How advanced research drive technology development and business success ?

2015 Personal Care Summit

Jun. 26th, 2015 Shanghai

Xianghong Yan, Senior Manager/Principle Scientist

SK-II Global Technical Marketing/P&G

Today’s Agenda

- Introduction: Global Overview of Skin Care Market
- World Wide Skin Aging Research
- Functional Ingredients with Cut-Edge Science

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- Introduction: Global Overview of Skin Care Market
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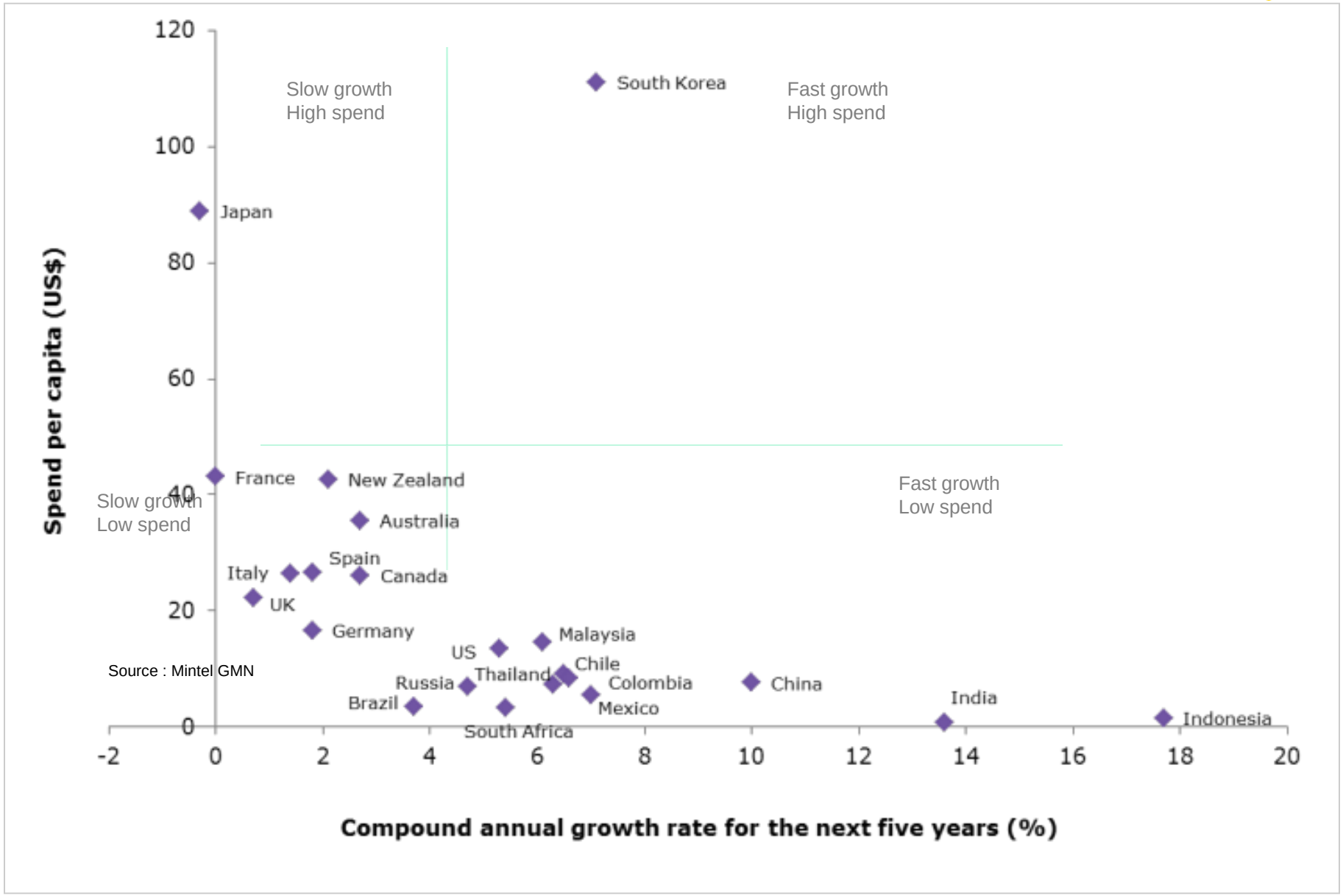
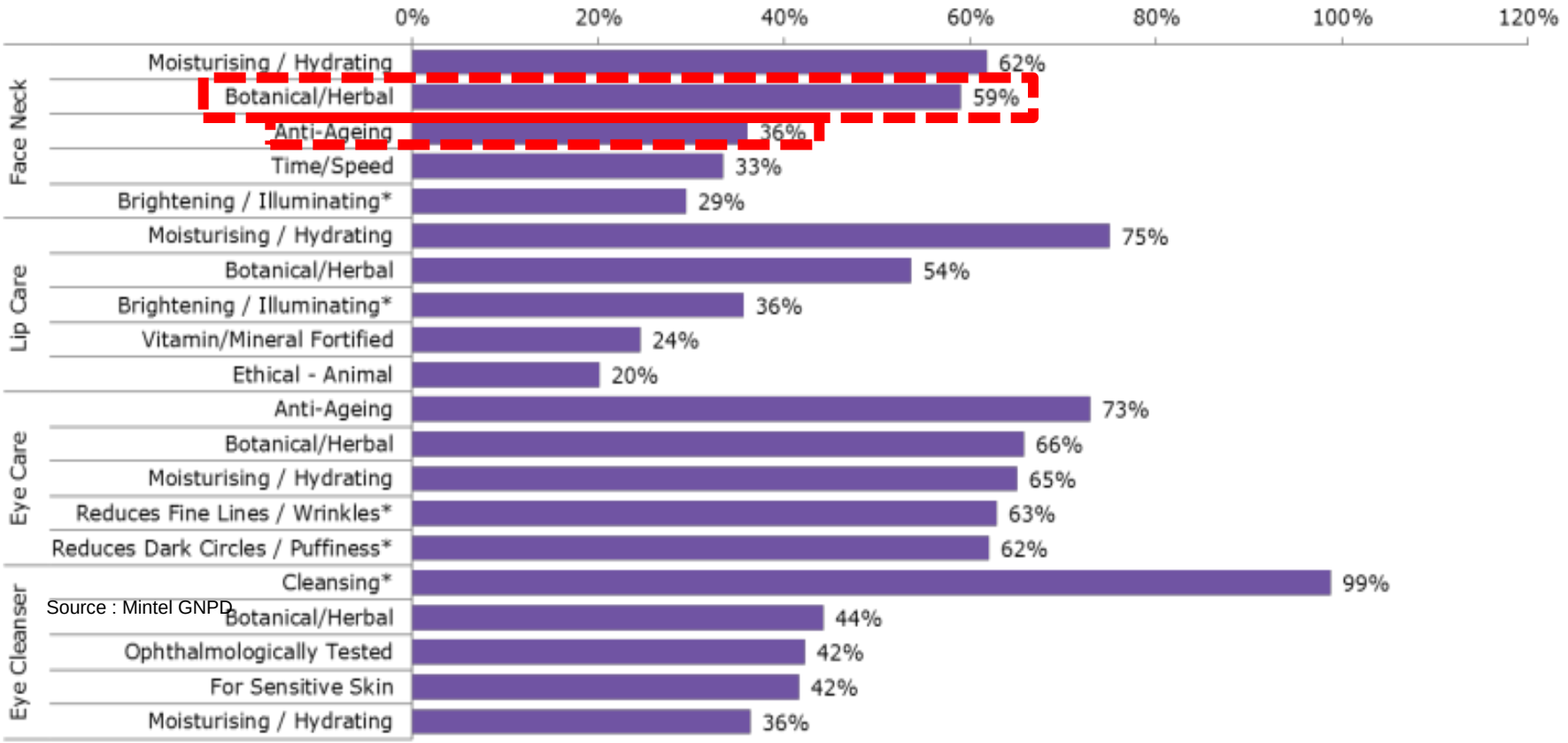
GLOBAL OVERVIEW

- Global markets
- Anti-ageing is the fastest growing segment of facial care

Global markets 2012

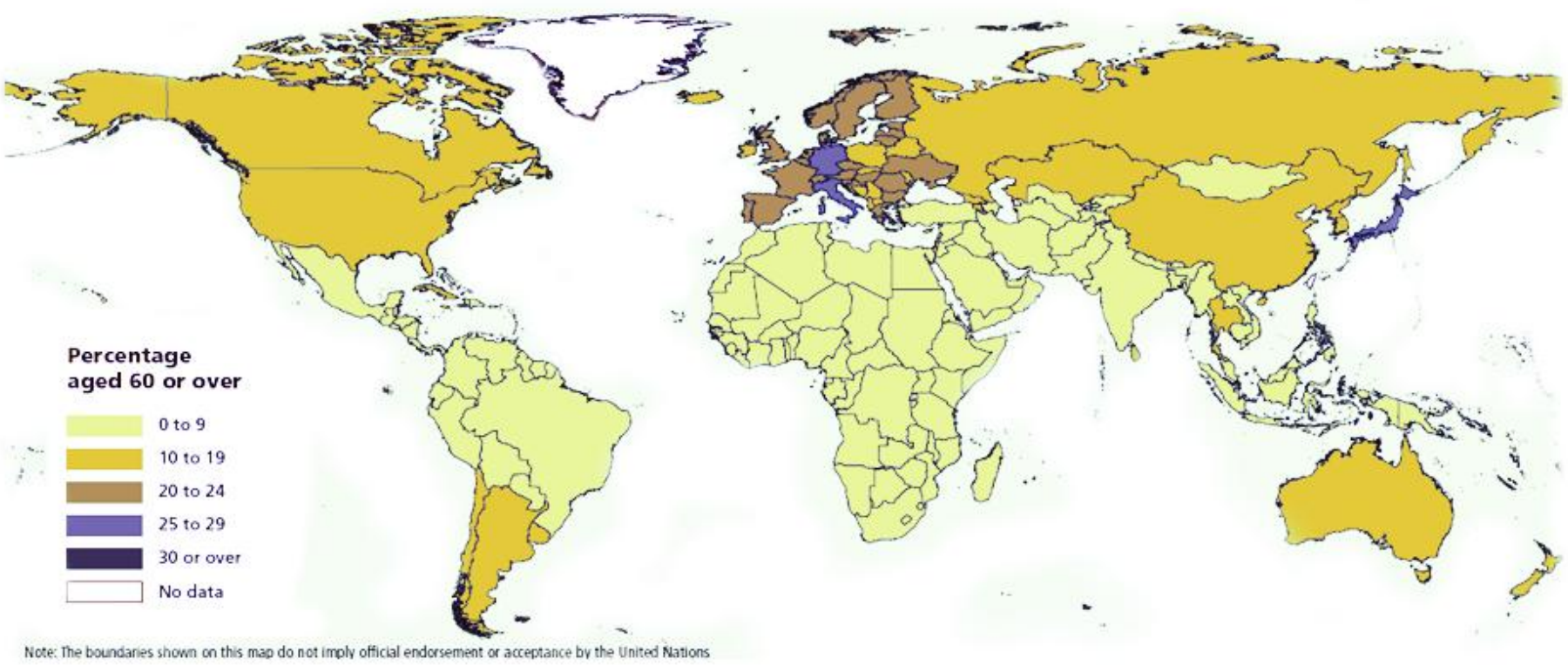


Top five claims for each facial care sub-category



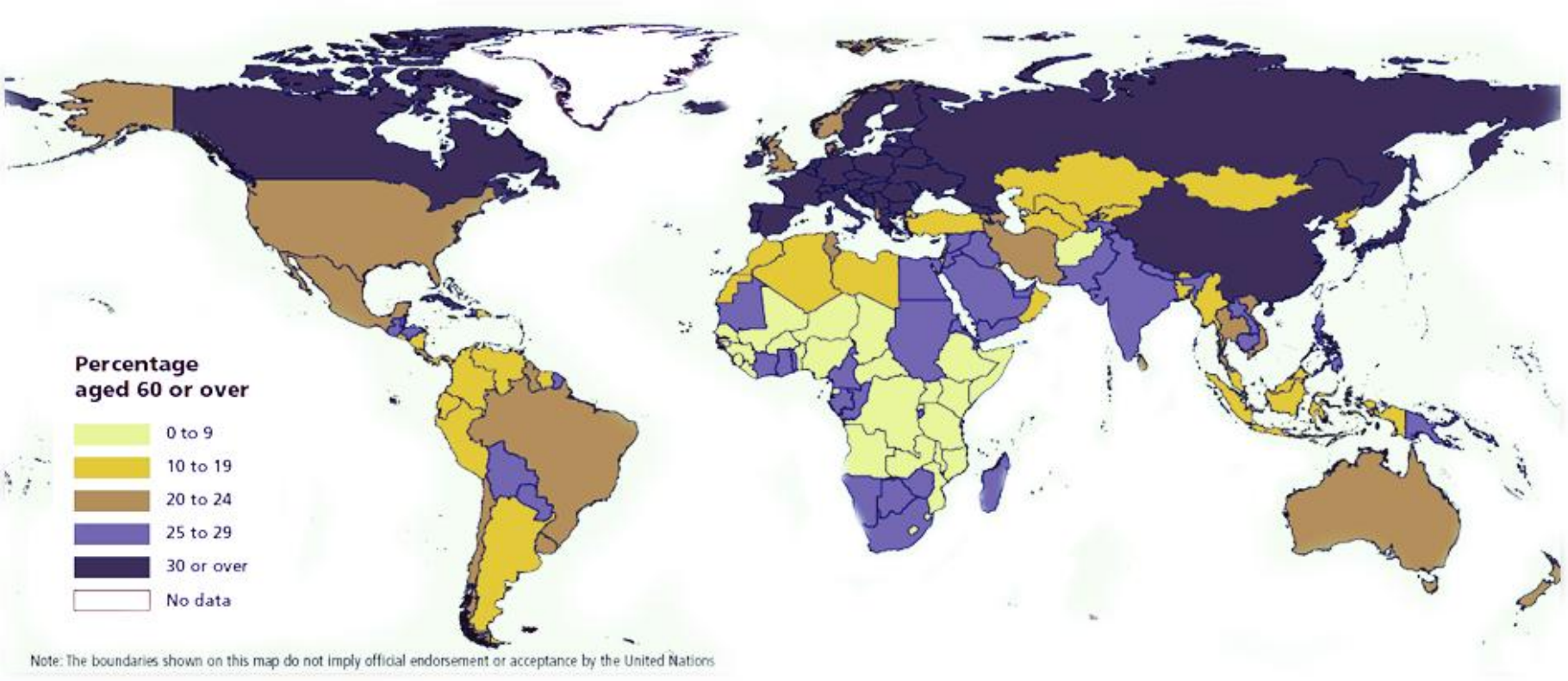
Source : Mintel GNPD

60+ in 2009



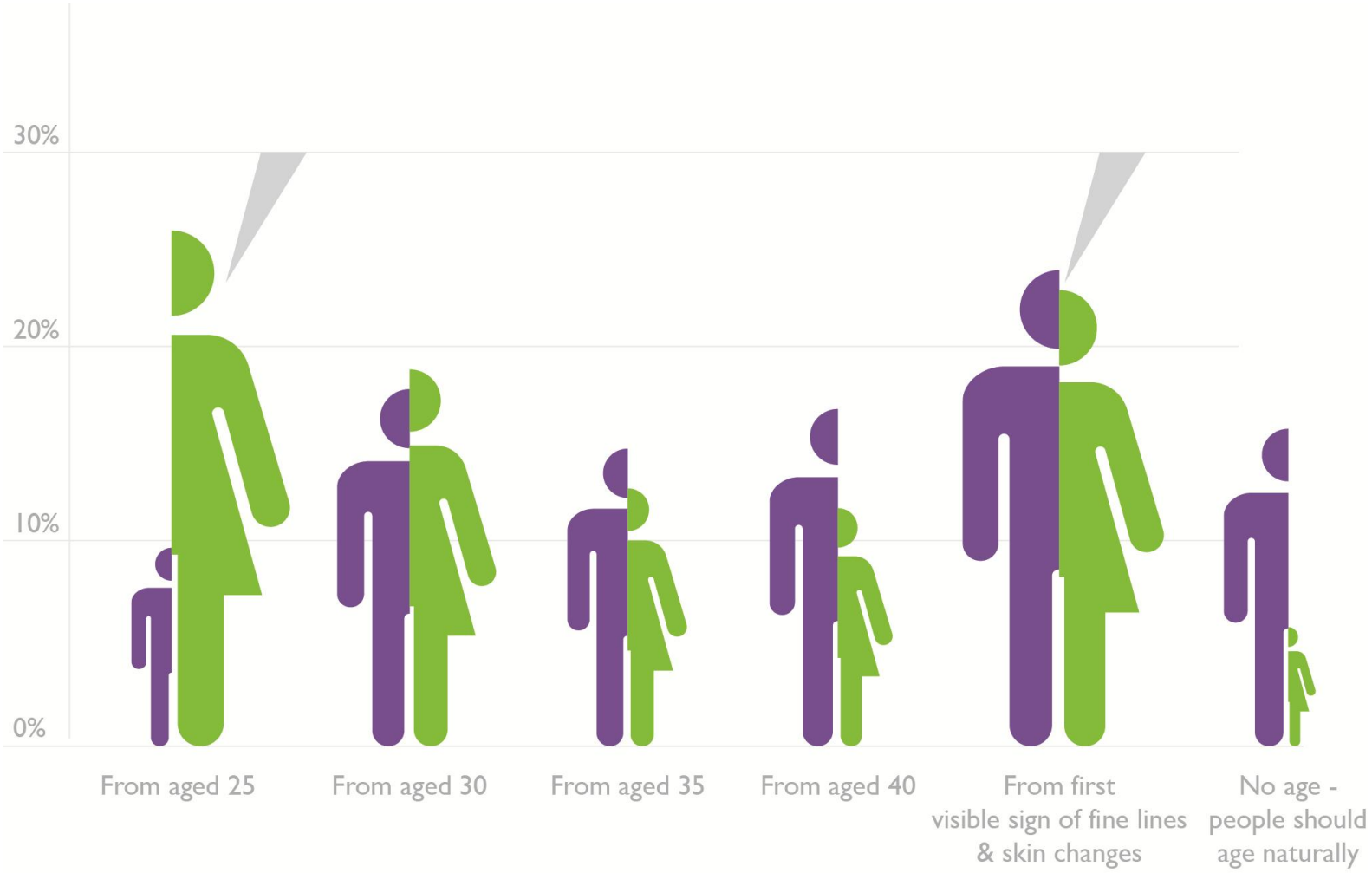
SOURCE: DANISH AGEING RESEARCH CENTRE; LANCET MEDICAL JOURNAL; OFFICE FOR NATIONAL STATISTICS UK

60+ in 2050



SOURCE: UN

WHEN SHOULD YOU START USING ANTI-AGEING SKINCARE, ACCORDING TO US CONSUMERS?

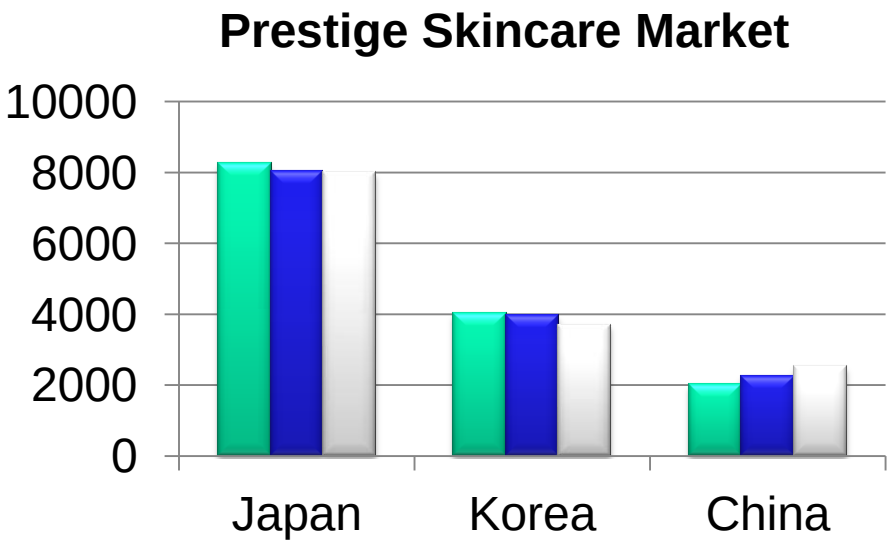


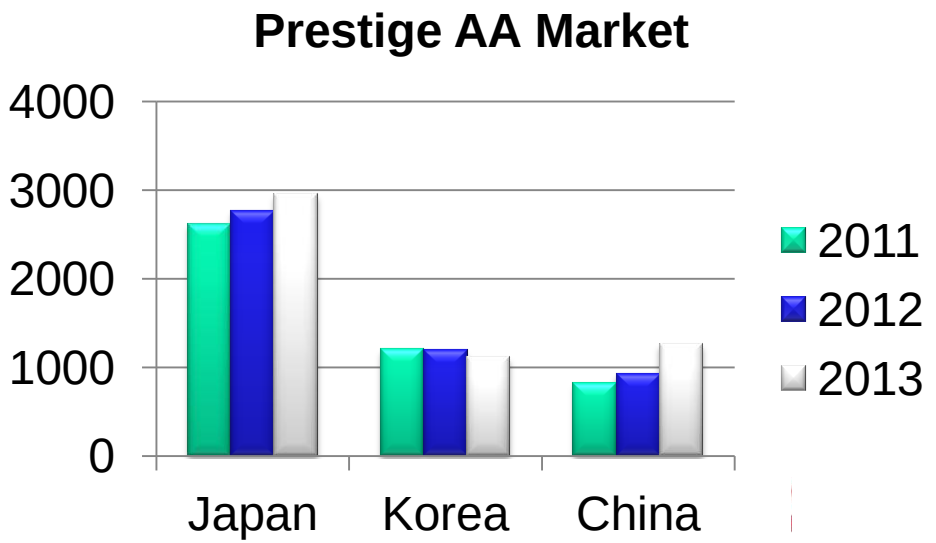
Source: Mintel Oxygen report Anti-ageing skincare - US - February 2011

Market Landscape in Asia

•Total Prestige Skincare in general is shrinking. Only China is still growing.

• Prestige AA is approximate 35% of the total prestige skincare market. AA continues to be big in Asia with growth in Japan and China faster than total prestige skincare.





Today’s Agenda

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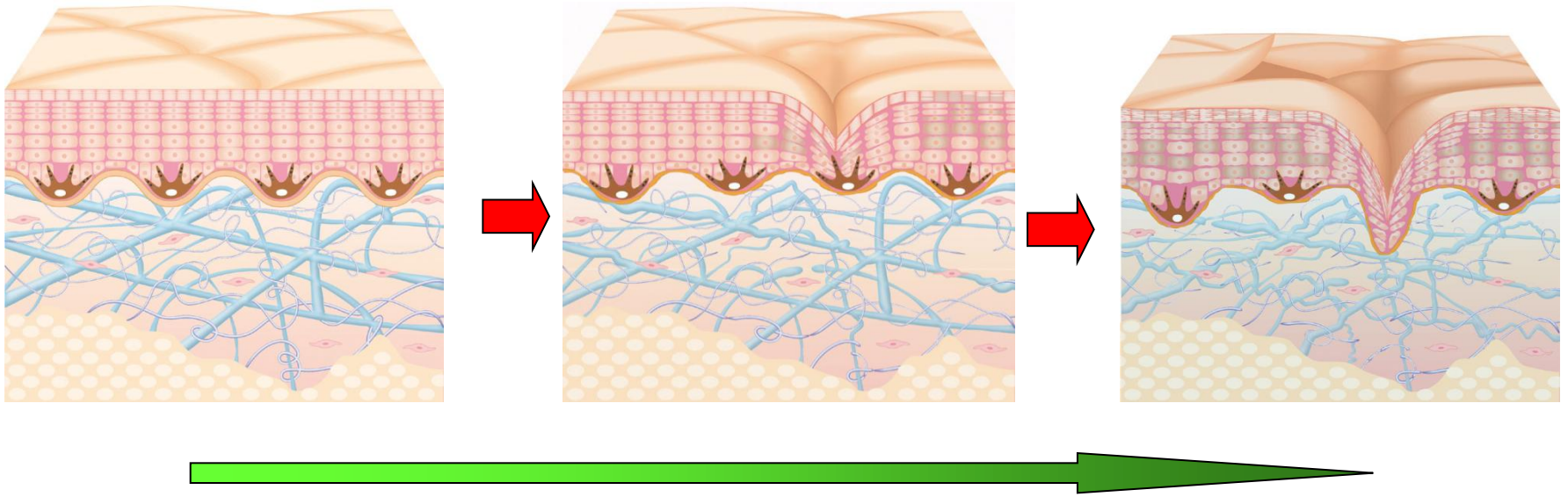
- World-Wide Skin Aging Research
- Functional Ingredients with Cut-Edge Science

A Quick Review of Skin Aging

Skin Aging: Components Deterioration



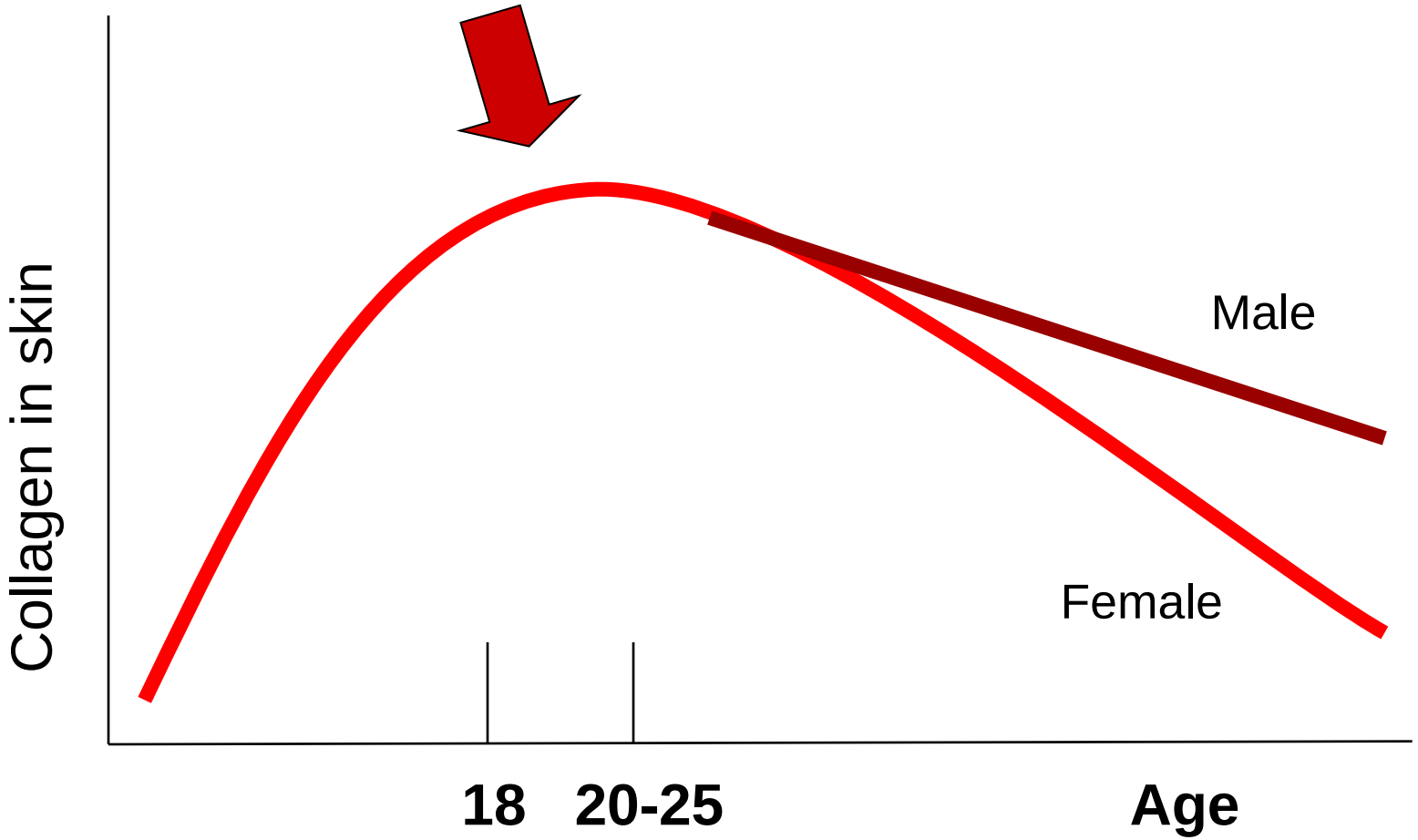
Skin Components change:

Epidermis: Turn thinner in irregular

DE Junction: Loose tightness

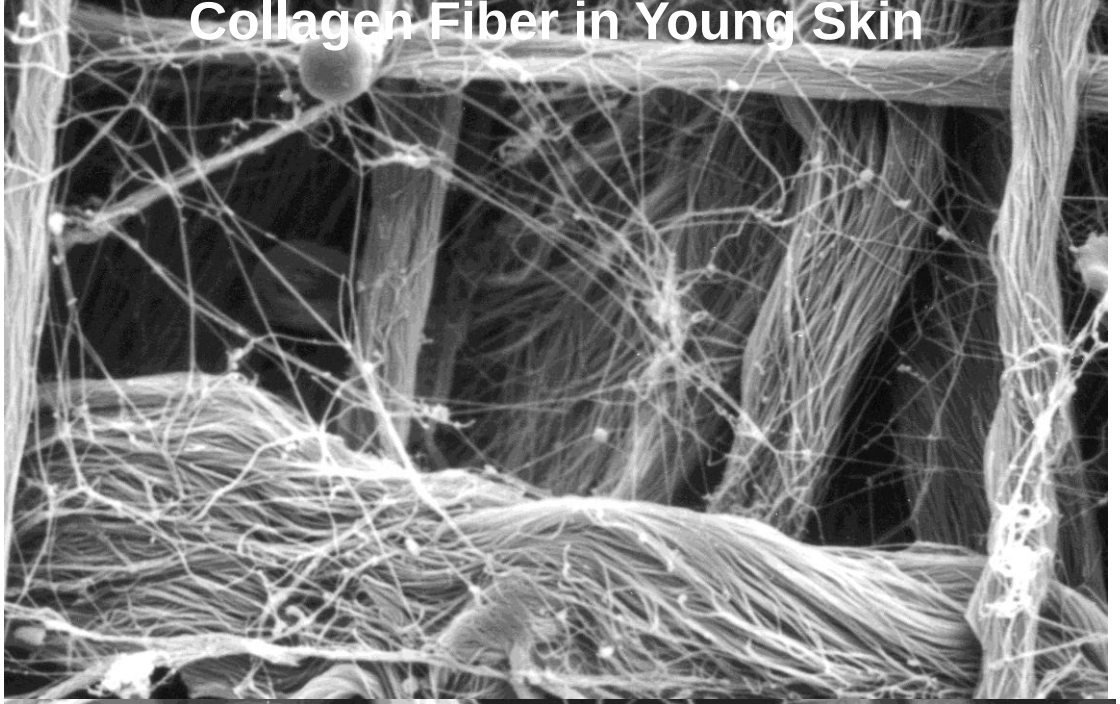
Dermis: Matrix quality and quantity downgrade

Dermis component change via skin aging
Collagen quantity decrease



Rook Textbook of Dermatology P. 90
Molecular Cell Biochemistry 1999 April 184 (1-2): 99-108

Collagen Quality Degrade

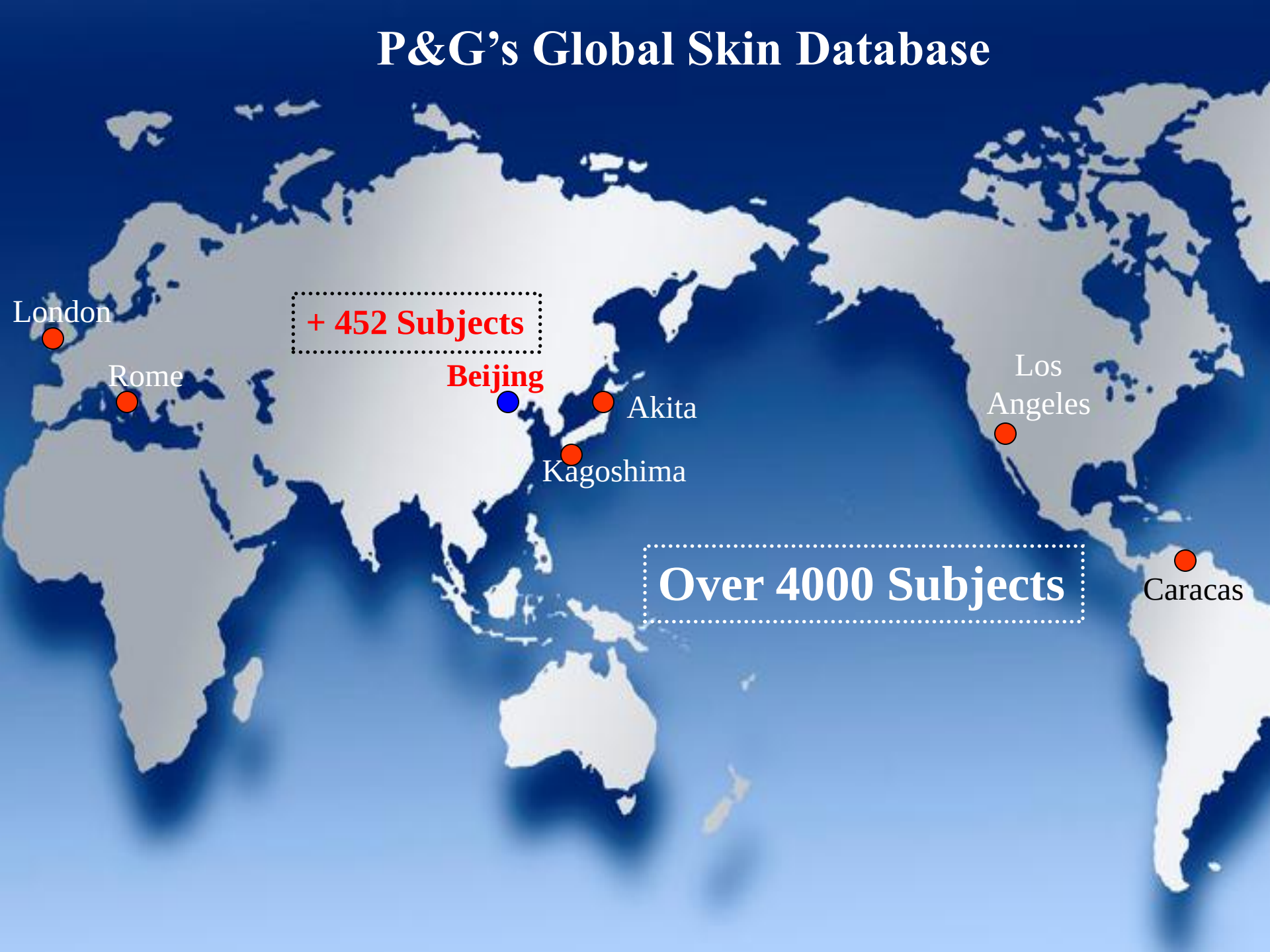


A Hypothetical Explanation for the Aging of Skin

Shuhei Imayama and Irwin M. Braverman

World Wide Skin Aging Research

P&G's Global Skin Database



Epidemiology Study in Beijing

- P&G and CAIQ (Chinese Academy of Inspection and Quarantine)
- Oct 28 - Nov 11, 2006
- 452 Healthy Chinese females, Ages 10-70 (75 per decade)
- Measures
  - Visible facial features (Wrinkles)
  - Biophysical parameters (Hydration, Elasticity, Firmness, L*)
  - Host and environmental factors (questionnaire)








Facial aging

Wrinkles, spots take independent courses

By John Jesitus
Senior Staff Correspondent

QuickREAD

In a recent study of Chinese women, facial age spots have proven to be no predictor of facial wrinkling and vice versa, a study author says.

San Antonio — A study of facial aging in Chinese women shows that wrinkles are no predictor of age spots, and vice versa, a study author says.

"Each of us ages differently. Some people are more prone to skin wrinkling; others, age spots; others, both. It may be that for some, their skin reacts to chronic sun exposure over a lifetime by mounting a defense in the form of persistent hyperpigmentation or age spots," which stem from an unevenly distributed increase in melanin production, says Greg G. Hillebrand, Ph.D., principal scientist in skincare product development with Cincinnati-based Procter & Gamble.

Dr. Hillebrand

"That increase in melanin, while unwanted, may help protect the underlying basal keratinocytes and dermal fibroblasts, as well as col- … the world," he says.

Procter & Gamble has also studied populations from Japan, Europe and the United States, he says.

"Since we have a fast-growing skincare business in China," Dr. Hillebrand says, "it's important for us to understand the skin condition of the Chinese population, to allow us to potentially make better products that meet their needs."

The single-visit observational survey — involving 452 healthy Chinese females, ages 30 to 70, who had lived most of their lives in Beijing — employed various tools and objective measurements. These included, but were not limited to, VISIA Complexion Analysis (Canfield Scientific) of wrinkling, visible spots and UV spots on the right and left cheeks; cutometer measurements of left cheek and upper inner arm elasticity; and corneometer measurements of stratum corneum hydration on the left cheek.

"The result I found most interesting, and surprising, was that a person's facial wrinkling does not predict their facial hyperpigmentation, and vice versa — there was no correlation," Dr. Hillebrand says.

In prior studies, he says, "I've assessed the change in wrinkling and hyperpigmentation with age.

> **"The result I found most interesting, and surprising,** was that a person's facial wrinkling does not predict their facial hyperpigmentation, and vice versa."
>
> —Greg G. Hillebrand, Ph.D. Cincinnati

And one could see that as we age, we get more wrinkles and spots, just as we would expect."

However, he says these results come from comparing population means for patients of older ages to those of younger ages.

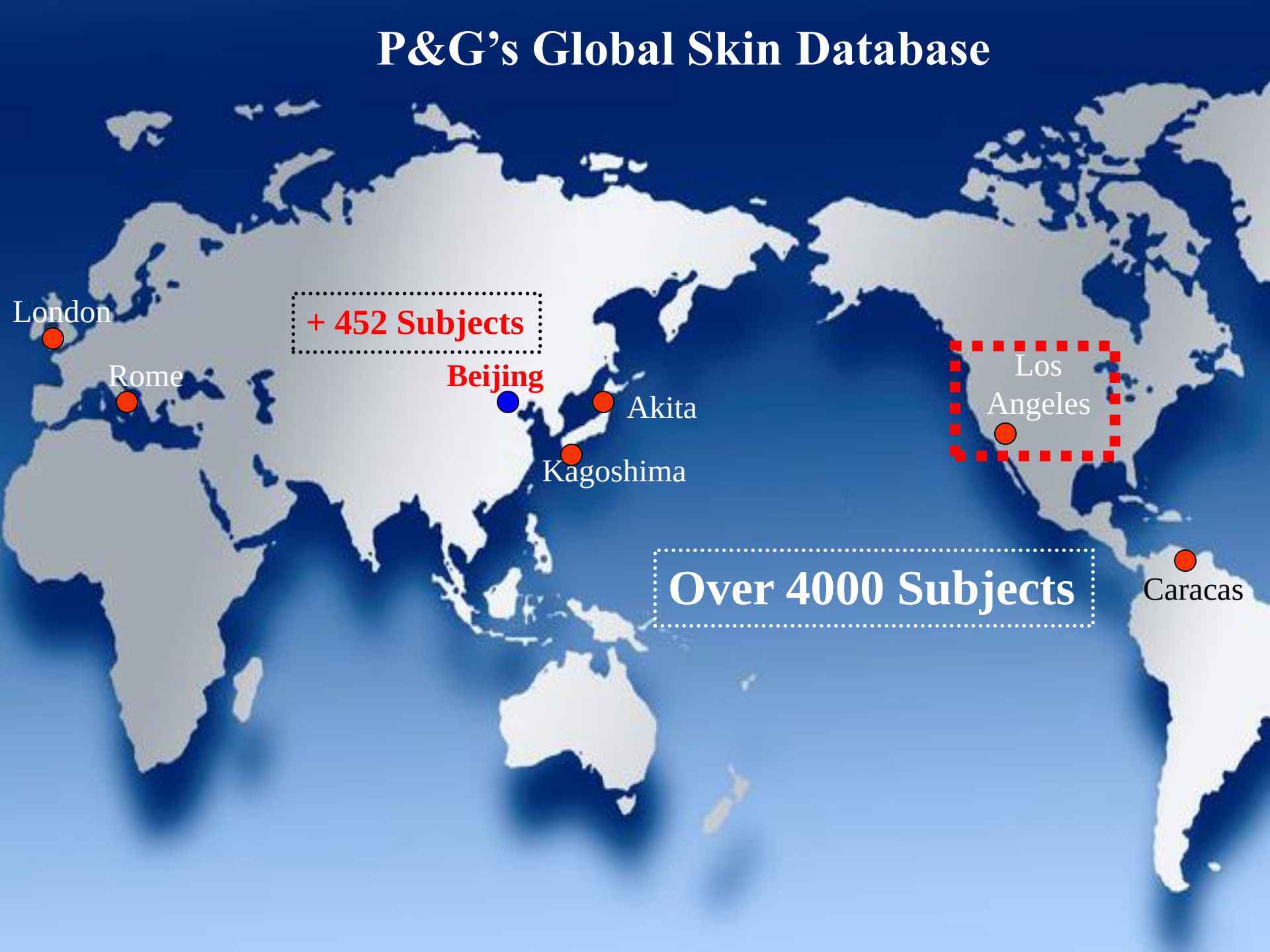
Aging continues page 63

QUOTABLE

"What you're looking for are cosmetically

An 8-year longitudinal study on facial wrinkling

P&G's Global Skin Database



An 8-year longitudinal study in LA

1999 vs. 2008

OBJECTIVES

- To determine the progression of facial wrinkling, both temporary and persistent, on the same population of people over several years.
- To identify host and environmental factors significantly associated with the rate of change in facial wrinkling.

METHODS

-Same high resolution digital facial imaging system
-122 same women covering 4 ethnic populations
-Skin biophysical parameters were measured in 1999
-A QOL related standard questionnaire was done in 2008

BJD British Journal of Dermatology

New wrinkles on wrinkling: an 8-year longitudinal study on the progression of expression lines into persistent wrinkles

G.G. Hillebrand, Z. Liang,* X. Yan* and T. Yoshii*

The Procter & Gamble Company, Cincinnati, OH 45241, U.S.A.
*The Procter & Gamble Company, Kobe, Japan

Summary

Correspondence
Greg Hillebrand.
E-mail: hillebrand.gg@pg.com

Accepted for publication
4 February 2010

Key words
epidemiology, imaging, menopause, wrinkles

Conflicts of interest
All authors are employees of the Procter & Gamble Company. This work was funded by the Procter & Gamble Company, Cincinnati, OH.

DOI 10.1111/j.1365-2133.2010.09709.x

Background While cumulative lifetime sun exposure is well recognized as having an important role in the progression of facial wrinkling, the role of facial expression has largely been overlooked, in part due to the lack of comprehensive longitudinal data on the change in both expression lines and persistent wrinkles with age.
Objectives To track the detailed pattern of facial wrinkling in the same group of people over several years and to verify that expression lines evolve into persistent wrinkles. In addition, to identify factors predictive of a faster or slower rate of wrinkling.
Methods Standardized images were captured at baseline and at 8 years of 122 women (ages 10–72 years, skin types I–VI) with and without a smiling expression. The wrinkle pattern with expression at baseline was compared with the pattern without expression at 8 years. Severity of facial wrinkling was quantified using computer-based image analysis. Skin colour, hydration, sebum and pH were measured at baseline. A structured questionnaire captured demographic and lifestyle data at baseline and at 8 years.
Results Each subject's unique pattern of persistent facial wrinkling observed without expression at year 8 was predicted by the pattern of lines observed with a smiling expression at baseline. Having a drier, more alkaline stratum corneum, a lighter complexion, being middle-aged (40s) or becoming menopausal were associated with faster persistent wrinkling.
Conclusions Repeated skin flexure during facial expression causes persistent wrinkles. The pattern of expression lines predicts the pattern of future persistent wrinkles. Certain intrinsic and extrinsic factors are not causative, but influence the rate, of facial wrinkling.

Akita 11-Year Skin Aging Longitudinal Study

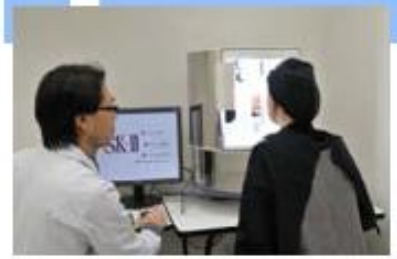
P&G's Global Skin Database

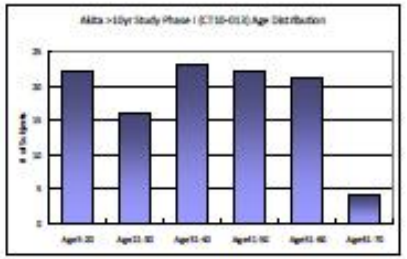
Akita 11-Year Longitudinal Study

- Subjects: 108 Japanese females were selected from the original 1999 facial aging study, ages 15-76 (age 5-65 in 1999) (Ave. 37.9 at 2010)
- Facial skin appearance and physical properties were measured in subjects at both time points under the same conditions

1st measurement 1999

2nd measurement 2010
(11 yrs later)





BIS - Facial Imaging system

Hydration/Elasticity/TEWL

Subject age distribution

Akita Interface Co. Ltd. (Northern Part of Japan) Clinical Facility

Same clinical condition as 1999

Other skin physical measures

Characterization of comprehensive appearances of skin aging: An 11-year longitudinal study on facial skin ageing in Japanese females at Akita

Kukizo Miyamoto[a], , Yasuko Inoue[a], Kesyin Hsueh[a], Zhiwu Liang[a], Xianghong Yan[a], Takashi Yoshii[a], Masutaka Furue[b]

[a] Prestige and Female Beauty R&D, P&G Innovation Godo Kaisha, 1-17 Koyo-cho Naka, Higashinada-ku, Kobe 658-0032, Japan

[b] Department of Dermatology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Received 9 May 2011. Revised 2 September 2011. Accepted 19 September 2011. Available online 29 September 2011.

Summary

Background

Facial appearance is regarded as a typical index of ageing. However, people of the same age do not necessarily show the same degree of the facial appearance. The ageing of facial skin proceeds relatively slowly and therefore requires long-term follow-up to elucidate the mechanism of ageing changes.

Objectives

The purpose of this study was to identify facial skin parameters contributing the subjective impression of the overall ageing and characterize the degree of skin ageing by a 11 year longitudinal skin monitoring.

Methods

One-hundred-eight healthy Japanese females excluded outside workers aged 5–64 at 1999, and lived in Akita, Japan till 2010 were enrolled. Facial images were collected to quantify various skin optical parameters. Skin colour, hydration and barrier function were measured with Chromameter, Corneometer and TEWAmeter, respectively. The visual evaluation of the overall facial skin ageing impression was also carried out. The skin parameters contributing visible impression of skin ageing were identified by variable importance in projection analysis, and the degree of facial skin ageing over 11 years was statistically classified by a cluster analysis.

Results

Facial skin parameters that comprehensively influenced visible skin ageing, including hyperpigmented spots, wrinkles and texture were studied. The Skin Ageing Score calculated from these three skin factors was used to classify the subjects into a mild, age-appropriate, and severe skin ageing group. The mild skin ageing group maintained significant better both skin optical and physical conditions.

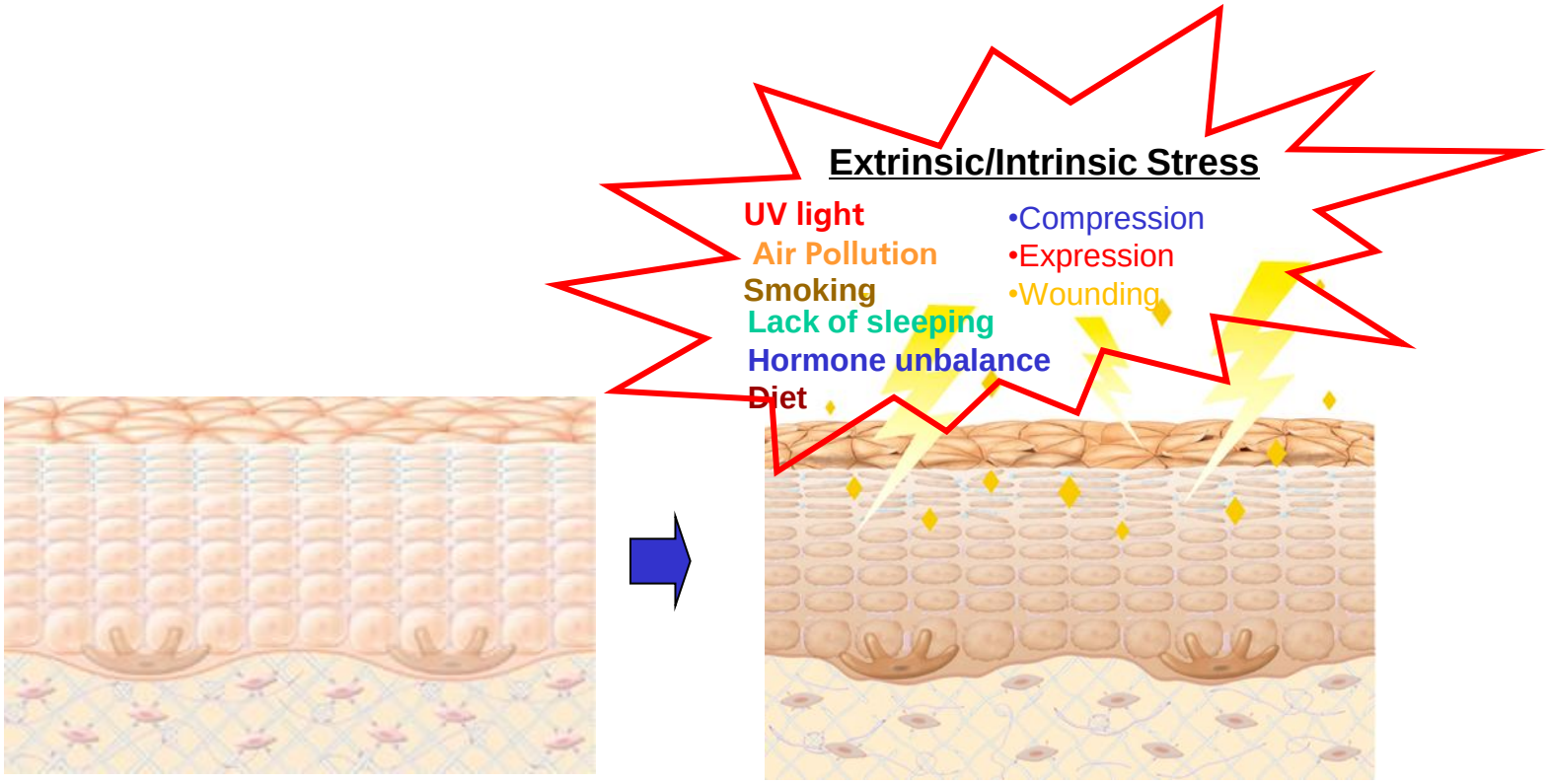
Conclusions

Variability and classification of the degree of facial skin ageing appearance were studied from this longitudinal research.

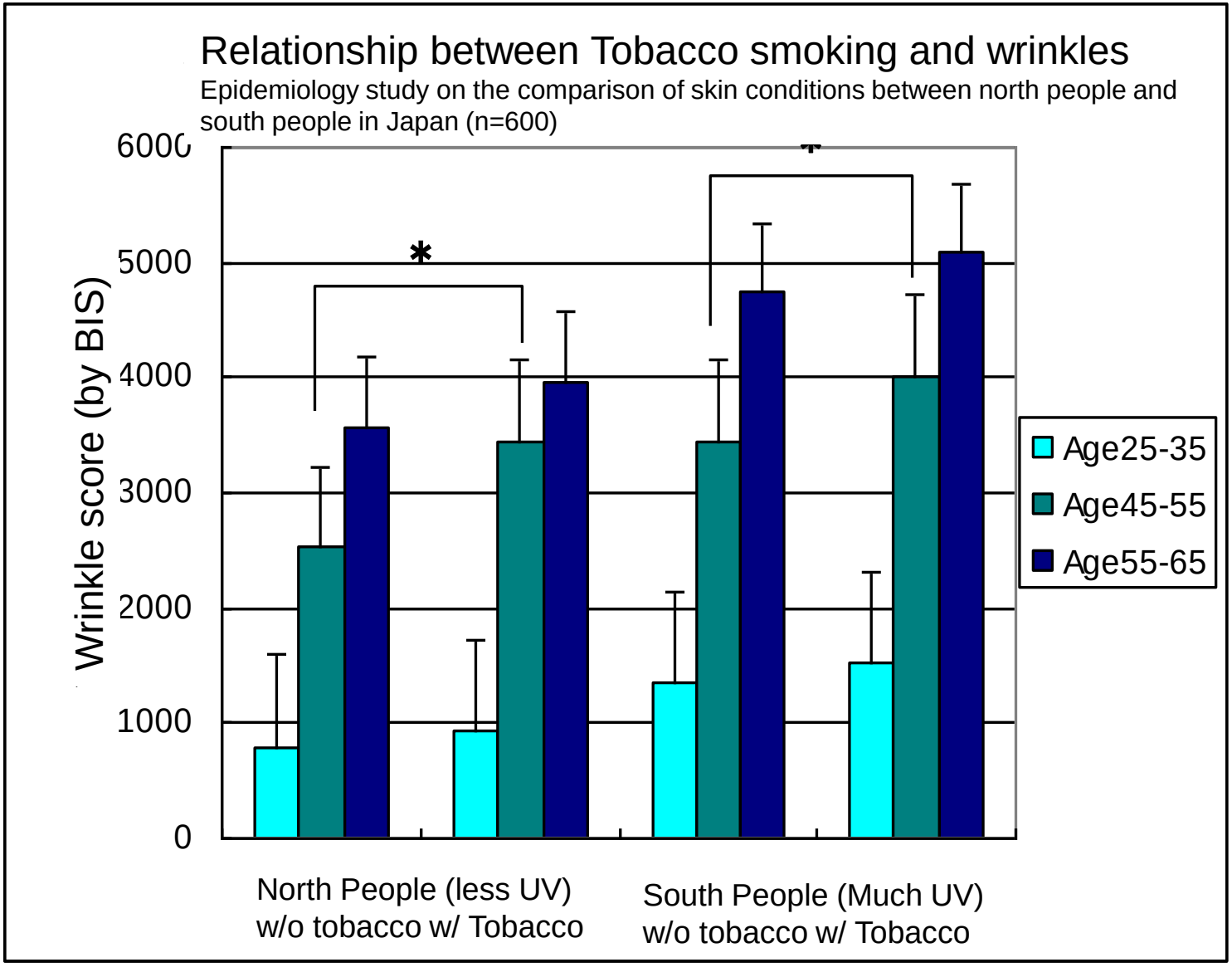
Skin Aging hugely varies by individual,

Can we help women successfully age ?

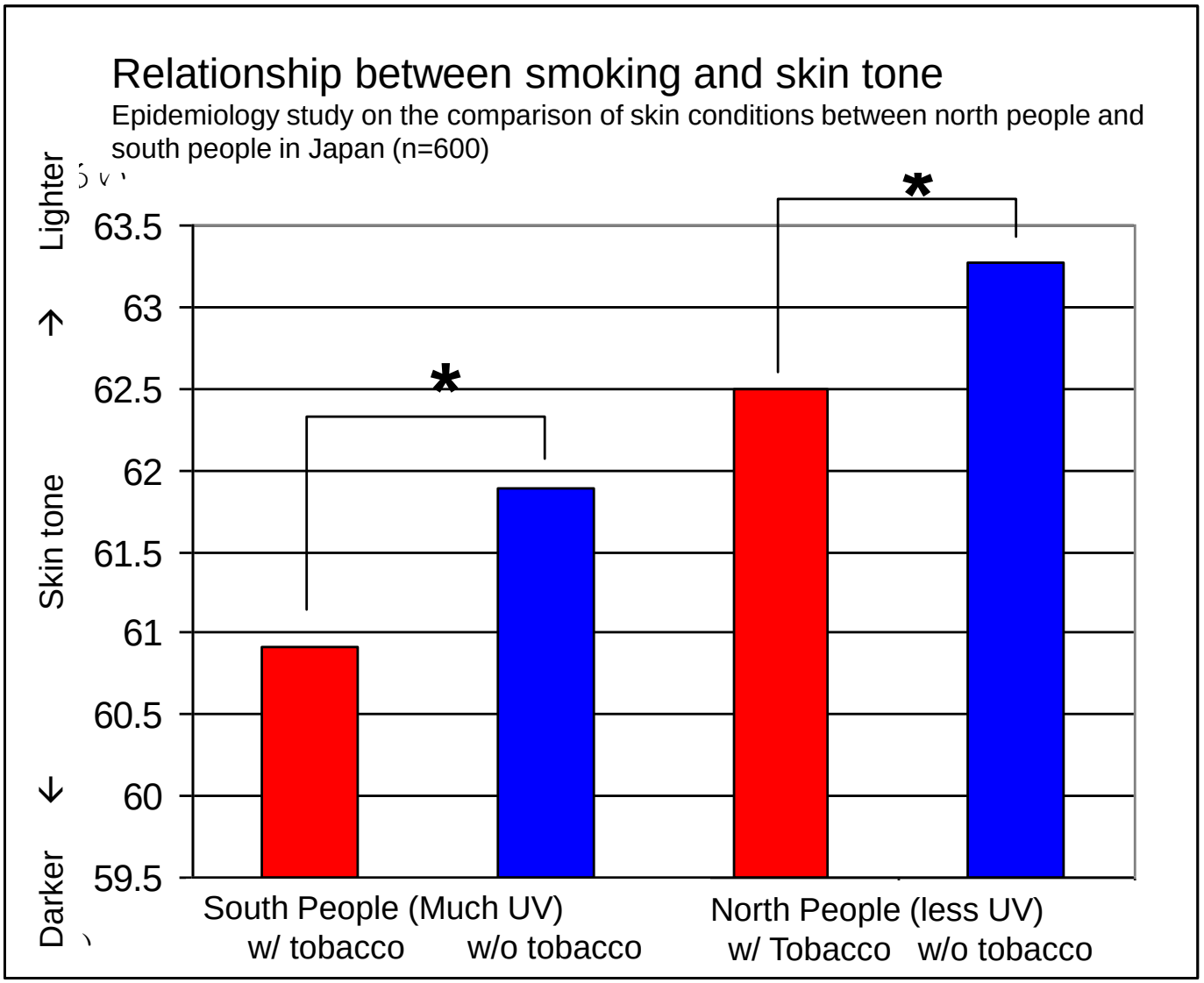
Cause of Skin Aging



For example: UV and Smoking Influence



For example: UV and Smoking Influence



Genomic Study on Skin Aging

20’s・60’s Skin Biopsy

Non UV Exposure

Non UV Exposure

UV Exposure

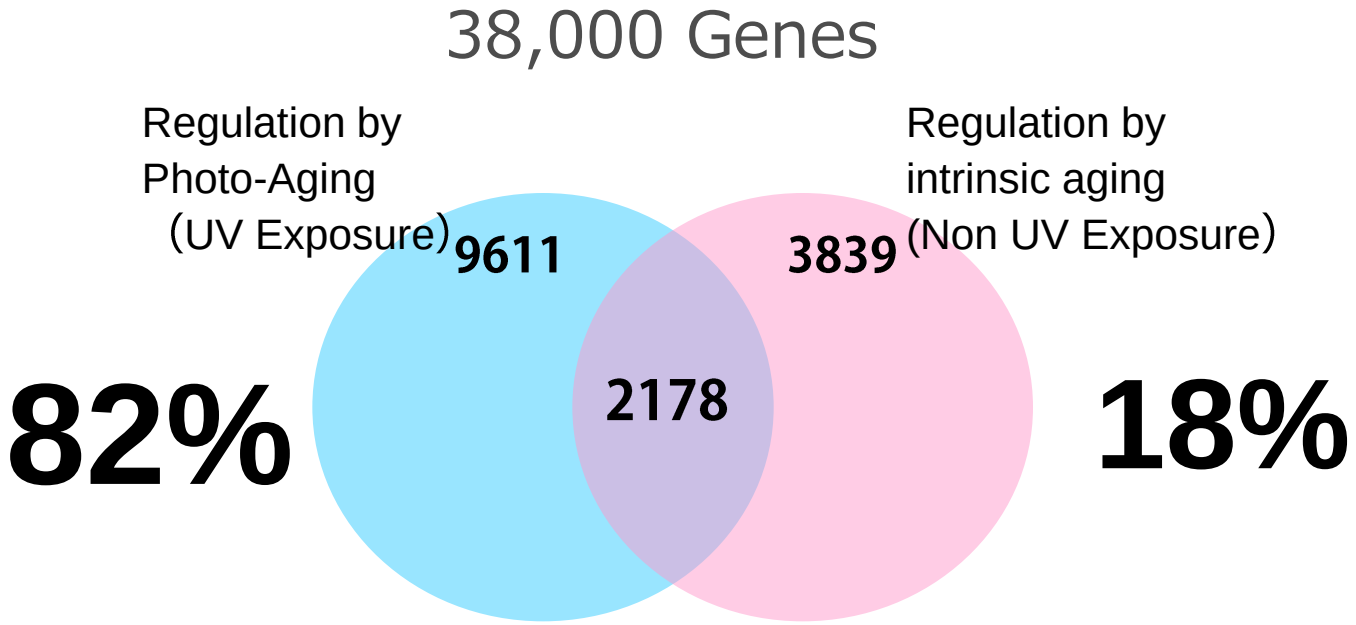
UV Exposure

20’s

60’s

Gene Chip

Comparison of Gene Expression Aged and Young Skin



Today’s Agenda

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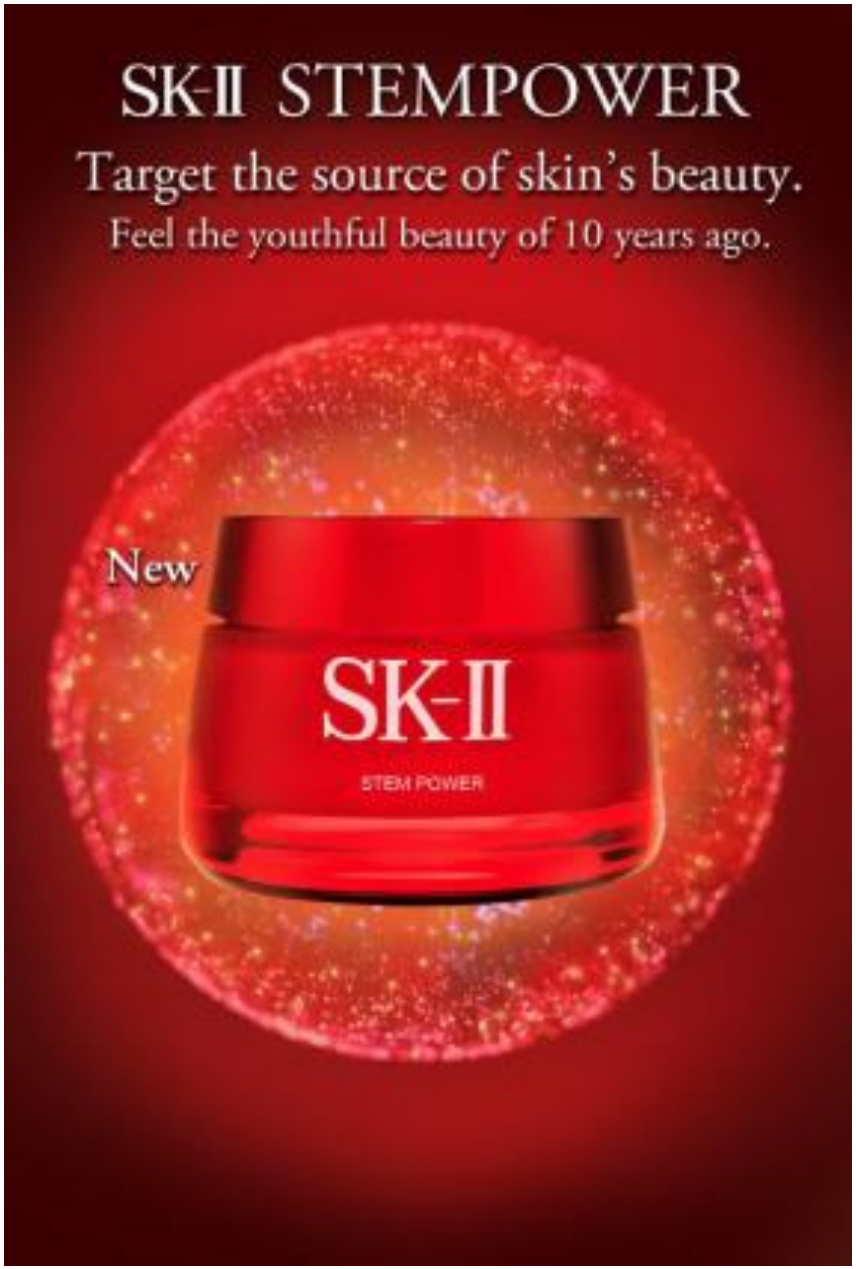
- World Wide Skin Aging Research
- Functional Ingredients with Cut-Edge Science

1. Stem-Acanax from Siberian Ginseng

Business Success, Rooted in Advanced Science



2. Artichoke Extract

Cynaropicrin, an extract from artichoke, inhibits UVB-induced oxidative stress in cultured human keratinocytes.

G. Tsuji[1], M. Takahara[1], X. Yan[2], A. Hachiya[1], H. Uchi[1], S. Takeuchi[1], F. Yasukawa[1], K. Takei[1], Y. Moroi[1], M. Furue[1]

1. Dermatology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan.
2. P&G Design Center Godo Kaisha, Kobe, Japan.

Abstract

Cynaropicrin, a bioactive compound from artichoke leaf extract, has been reported to have a potent anti-inflammatory activity, however, the precise mechanism remains unclear. Several studies have shown that some phytochemicals modulate aryl hydrocarbon receptor (AhR) signaling, which results in inhibition of reactive oxygen species (ROS) production in vitro and vivo. Further, we have demonstrated that AhR signaling regulates ROS production via Nrf2 and SIRT1 activation, which turns on a redox machinery against ROS-induced oxidative stress in human keratinocytes. Therefore, we examined whether cynaropicrin exerts its anti-inflammatory effect via AhR-mediated Nrf2 and SIRT1 activation in human keratinocytes. Cultured normal human epidermal keratinocytes (NHEKs) were treated with cynaropicrin (100nM-10μM). We found 1) that cynaropicrin upregulated Nrf2, Nqo1 and SIRT1 mRNA expression in real-time PCR assay, 2) that cynaropicrin induced nuclear translocation of AhR and Nrf2 in confocal microscopic analysis, and 3) that knockdown of AhR using siRNA transfection cancelled cynaropicrin-induced Nrf2 and Nqo1 mRNA upregulation in real-time PCR assay. Taken together, we have revealed that cynaropicrin is an AhR-Nrf2 signal activator in NHEKs. Furthermore, to examine its anti-inflammatory effect, NHEKs were exposed to ultraviolet (UV) B radiation which produces ROS attributing to skin aging, inflammation and carcinogenesis. As UVB has been reported to induce skin inflammation via AhR-mediated COX-2 expression, we hypothesized that cynaropicrine might prevent UVB-induced AhR activation antagonistically. We found that cynaropicrin (1μM) inhibited UVB-induced ROS and inflammatory cytokine (IL-1α, IL-6, IL-8 and TNF-α) production in NHEKs. In conclusion, these findings indicate that cynaropicrin may be a useful agent for preventing the UVB-induced skin aging, inflammation and carcinogenesis via AhR-Nrf2-mediated mechanism.

Introduction

Aryl hydrocarbon receptor (AhR), a receptor for dioxins, induces multiple gene expression related to cytoprotection against oxidative stress as well as gene expression of drug metabolizing enzymes.
Oxidative stress caused by reactive oxygen species (ROS) has a very important role in skin inflammation, infection and aging. Since keratinocytes, the outermost barrier of body, are exposed to various stimulants causing oxidative stress such as pathogens, chemicals and ultraviolet ray (UV), a targeted therapy against oxidative stress may be beneficial to improve ~~many~~ skin disorders (Fig 1).
Our previous studies have demonstrated that AhR modulates expressions of nuclear factor erythroid 2-derived 2-like 2 (Nrf2), a master switch of a redox machinery, and small mating type information regulation 2 homolog 1 (Sirt1), a mediator of inflammatory reaction and cell differentiation via regulation of ROS production.
Cynaropicrin (Cyn), an active compound of artichoke leaf extract, is known to have a potent anti-inflammatory effect. According to reports that AhR is activated by phytochemicals as well as dioxins, we hypothesized that Cyn may exert protective effect against ROS production by activating AhR (Fig 2).

Fig 1. Keratinocytes are the first line to protect human body from oxidative stress.

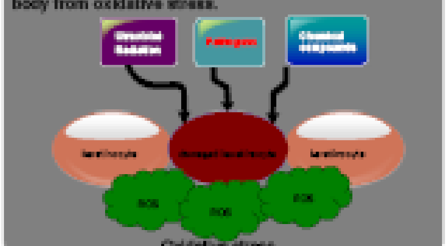
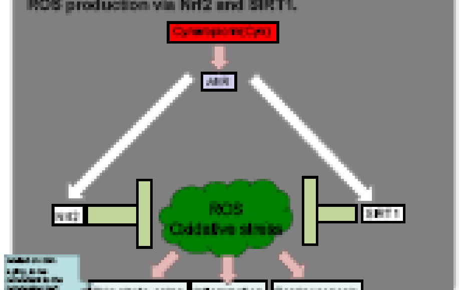
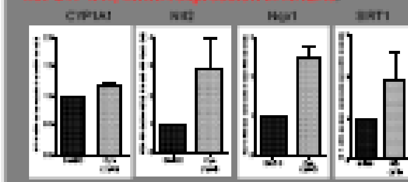


Fig 2. Aryl hydrocarbon receptor (AhR) modulates ROS production via Nrf2 and SIRT1.



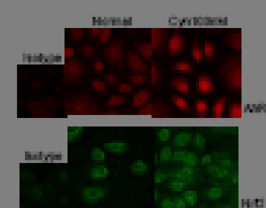
Results

Fig 3. Cyn upregulated Nrf2, Nqo1 and SIRT1, but not CYP1A1, mRNA expression in NHEKs.



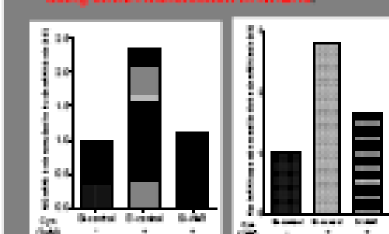
Real-time PCR analysis: NHEKs treated with Cyn (1μM) for 6 hrs were examined whether Cyn upregulates CYP1A1, Nrf2, Nqo1 and SIRT1 mRNA expression. Nqo1 is a downstream gene of Nrf2 inhibiting oxidative stress.

Fig 4. Cyn induced nuclear translocation of AhR and Nrf2 from cytoplasm of NHEKs.



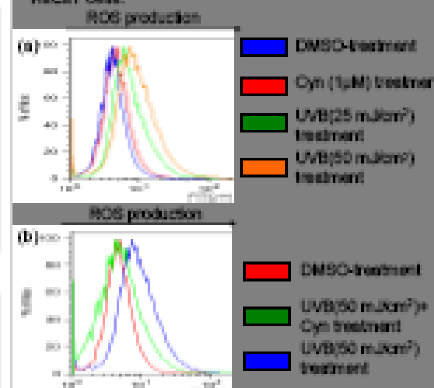
Confocal microscopic analysis: NHEKs treated with Cyn (1μM) for 6 hrs. Nuclear translocation of AhR or Nrf2 which is required for AhR or Nrf2 activation was demonstrated by Cyn treatment, respectively.

Fig 5. Cyn-induced Nrf2 and Nqo1 mRNA upregulation was canceled by AhR knockdown using siRNA transfection in NHEKs.



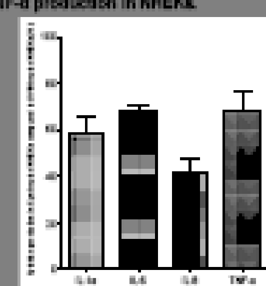
Real-time PCR analysis: NHEKs were transfected with siRNA against AhR for 48 hrs to knockdown AhR expression. AhR knockdown NHEKs were unresponsive to Cyn (1μM), showing Cyn-induced Nrf2 and Nqo1 mRNA expressions were AhR-dependent.

Fig 6. Cyn inhibited UVB-induced ROS production in HaCaT cells.



Flow cytometry analysis: (a) HaCaT cells were treated with DMSO (control), Cyn (1μM), or different doses of UVB (25-50 mJ/cm²). After 6 hrs, HaCaT cells were incubated with H2DCF. ROS production changes H2DCF into a detectable form as a green fluorescence using flow cytometry. (b) Cyn inhibited UVB-induced ROS production in HaCaT cells. After the UVB irradiation, HaCaT cells were treated with DMSO (control) or Cyn for 6hrs.

Fig 7. Cyn inhibited UVB-induced IL-1α, IL-6, IL-8 and TNF-α production in NHEKs.

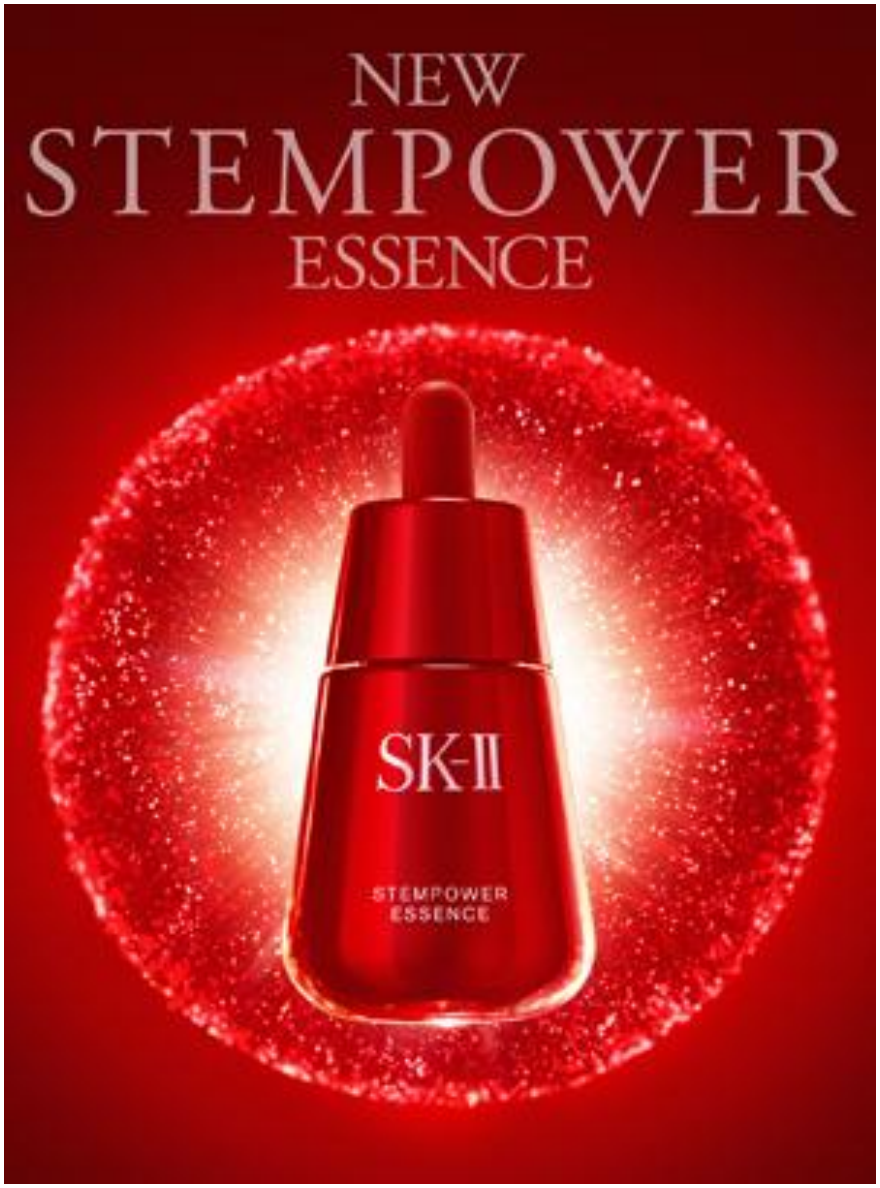


ELISA analysis: UVB(50 mJ/cm²) irradiated NHEKs were treated with DMSO or Cyn (1μM) for 6hrs. Inflammatory cytokines production in culture supernatant were measured by ELISA. Treatment with Cyn clearly reduced the production of IL-1α, IL-6, IL-8 and TNF, when compared to DMSO control.

Conclusion

These findings indicate that cynaropicrin may be a useful agent for preventing the UVB-induced oxidative stress leading to skin aging, inflammation and carcinogenesis.

Another Hero, Rooted in Advanced Science



Recap

- **Global Overview of Skin Care Market**
  Anti-aging is the fastest growing segment

- **World Wide Skin Aging Research**

1. Epidemiology Study
2. Longitudinal Study

- **Functional Ingredients with Cut-Edge Science**

1. Stem Acanax
2. Artichoke Extract

Thank you for your attention