

The Secret of Exceptional Skin Agers – Genes or Skincare?



By Lois Rogers,
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Women who look mysteriously young for their age always attract unspoken questions: Is it genes or a magic face cream?

Olay scientists are showing it is both. P&G scientists have turned to gene expression profiling to identify key factors in the skin aging process. With a better understanding of the genes and molecular pathways underlying the skin aging process, Olay can identify and closely examine ingredients to optimise skin care regimens for any age.

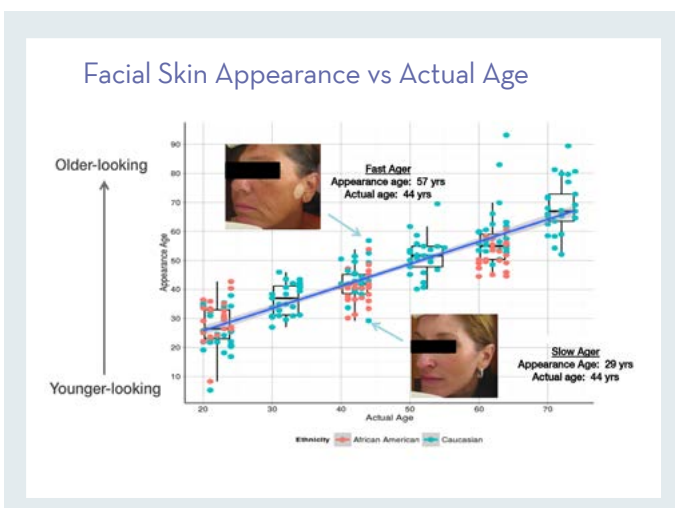
In a unique project, Olay scientists working with Harvard Medical School and Massachusetts General Hospital have discovered a gene expression fingerprint unique to younger than average looking women, and are now investigating if and how their benefits can be passed on to everyone in the future.

Their work has identified a constellation of 2,100 extra hard-working genes that confer exceptional skin quality. These discoveries were unveiled in a series of findings presented to the World Congress of Dermatology in June 2015. Now the scientists involved are well on the way to working out how to boost the activity of these same genes in the rest of us.

The project follows decades of effort during which Olay's parent company Procter and Gamble has invested more than £1 billion every year in the emerging science of molecular biology. P&G now employs 8,000 world class researchers, representing just 1% of all the scientists who apply to join their team.

Here we describe the exciting progress they have made so far in decoding the secrets of 'exceptional agers,' women whose skin is naturally resistant to the ravages of time, and how that knowledge is being used to develop a new generation of products with unprecedented efficacy.

This advance could lead us into an age of genetically-tailored personalised skincare where educated consumers will be able to obtain high-performance products uniquely adapted to their individual requirements.



The Multi Decade and Ethnicity (MDE) Study

For the past five years, Olay scientists working with top experts from the global genetics company 23andMe have been engaged in planning and carrying out the largest ever project to understand the biology of skin ageing.

23andMe has a database of almost a million individuals around the world. These are ordinary people who have elected to be genetically profiled to find out their ancestral origins, and inherited risk of disease so they can head off such risks where possible by making lifestyle changes.

Using skin samples collected by Professor Alexa Kimball and her team at Harvard Medical School, the Olay scientists performed an advanced analysis of 20,000 genes to study those which are responsible for major skin maintenance functions including DNA repair, cell energy production, skin barrier preservation; and production of elements called lamellar bodies that produce lipids, which are molecules containing fats, waxes and nutrients that help to keep the skin moist.

It was found 20% of black women and 10% of white women showed a unique gene expression profile which correlated to their significantly younger looking skin¹. This new understanding will enable the creation of the next generation products to better prevent and correct visible skin aging by offering more personalised solutions.

"The information from the MDE study is giving us a huge competitive advantage," said Frauke Neuser, Principal Scientist at Olay. "We not only know what a wrinkle is, we know how it is formed and what happens in the skin five years earlier, so we can come up with targeted products to help stop the process from happening."

Until now it has been believed that people's genetic inheritance was more or less reflected in their faces, but the Olay scientists proved that skin colour may be misleading.

One MDE study of 75 random black volunteers showed only one of them was 100% African. The others carried a mixed variety of Mediterranean, Middle Eastern and North African genes².

These studies indicate that women who see themselves as black or dark-skinned may have a white ancestry which puts them at almost as much risk of sunburn as a pale-skinned Northerner.

At the same time, pale-skinned women with African genes may also be advised to take extra care with cuts because of a tendency to a type of severe scarring that does not affect genetically white skins.

Body maintenance and repair mechanisms generally decline with age, but the Olay team found that a key characteristic of these 'exceptional agers' was that the genes responsible for skin moisture barrier formation became more rather than less active with age, or at least stayed at the same activity level as in other women in their 20s¹.

The first product to benefit from these advances, Olay Regenerist, is already on the market, but many more will follow in a series of developments that will keep P&G at the vanguard of the skincare revolution.

Systems biology

The specialists engaged in this ambitious project are working in the field of systems biology: an approach in biomedical research to understanding the larger picture – be it at the level of the organism, tissue, or cell – by putting its pieces together. Understanding the complex and changing interaction of the skin's molecules and cells is helping Olay products to offer ingredients from the cutting edge of anti-ageing technology. As more of us look forward to an extended lifespan, it is important we find ways of maintaining the vital bloom of youth, not just to preserve well-being and self-confidence but also to protect ourselves from damage to our health if the skin barrier is compromised.

Bioinformatics

Bioinformatics is a discipline that represents a marriage between biotechnology and computer technologies and has evolved through the convergence of advances in each of these fields. Today bioinformatics is a field that encompasses all aspects of the application of computer technologies to biological data. Computers are used to organise, link, analyse and visualise complex sets of biological data. With the advent of high throughput technologies such as Next Generation Sequencing and proteomics, bioinformatics has become essential to the biological sciences in general.

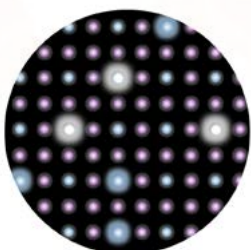
One of the analyses achieved through this technology has shown that menopause has a less ageing effect on the skin of black women than it does on white skin³.

Gene chips

Olay scientists were among the first in the world to realise the potential of the new generation of gene probes to understand genes involved in skin maintenance and repair, which of them were still functioning well in older women, and which had 'gone to sleep.' This high-tech method allows thousands of gene variations from different individuals to be screened simultaneously. The objective of this research is to understand how the ingredients that have already been added to Olay Regenerist work to improve the appearance of skin.

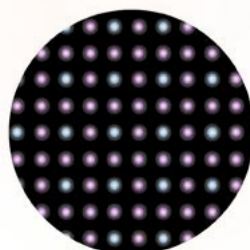


Gene Activity Changes Over Time



When we are young, some genes are much more active

They might be sending the message "MAKE A LOT OF COLLAGEN"



With age, these genes become weaker

They might be sending the message "make a little bit of collagen"

The "omics" revolution

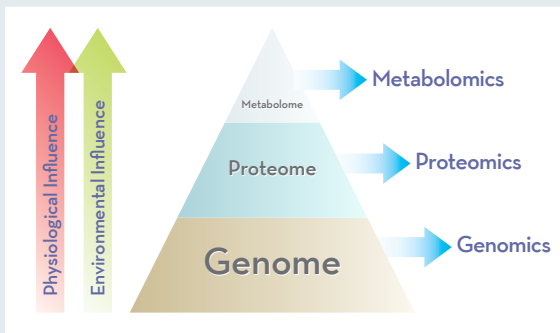
The study of genetics has moved on from identifying single genes. Giant strides have been made in using bioinformatics data to investigate the function and structure of the complete set of DNA within each cell, known as its genome.

Which genes are switched on and actively functioning at any given moment is called gene expression or the transcriptome. One of the dozens of studies in the MDE project revealed that black and mixed race women have a different transcriptome profile than their white-skinned counterparts. While skin cell maintenance and repair genes were slowing down in middle-aged white women, in those of the same age with more pigmented skin these genes were still functioning at maximum efficiency meaning some of them looked up to ten years younger than Caucasians of the same age².

The “omics” revolution *(Continued)*

The study of genomics has led to the rise of proteomics, the study of sets of proteins produced as a result of cellular genome activity in different circumstances. Studies have shown that in skin this may be altered by exposure to cold or heat and sunlight; cigarette smoke, urban pollution, hormones and ageing⁴.

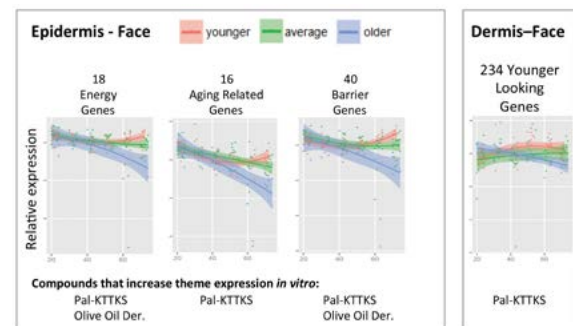
The third layer of this pyramid is metabolomics, the study of chemicals that regulate the processes of cell growth, development and reproduction, and their by-products. These could be anything from fatty acids and sugars, to the pigments that cause freckles and age spots.



An additional factor uncovered by the MDE project is the role of the ‘microbiome’, the surface bacteria on skin. The variety of different strains of bacteria increases with age, indicating a declining immune system and the loss of the skin’s ability to protect itself⁵. The effect of this is still being investigated, but it may explain why there are higher levels of inflammation and more uneven skin tone in older women.

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Matching ‘Exceptional Agers’ Profiles *In Vitro*



Olay has benefitted from the fast-expanding field of high throughput screening, where thousands of substances are tested for their capacity to affect pathways associated with skin aging and stimulate regenerative cellular activity.

Olay scientists have identified a number of ingredients associated with findings from the MDE project which are already being incorporated in Regenerist Three Point Treatment Cream:

Olivem

Contains specific long chain fatty acids found in olive oil which stimulate expression of the protective enzymes that are made naturally by the exceptional agers. The researchers have found a way to modify these fatty acids so they can be incorporated into a formula absorbed by the skin. Studies have shown that skin pre-treated with these fatty acids retains resistance to damage from sunlight⁶.

Niacinamide

A vitamin B3 derivative with beneficial skin properties that have been confirmed by more than 700 published studies. Niacinamide reduces redness and inflammation and has been shown to protect against non-malignant melanoma skin cancer^{7,8}. The Olay formulation has been refined to maximise skin absorption, boosts cell energy and cell turnover.

Lyslastine

Lyslastine is a new ingredient found in the herb dill, that replicates one of the linking elements of elastin, a support structure of skin that degrades with age.

Like many other new compounds occurring in nature that mimic the effects of molecules in the human body, its effect was discovered by the high throughput computerized screening that is revolutionising skincare⁹.

Pal KTTKS

A remarkable ingredient, palmitoyl pentapeptide has been the subject of 15 published scientific studies demonstrating its function, four of them co-authored by Dr. Rosemarie Osborne, P&G Beauty Technology Fellow. Pal-KTTKS is proven to boost cell regeneration and replicate the gene product that renews the extracellular matrix, the spongy cushion between the cells¹⁰.

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“These advances mean that women can now have more control over what happens to their skin - the ability to compensate for sluggish gene activity that comes with aging,” says Dr. Osborne, “There are now ways we can enhance skin cells to make them behave like younger versions of themselves.”

The future for ever more effect anti-ageing skincare looks bright indeed. But in order for women to be fully prepared in advance for the risks on the horizon from genes that slow down, they will need to know their genetic ancestry to select the correct skincare cocktail. It is an advance Dr Jay Tiesman P&G's genomics group leader, says is just around the corner:

“At our current rate of discovery, customised skincare could be with us within the next five years.”

“Companies like 23andMe are already offering postal gene tests for \$199. I can see this technology merging with our deep understanding of skin biology to provide a woman the ability to customise her skin

care based on her genetics. Perhaps even a smart phone app with the equivalent of a quick response code. You will be able to match this up with labels on products to identify the ones suitable for your genotype.”

There are already companies claiming to offer skin care advice and products based on a small handful of genes but Dr. Tiesman warns,

“Most of these companies have very little real research behind their claims. For instance, although it makes sense that a particular gene like collagen is important to your skin, just having a variant somewhere in this gene doesn't necessarily mean that you will have skin issues. We need to do the hard work of connecting the dots between your genes and your skin before we can give any real advice on what skin products work with your genes.”

Studies have shown that approximately 80% of skin ageing is environmental and only 20% genetic¹. Dr. Neuser says this makes the MDE findings all the more important.

“ You can be dealt a really good poker hand, but if you don't know how to play poker you can still lose. We are showing women how to win with anti-ageing skincare whatever the hand they've been dealt ”

Frauke Neuser, Principal Scientist at Olay

Proven Olay REGENERIST technology has been shown to help skin look and behave like that of an “Exceptional Skin Ager - even if, genetically, you're not...”



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¹Osborne *et al.* Genomic and Genetic Profiling of Women Whose Facial Skin Appearance Sets Them Apart As Successful Agers - The Multi-Decade and Ethnicity Study; Poster #2983434. 23rd World Congress of Dermatology, 2015, Vancouver, Canada.

²Osborne *et al.* Racial Similarities and Differences in Gene Expression Related to Aging - The Multi-Decade & Ethnicity Study; Poster #3445. American Academy of Dermatology 2016 Annual Meeting, Washington, D.C, USA.

³Wolff *et al.* Skin wrinkles and rigidity in early postmenopausal women vary by race/ethnicity: baseline characteristics of the skin ancillary study of the KEEPS trial. Fertility and Sterility (2011); 95(2), 658-662.e3

⁴Kimball, A., Johjn, M. The Omics Revolution. Br J Dermatol (2012); 166 (suppl. 2), 41-45

⁵Osborne *et al.* Decade by Decade Ageing Associated Changes in the Human Skin Microbiome. Agers - The Multi-Decade and Ethnicity Study; Poster #2985150. 23rd World Congress of Dermatology, 2015, Vancouver, Canada.

⁶P&G Data on File

⁷Bissett *et al.* Topical niacinamide reduces yellowing, wrinkling, red blotchiness and hyperpigmentation spots in ageing facial skin. Int J Cosmet Sci (2004); 26, 231-238.

⁸Martin *et al.* Oral nicotinamide to reduce actinic cancer: A phase 3 double-blind randomized controlled trial. J Clin Oncol (2015); 33 (suppl; abstr 9000).

⁹Cenzio *et al.* LOXL as a target to increase the elastin content in adult skin: a dill extract induces the LOXL gene expression. Experimental Dermatology (2006); 15(8), 574-81.

¹⁰Osborne *et al.* Appearance of uneven facial texture is improved by a facial moisturizer

containing cosmetic ingredients that boost cellular energy. Poster presented at the Journal of American Dermatology, 2013, Miami Beach, Florida.

¹¹Flament *et al.* Effect of the sun on visible clinical signs of aging in Caucasian skin. Clin Cosmet Investig Dermatol (2013); 6: 221-232.