Stem cells of the skin - Novel approaches to increase their performance
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Personal Care
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Outline agenda

1. Claiming stem cell in cosmetics - a current trend
2. Background on skin stem cells
3. Cosmetic ingredients to increase stem cell performance
Stem cells in Cosmetics

- On finished product level: Cosmetics supporting skin stem cells activity
- On ingredient level:
  - Ingredients based on plant stem cells
  - Other approaches
Cosmetics are cashing in on the magic allure of the words “stem cell” as a route to youth.

Various market examples for finished products making stem cell claims

"will help restore the potential of skin stem cells and bring back the skin of youth."

"convert resting adult stem cells to fresh newly minted cells for a firmer, more defined appearance."

"works on skin stem cells to better repair wrinkles"
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Stem cells are undifferentiated cells that can develop into various cell types

- **Totipotent stem cells**: Can differentiate in any cell type
  Known as embryonic stem cells
  No cosmetic relevance

- **Multipotent stem cells**: Can differentiate in several cell types
  (e.g. liver cell, nerve cell)
  Example: Dermal stem cells
  High cosmetic relevance

- **Unipotent stem cells**: Differentiate in one particular cell type
  Example: Epidermal stem cells
  High cosmetic relevance
Self-renewal and differentiation of adult stem cells

- Give rise to more stem cells
- Differentiate into specialized cell (e.g. Keratinocytes)

Adapted from: C.C. Zouboulis et. al. / Experimental Gerontology 43 (2008)
Overview on skin stem cells

- Epidermal interfollicular SC
- Follicular epidermal/bulge SC
- Dermal mesenchymal SC
- Follicular mesenchymal SC
- Adipose derived SC

Healthy skin involved the activity of different types of stem cells
Stem cell differentiation

Epidermal stem cell differentiation

Stem cell → Progenitor cell (Transit Amplifying (TA) cell) → Differentiated cell

Dermal stem cell differentiation

Stem cell → Progenitor cell → Differentiated cell → Apoptosis
Homeostasis in the skin

The major roles of the epidermis are as follows:
- protecting effect against water loss
- protecting effect against microorganism infection
- providing information about the species, gender and social status

The major roles of the dermis are as follows:
- giving mechanical protection to the body; collagen has an important role
- providing oxygen and nutrients to the living part of the epidermis
- removing waste products of metabolism from the epidermis
- providing shape and form to the body
- skin sensations of touch, pain, heat and cold

The process that ensures the epidermal and dermal functionality is called Homeostasis

Epidermal homeostasis: a balancing act of stem cells in the skin

* C. Blanpain; Nature Reviews Molecular Cell Biology 2009
Role of Epidermal interfollicular stem cells

- Epidermal stem cells occur in the basal layer of the epidermis and at the base of hair follicles.

- The epidermal stem cells give rise to keratinocytes, which migrate to the surface of the skin and form a protective layer the stratum corneum.

Epidermal stem cells are responsible for tissue maintenance and repair
Role of dermal mesenchymal stem cells

- Dermal stem cells are able to undergo multipotent differentiation
- Fibrocytes are understood as progenitors of Fibroblasts
Do stem cell age?

- Stem cell number and self-renewal capabilities do not decline with age necessarily
- The ability to produce progenitor and differentiated cells decline
- Reduced functionality is mainly caused by:
  - Direct effects such as DNA damage, oxidative stress
  - Effect on their supporting niches

Reduced stem cell functionality leads to imperfect homeostasis which results in typical signs of aging
Outline agenda

1. Claiming stem cell in cosmetics - a current trend
2. Background on skin stem cells
3. Cosmetic approach related to stem cell functionality
1. Actives protecting and preserving stem cell functions

- Synthetic peptides to maintain the skin stem cell environment (niche)*
- Increase stem cell activity
- Maintain self renewing capacity through DNA protection **

* A. Weber Cossma 9/2010
** C.C. Zouboulis et.al./Experimental Gerontology 43 (2008)
Synthetic peptides to maintain the epidermal stem cell environment (niche)

SYN®-TACKS is suitable to maintain a healthy environment for epidermal stem cells through DEJ strengthening
SYN®-TACKS stimulate major DEJ Proteins (in vitro efficacy)

Stimulation of DEJ protein expression in vitro by:
Peptide 2: Palm-Lys-Val-Dab-Thr-OH (50 μM, in red, RNA level)
Peptide 3: Palm-Lys-Val-Dab-OH (100 μM, in orange, Protein level).

Major DEJ proteins are significantly up-regulated
SYN®-TACKS benefits on epidermal stem cells

(Palmitoyl Dipeptide-5 Diaminobutyroyl Hydroxythreonine, Palmitoyl Dipeptide-5 Diaminohydroxybutyrate)

- Strengthen the DEJ
- Tightens dermis to epidermis to improve communication and cellular nourishment

SYN®-TACKS promotes an ideal environment for differentiation of epidermal stem cells to basal cells and their further proliferation and final differentiation to Corneocytes
Peptides to maintain the dermal stem cell environment (niche)

Collagen as major structural element of the dermis has a key function to maintain skin firmness
Peptides to maintain the dermal stem cell environment (niche)

1. Boost collagen production
2. Protect collagen from degradation

SYN®-COLL dual-mechanism for maximal effect on collagen
SYN®-COLL stimulates the Collagen I synthesis (in vitro efficacy)

SYN®-COLL effectively induces collagen synthesis
SYN®-COLL benefit on dermal stem cells

( Palmitoyl Tripeptide-5)

- Stimulates collagen synthesis and strengthen the extracellular matrix
- Reduces Collagen breakdown

SYN®-COLL promotes an ideal environment for freshly differentiated dermal stem cells and promotes dermis regeneration
Energizing of stem cells

- Stem cells and progenitor cell proliferation requires high cellular energy

- Reduced proliferation potential and finally skin aging is a consequence of the loss of skin stem cell activity

PEPHA®-CTIVE increase cellular activity which directly supports proliferation capabilities of skin stem cells.
PEPHA®-CTIVE increases cell turnover

Biotechnologically produced microalgae extract (Dunaliella salina) protects and stimulates mitochondria by increasing ATP levels.
PEPHA®-CTIVE benefit on stem cells

- Supports the proliferation capabilities of stem cells and their progenitor cells
- Increase cellular activity
Recent data suggest that we age, in part, because our self-renewing stem cells grow old as a result of heritable intrinsic events, such as DNA damage, as well as extrinsic forces, such as changes in their supporting niches.

**PEPHA®-PROTECT** protects the DNA of skin cells from daily stress.
PEPHA®-PROTECT protecting effect of on human Keratinocytes

INCI: Water, Glycerin, Citrullus Lanatus (Watermelon) Fruit Extract

COMET assay

Principle

- Cellular stress leads to DNA fragmentation
- fragmented DNA migrate from nucleus
- migrated DNA pieces form a COMET

Destroyed DNA

Protected DNA

no PEPHA®-PROTECT

plus PEPHA®-PROTECT
PEPHA®-PROTECT benefit on dermal stem cells

- PEPHA®-PROTECT help to protect the skin stem cells from DNA damage
- PEPHA®-PROTECT ensure their self-renewing capacity of stem cells and their progenitor cells

PEPHA®-PROTECT delays the epidermal aging process induced by DNA damage
# Take home message

<table>
<thead>
<tr>
<th>Product</th>
<th>Main activity</th>
<th>Benefit for SC</th>
<th>Cosmetic benefit</th>
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</table>
| SYN®-TACKS    | • Strengthen the DEJ (BM)  
• Anchoring function for Epidermal basal cells | Dermal -epidermal cross talk improved               | Regeneration and rejuvenation for smooth looking skin  |
| SYN®-COLL     | • Improves Collagen synthesis  
• Protects Collagen network                                                    | Provides ideal environment for stem cell niche      | Firm skin appearance                                  |
| PEPHA®-CTIVE  | • Protects mitochondria  
• Fibroblast and Keratinocyte stimulation                                   | Stimulates epidermal regeneration (homeostasis)     | Natural beautiful skin look                           |
| PEPHA®-PROTECT| • DNA Protection                                                               | Protect stem cells for external damage (photo-ageing)| Delays skin ageing                                    |
Thanks for your attention

Thanks for supporting:

• Dr. Manuela Pflaumbaum
• Dr. Göde Schüler
• Rainer Voegeli
• Dr. Dominik Imfeld
• Dr. Remo Gräub

For more information please visit us at booth F40
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