis revealed significant changes in gene expression at the earliest age transition evaluated (20s to 30s);⁵ the extent of change continued into later years. The data also reveal distinct gene expression tipping points that occur in each decade as we age:⁵



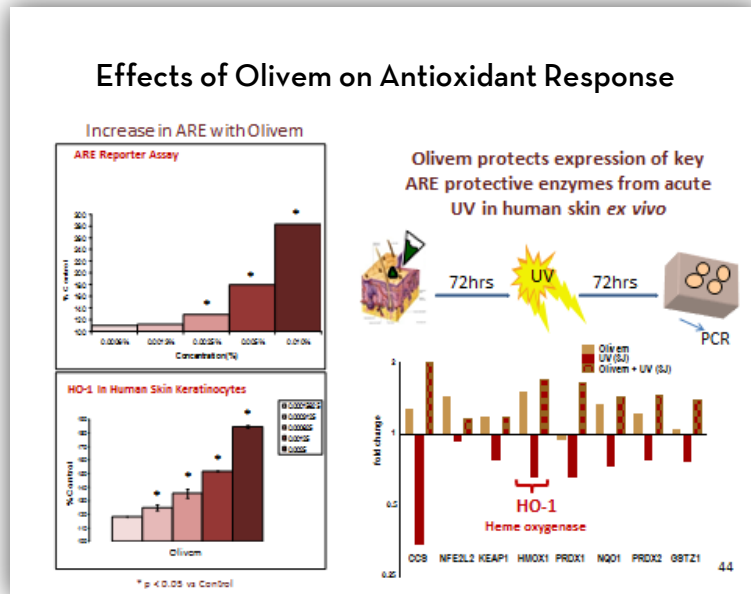
| CHANGES IN GENE EXPRESSION WITH AGING | EFFECT ON SKIN |
|--|--|
| Decline in antioxidant response (20s) | Skin cells more susceptible to free radical damage. |
| Decline in skin bioenergy (30s) | Skin becomes less responsive to anti-aging treatments. |
| Increase in cellular senescence (40s) | Decreased regeneration and renewal capacity of skin. |
| Decline in skin barrier function (50s) | External factors can damage and weaken skin more easily. |
| Acceleration of all the above (60s) | All of the above processes are increased. |

Data from women of African, Asia and Hispanic decent is currently being gathered and analyzed to compare the occurrence of tipping points across the different skin types.

Targeted Ingredients Maximize Skin Care Benefits at Any Decade of Life:

With a better understanding of the genes and molecular pathways underlying the skin aging process, Olay can identify and more closely examine ingredients to optimize skin care regimens for any age.

Olay has been screening compounds that possess potent anti-aging effects. For example, Olivem, Lyslastine and pal-KTTKS (penta-peptide) are ingredients that Olay has been studying and applying to the learnings of the MDE study. Olay scientists found that Olivem activates the intracellular antioxidant response, such as HO-1, in human skin *in-vitro*.⁹

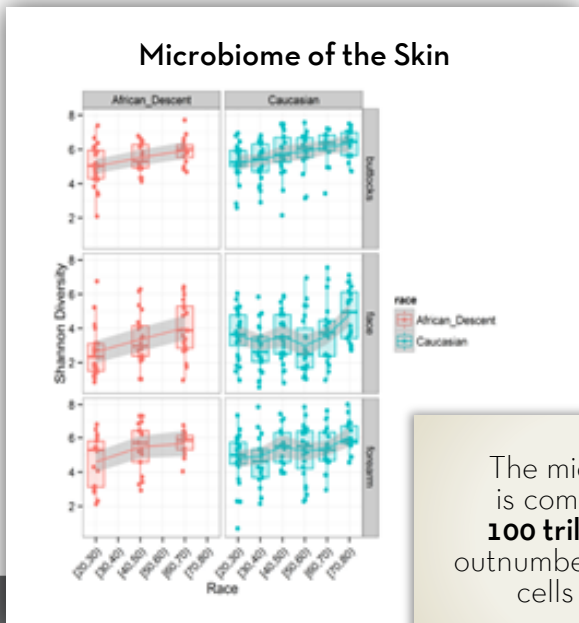


Research conducted *in-vitro* has confirmed that **Olay's top-performing ingredients**, such as Niacinamide (vitamin B3),¹⁰⁻¹¹ pal-KTTKS (penta-peptide), Olivem and Lyslastine are **key components** to address skin aging.⁹

Additionally, pal-KTTKS (penta-peptide) induce dermis development related genes and Lyslastine elevates expression of genes involved in the skin's defense-response.⁹

Age-Associated Changes in the Human Skin Microbiome:

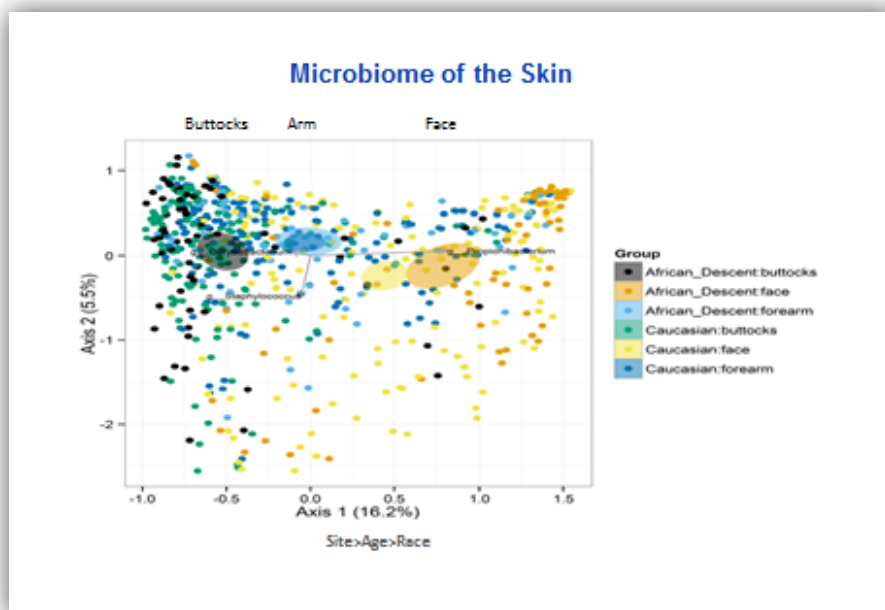
The microbiome is a snapshot of the commensal, symbiotic and pathogenic microorganisms that reside on various organs such as the skin. A newly emerging field, the microbiome is being investigated in various conditions and body sites. The MDE study demonstrated that the microbiome diversity increases with age.¹²



The microbiome is composed of **100 trillion cells**, outnumbering human cells 10 to 1.



Additionally, researchers found that the microbiome profiles from the buttocks and arms are similar in African-descended and Caucasian women but drastically differ in samples collected from the face.⁷



CONCLUSION

With the most comprehensive study to date, Olay is positioned at the forefront of skin biology research. Through partnering with more than a dozen independent research institutions and companies, Olay is a leader in Systems Biology approaches to understand and answer the complex topics surrounding skin biology and aging.

The identification of the “exceptional skin ager” as well as the tipping points that occur at each decade as we age are just the initial findings. Once completed, the MDE study will have examined six distinct decades across four different ethnicities to allow for broader and more in-depth findings than ever before. Combined, these findings will help inform and guide Olay in creating next-generation products that are optimized and eventually personalized to delay the onset of visible skin aging and can help empower every woman to be exceptionally ageless.

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