How senescence science is redefining skin longevity

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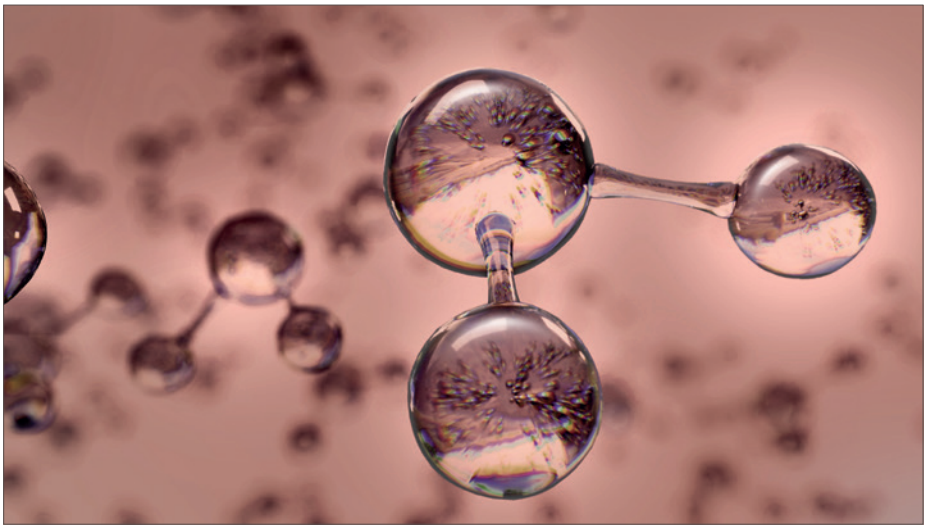
The beauty industry is undergoing a fundamental transformation. Driven by holistic approaches to skin health and longevity, it is moving away from the traditional, unwinnable anti-ageing narratives to a science-driven approach that is focused on understanding the root causes of the signs of ageing and tackling them early enough to slow or prevent these processes.

This change in perspective is driven by increased life expectancy, health-conscious consumers across all demographics and results from pharma-inspired scientific studies.

Skin longevity plays an important part in the perception of age. A recent multiethnic study involving women from diverse backgrounds aged 50–65 years, demonstrated that maintaining a healthy skin appearance – defined by smooth texture, even tone, and minimal wrinkles – can extend the perception of youth.

Despite having the same chronological age, volunteers were judged significantly younger or older depending on the visible condition of their skin (Figure 1). Ultimately, longevity in skin translates into being perceived younger for longer.[1]

The holistic health movement encourages people not to strive for perfection, but to be their best possible selves at every stage of life. Skin longevity follows the same thinking. It is about ageing well and feeling good about your skin regardless of how old you are.



Based on a holistic scientific view, skin is now seen as part of an interconnected system influenced by genetics, environment, lifestyle, and emotional wellbeing. Rather than treating skin in isolation, this perspective recognizes that vibrant, healthy-looking skin comes from supporting your overall health and wellbeing throughout life.[2]

In this context, new holistic skin models are emerging to provide a comprehensive framework that unites all the factors impacting skin health, which in the era of anti-ageing, were often addressed independently.

Figure 2 shows the DSM-Firmenich 360° Skin Ecosystem, which exemplifies the holistic-interconnected scientific strategy now being used in advanced skin care. Healthy-looking skin is when these physical, environmental, and emotional elements are in harmony.

This comprehensive framework integrates intrinsic influences (genetically programmed, time-driven), extrinsic elements (environment and lifestyle-driven, as encompassed by the exposome), and emotional factors, to account for all the variables that impact skin health.

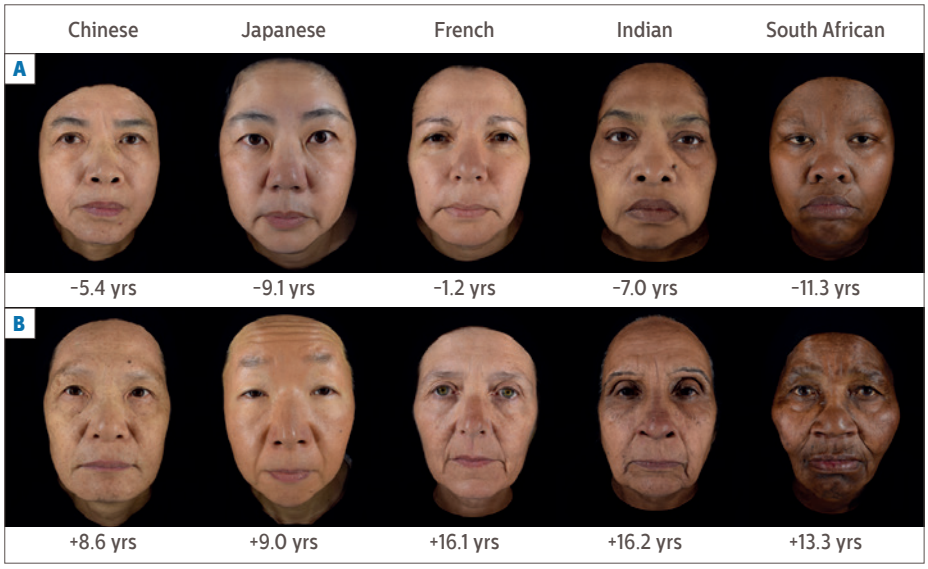


Figure 1: Differences between estimated and chronological age in women aged 50-65 years across five ethnic groups. Women in each column have the same chronological age, with numbers showing how many years older (+) or younger (-) they were perceived compared to their actual age

The hallmarks of ageing

The conventional separation of intrinsic and extrinsic ageing has now been superseded by the twelve hallmarks of ageing,[3] which offer a far more comprehensive framework of interconnected molecular mechanisms that drive cellular and tissue decline (Figure 3).[4]

Because these mechanisms are interdependent, when one area becomes compromised, it can trigger a cascade of problems in other areas that may lead to unhealthy looking skin, to overall poor health and in some extreme situations, be life changing.[5]

Cellular senescence: the key to healthy looking skin

Cellular senescence is a major hallmark of

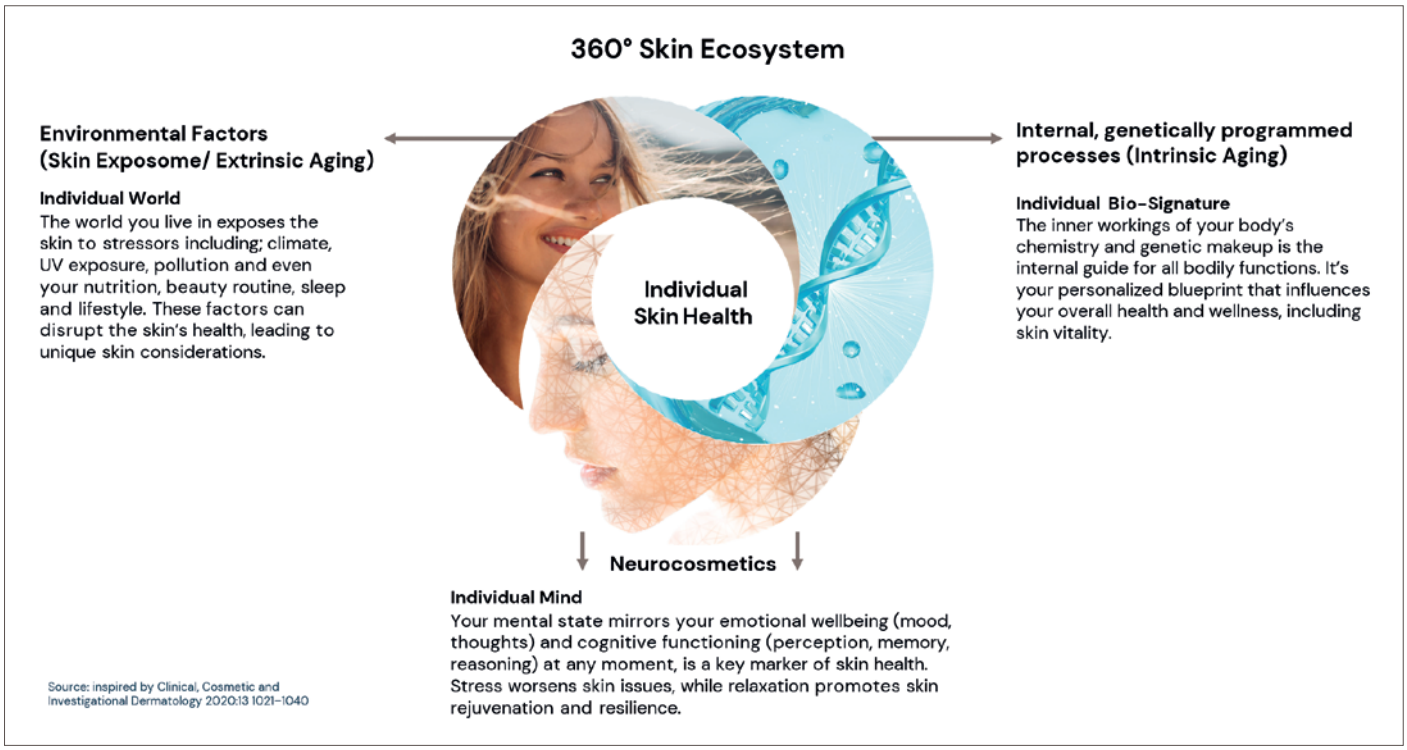


Figure 2: DSM-Firmenich 360° Skin Ecosystem

ageing with direct effects on skin function and appearance, acting alongside other interconnected hallmarks that together drive the ageing process. Cellular senescence occurs when damaged cells enter a permanent state where they cannot divide or enter programmed cell death and die (apoptosis).

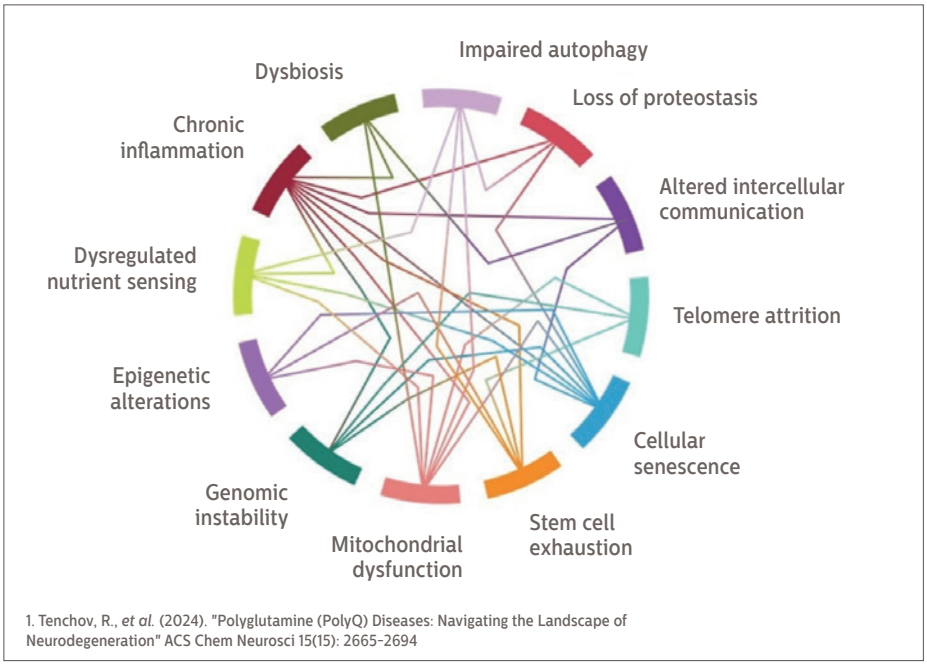
Instead, they remain metabolically active, releasing toxic substances that damage tissue and trigger more cells to become senescent. They are central to the ageing process, and their presence is a strong biological indicator of tissue decline.

Senescent cells arise from both intrinsic and extrinsic factors and appear early in life and naturally accumulate over time. Intrinsic processes such as telomere shortening, oxidative stress, and DNA damage can transform normal cells into senescent cells.

Meanwhile, extrinsic factors including UV/infrared radiation, pollution, and mechanical stress can accelerate cellular senescence through three pathways: they can worsen damage from intrinsic factors, directly trigger senescence in healthy cells, or intensify existing cellular damage. As a result, senescent cells accumulate and drive many age-related changes throughout the body.[6]

The main toxic substances secreted by senescence cells are known together as SASP (senescence-associated secretory phenotype), which is a potent cocktail of pro-inflammatory cytokines (including interleukins), chemokines, growth factors, and matrix-degrading enzymes (MMPs) that breakdown tissue and is highly damaging to neighbouring cells. SASP disrupt tissue homeostasis, degrades the extracellular matrix, fuels inflammageing and impairs skin regeneration.

They trigger a cascade of damaging effects. Inflammation caused by released inflammatory



1. Tenchov, R., *et al.* (2024). "Polyglutamine (PolyQ) Diseases: Navigating the Landscape of Neurodegeneration" ACS Chem Neurosci 15(15): 2665–2694

Figure 3: Interconnected hallmarks of ageing

mediators disrupt intercellular communication, stem cells become exhausted creating local areas less able to regenerate.

Furthermore, once a chronic inflammatory state is reached it can contribute to dysbiosis, by affecting the composition and balance of the microbiome. Senescent cells, through the release of SASP, accelerate the appearance of visible signs of ageing, including wrinkles, loss of firmness, and enlarged pores.

This makes the removal of senescent cells important for maintaining healthy-looking skin. Potentially, their removal could even result in the reversal of some visible signs of ageing, making senescent cell clearance an important strategy for longevity.

Senolytic technology: the future of skin renewal and longevity

Senescent science represents a breakthrough in longevity. Not only do the senescent cells contribute to numerous ageing processes, but because researchers now have the tools to reliably detect and measure them, this research field has already challenged previous assumptions about cellular ageing.

Where cellular senescence was once considered irreversible, pharma-inspired

studies show that senescent cells can be induced by senolytic molecules to undergo apoptosis, leaving tissues free to regenerate and return to a healthier state.[7,8]

Scientists at DSM-Firmenich are experts in the understanding of the behaviour of senescent cells, and in ways they can be removed from skin. Through systematic screening for natural senolytic and senomorphic compounds, they have developed a powerful fully sustainable natural senolytic from the rare alpine plant Epilobium fleischeri, Eterwell™ Youth.

This innovation triggers programmed cell death in senescent cells by reducing levels of BCL-2, a protein that normally prevents apoptosis. This allows senescent cells to die and be removed through natural processes. Their pioneering studies demonstrate that cellular-level interventions can reduce populations of senescent cells, rejuvenate tissue, and improve appearance.

Senolytics: transforming the skin's response to anti-ageing actives

Intuitively, scientists at DSM-Firmenich hypothesized that, once senolytics, like Eterwell Youth, had cleared away senescent cells, they would create a new "fresh tissue landscape" where traditional cosmetic actives such as collagen-boosters, could be even more effective.

Research has now validated this approach, showing that senolytic science can significantly enhance the efficacy of established cosmetic ingredients. This synergy represents the future direction of skin care, when actives that remove barriers to renewal will be combined with traditional ingredients that address the hallmarks of ageing. The resulting boosted efficacy will set new standards for maintaining healthy, vibrant skin throughout life.

This ingenious idea of pairing senolytic with traditional skin care actives to enhance their effectiveness was successfully demonstrated using DSM-Firmenich's collagen booster SYN®-COLL CB (Palmitoyl Tripeptide-5), in a two-month, single-blind, randomized, half-face clinical study with 55 Chinese volunteers aged 45-65.

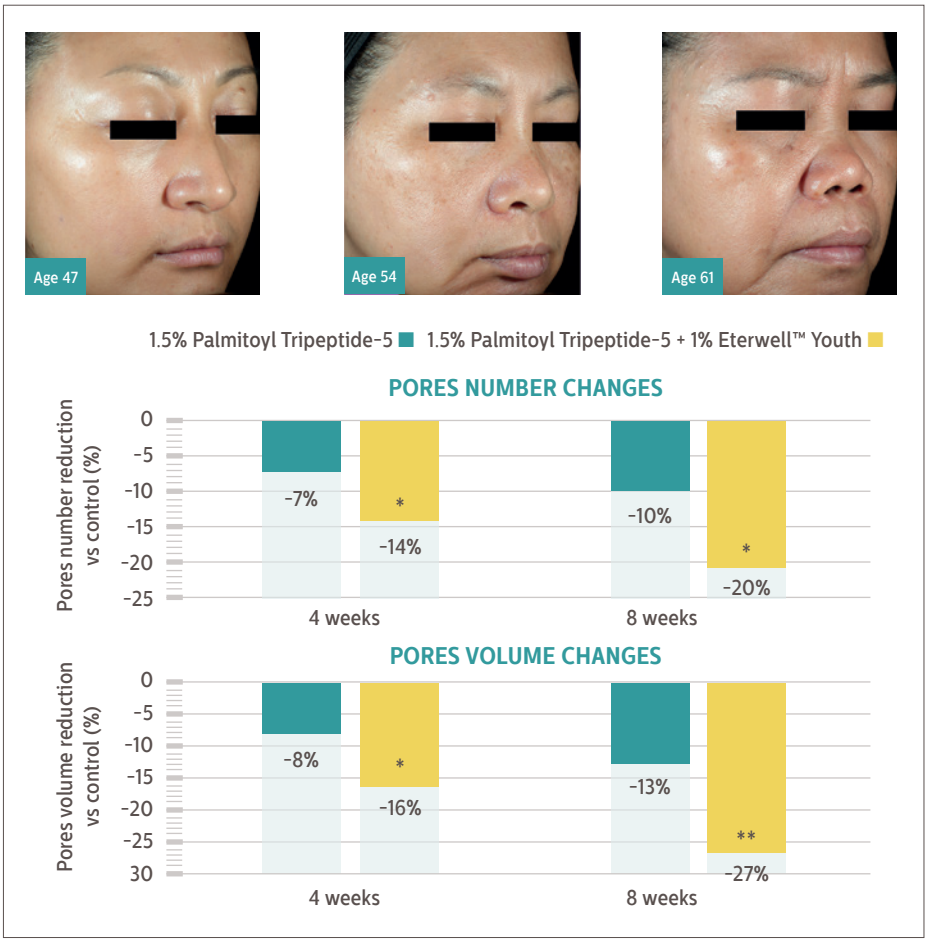


Figure 3: Interconnected hallmarks of ageing

Each volunteer had one side of their face treated with a test product formulated with either 1.5% Palmitoyl Tripeptide-5 alone or with 1.5% Palmitoyl Tripeptide-5 combined with 1% Eterwell Youth. While Palmitoyl Tripeptide-5 alone significantly improved collagen density

compared to untreated skin, when combined with 1% Eterwell Youth, as predicted, it boosted collagen production by an impressive 200%.

Despite being one of the most challenging signs of ageing to address, because pores become larger and more visible as collagen levels fall, both pore number and pore volume were also included in the study.

Pores enlarge as we age, and this can be clearly seen in the images taken over a lifetime shown in Figure 3. While pores can be considered as just another sign of ageing alongside wrinkles and fine lines, in some populations, particular in Asian communities, they actually take precedence over wrinkles as the main indicators of age. Pore size and volume were measured using the images taken during the clinical trial (Figure 4).

The test product with Palmitoyl Tripeptide-5 alone produced significant improvement in pore number and volume (-7% and -8% respectively), when compared to the untreated skin. However, as with collagen density, these improvements were boosted when 1.5% Palmitoyl Tripeptide-5 was combined with 1% Eterwell Youth. Again, remarkably, the inclusion of the senolytic doubled the efficacy.

The striking improvements achieved by combining 1.5% Palmitoyl Tripeptide-5 with 1.0% Eterwell Youth compared to both untreated skin and skin treated with Palmitoyl Tripeptide-5 alone is captured in the advanced Antera 3D® imaging shown in Figure 5.

Clearly, at four weeks and even more impressively, after eight weeks these troubling signs of ageing had been significantly reduced, and the volunteers skin looks healthier.

The combination of active and senolytic, also doubled the efficacy of the other characteristics (forehead wrinkles and crow's feet) measured in the study. Looking at the results for Palmitoyl Tripeptide-5 alone, where some parameters plateaued after initial improvement, it might be that senescent cells partially destroy the active and/or the newly synthesised collagen, acting as biological roadblocks, creating cellular resistance that limits traditional actives' effectiveness.

However, the breakthrough discovery lies in the synergistic relationship between senolytic and peptide active. Across every parameter measured this combination consistently delivered approximately double the improvement compared to the peptide alone.

Senescent cell clearance unlocks the peptide's full regenerative power, transforming limited responses into sustained, progressive improvements. This validates the pioneering approach of using senolytics to maximizes conventional skin care ingredients' long-term efficacy.

Conclusion

The beauty industry's transformation from anti-ageing to skin longevity represents more than just a shift in terminology. It is a fundamental change in how we approach skincare. It plugs into skin biology for targeted, effective, personalized solutions.

While the development of senolytic technology like Eterwell Youth marks an important advancement in cellular science, the most significant breakthrough lies in the discovery that senolytics can dramatically enhance the performance of traditional skin care ingredients.

Today, clinical evidence shows that senolytic compounds can double the efficacy of established actives—such as collagen-boosting peptides—by amplifying their impact on the main visible signs of ageing. By removing the biological roadblocks that limit conventional actives' effectiveness, senolytic-enhanced formulations represent the future of evidence-based skin care.

As the industry continues to embrace this holistic, science-driven approach, consumers can expect increasingly sophisticated solutions and truly personalised advanced skin care that does not just address the visible signs of ageing but actively support skin's long-term health and resilience. This is the promise of skin longevity, not the impossible pursuit of perfection, but the achievable goal of looking and feeling your best throughout life. **PC**



Figure 5: Antera 3D® images showing the effects of 1.5% Palmitoyl Tripeptide-5 alone and in combination with 1% Eterwell Youth on one volunteer's Pore size and volume

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