



Replexium®

Achieve your beauty aspiration

**Presented by
Manasi Chavan & Anne Young**

■ BASF

We create chemistry

Care
Creations™

Agenda

- **Understanding Consumers' Beauty Aspirations and Expectations**
- **Skin Aging – A Multi-faceted Phenomenon**
- **Solution: Replexium® - Skin Bioavailable Peptide Complex**
- **Efficacy Data & Conceivable Claims**
- **Product Information & Formulation**

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Consumers' Beauty Aspirations and Expectations



235 women (ages 40-73)

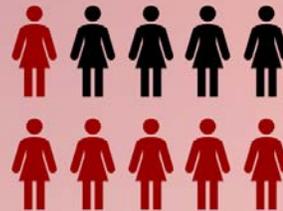
Close your eyes and picture yourself.
Now look into the mirror and tell us
“what is your aspired age?”

60%

wish to look

5-10 years

younger than their actual age



Tell us “How many years younger
can a quality skin care product
make you look?”

80%

expect to achieve

5-10 years

younger looking appearance



BASF Consumer survey

Consumers have high expectations from skin care products

Effective ingredients make quality skin care products



and offer non-invasive alternatives to consumers



Need for next-gen performance actives to address skin aging

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Skin aging - a multi-faceted phenomenon

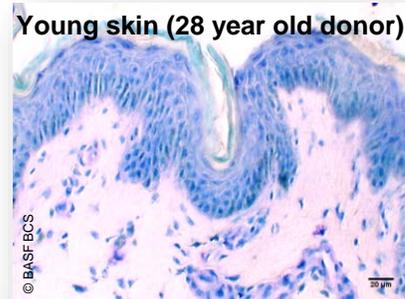
Visible changes

- Appearance of fine lines and wrinkles
- Loss of firmness and skin sagging
- Rough skin surface
- Deeper nasolabial folds



Age associated decrease of

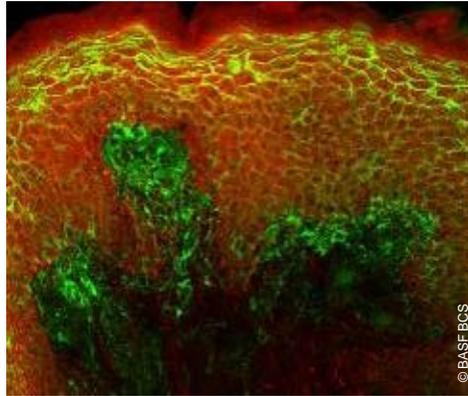
- Epidermal cohesion
- Flattening of dermal-epidermal junction
- Dermal density
- Extracellular molecules eg. collagen



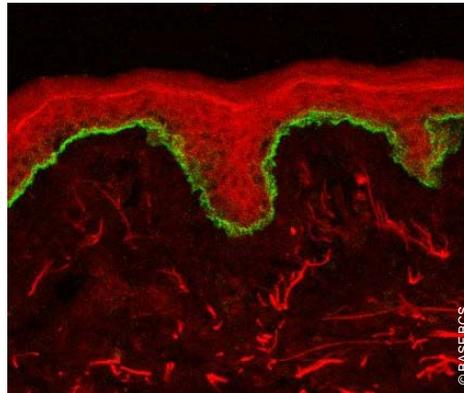
Need a multi-target approach to address skin aging concerns

Multi-target approach to address skin aging concerns

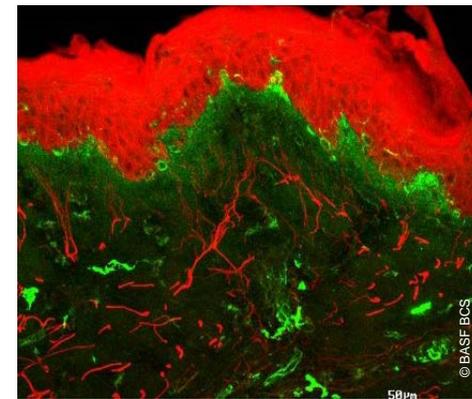
Epidermis



Dermal - epidermal junction



Dermis



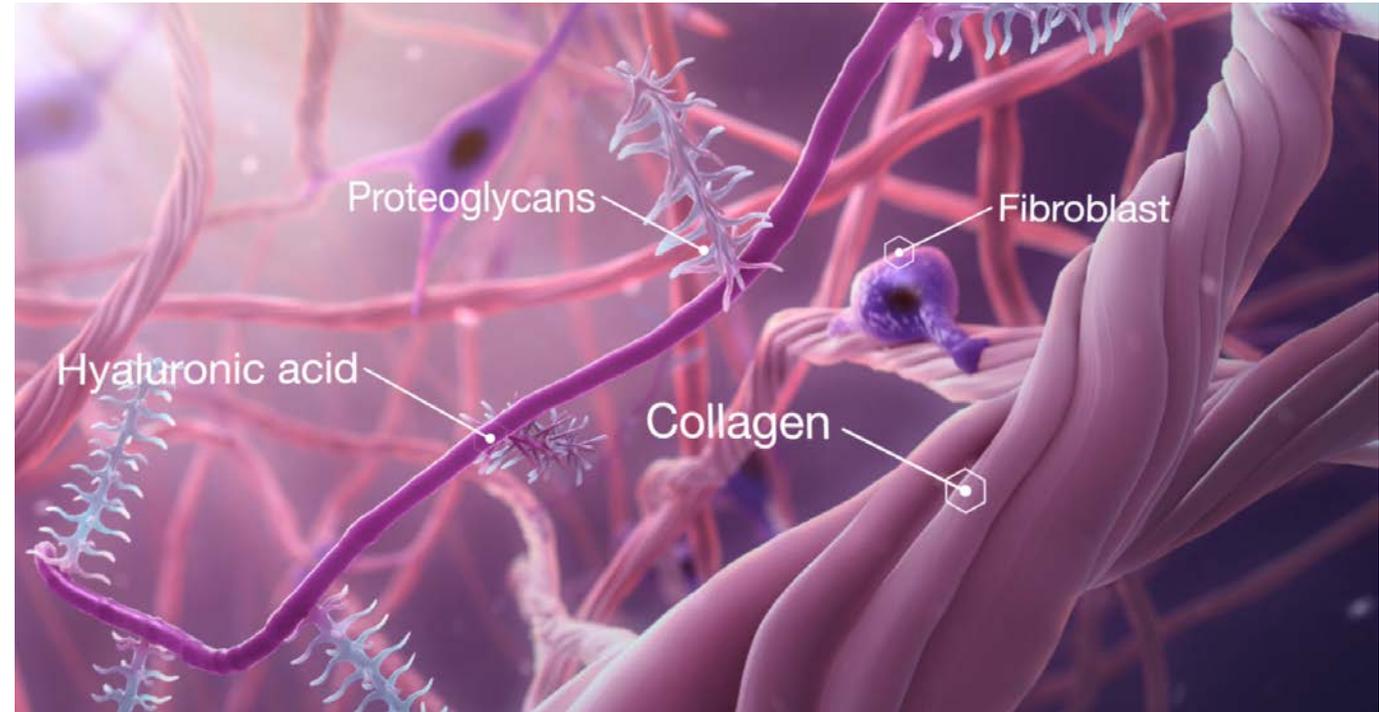
Proteoglycans - heavily glycosylated proteins in various skin layers

Functions

- proliferation, migration and differentiation of cells
- cell-cell interaction
- cell-extracellular matrix interaction
- tissue organization
- interact with collagen and hyaluronic acid
- provide biomechanical support
- act as filler between cells
- regulate water movement

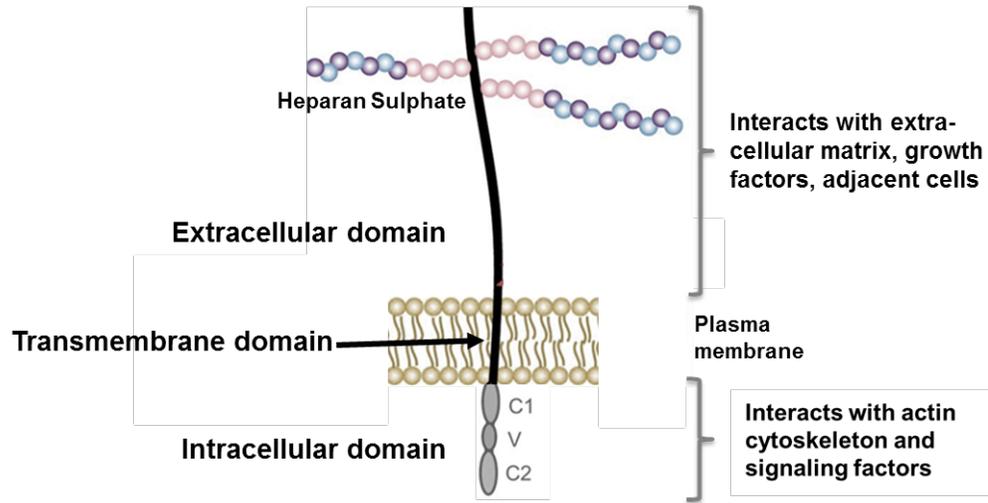
Two proteoglycans in focus

- **Syndecan-1**
- **Lumican**



Syndecan-1 involved in epidermal cohesion, decreases with skin aging

Syndecan-1 in epidermal cohesion

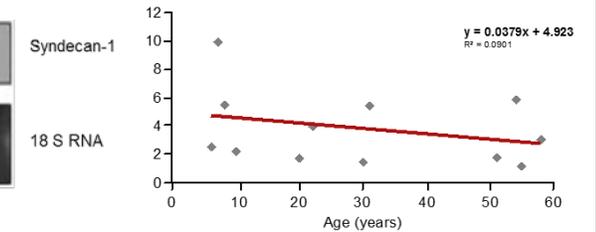
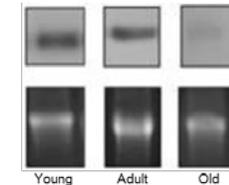


- Syndecan-1 is mainly expressed in the suprabasal layer of the epidermis
- Function - Modulation of epidermal cell proliferation and adhesion, and signaling of growth factors

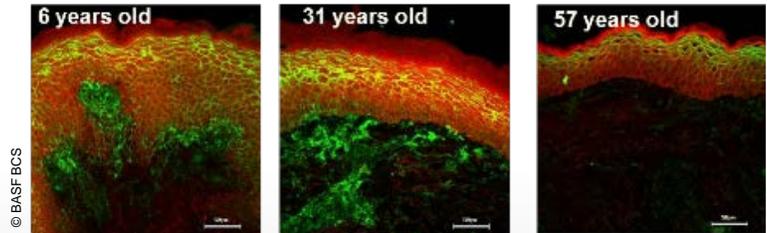
Syndecan 1 decreases with age in the epidermis

Method

Human cutaneous biopsies
0 to 58 yrs old
↓
Culture of primary culture)
↓
Quantification of Syndecan-1
mRNAs by Northern-blot



Human cutaneous biopsies
0 to 70 yrs old
↓
Cross sections
↓
Quantification by IHC and
confocal microscopy

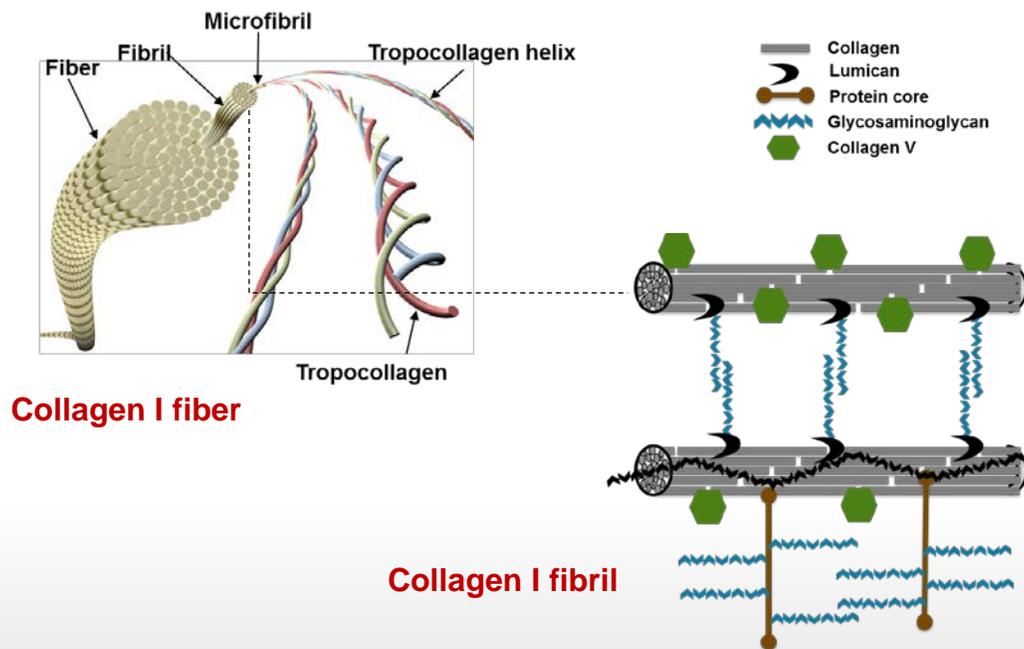


62% reduction of
Syndecan 1

Proper cellular signaling and cell-cell adhesion is altered, resulting in a decrease of epidermal cohesion.

Lumican, involved in collagen organization, decreases during skin aging

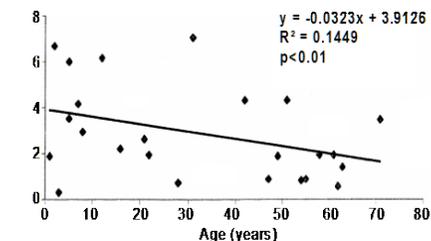
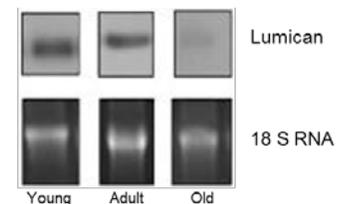
Lumican stabilizes collagen I



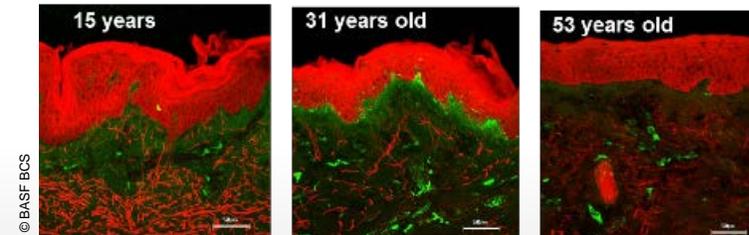
Lumican decreases with age in the dermis

Method

Human cutaneous biopsies
1 month to 83 yrs old
↓
Culture of dermal fibroblasts
(4 passages)
↓
Quantification of Lumican
mRNAs by Northern-blot and



Human cutaneous biopsies
1 month to 83 yrs old
↓
Cross sections
↓
Quantification by IHC and
confocal microscopy

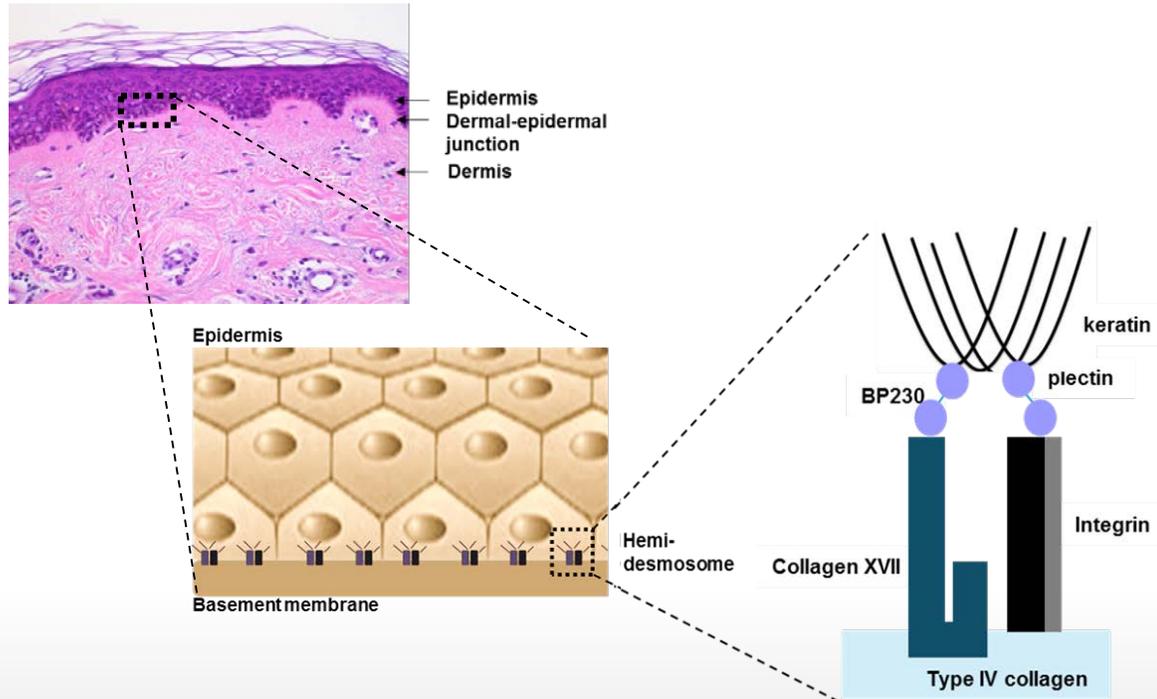


85% reduction of lumican

Organization of collagen fibrils is affected, resulting in a weakened extra cellular matrix.

Collagen XVII in the DEJ decreases with skin aging

Collagen XVII – structural component in the DEJ



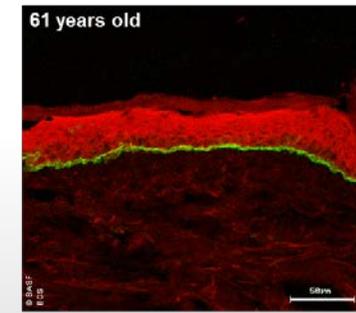
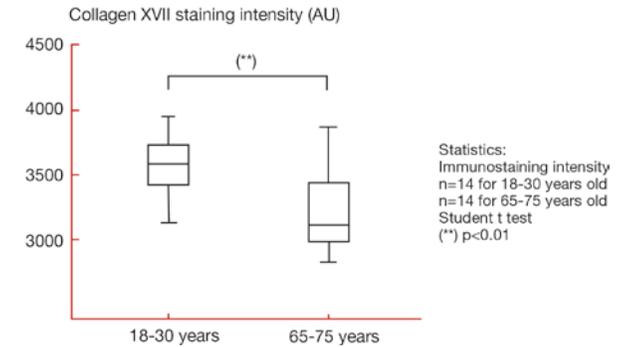
Function: cell-basement membrane adhesion through stabilization of the hemidesmosome complex.

Collagen XVII decreases with age in the DEJ

Method

Human cutaneous biopsies
0 to 70 yrs old
↓
Cross sections
↓
Quantification by IHC and
confocal microscopy

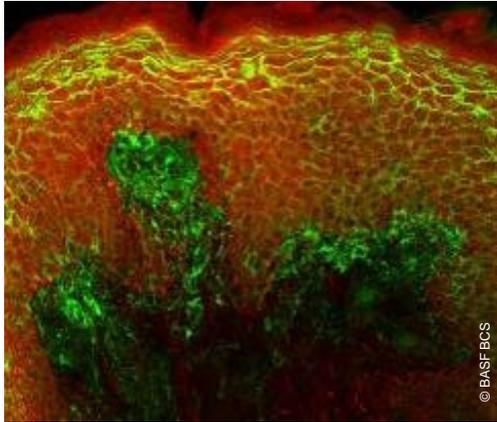
From Langton et al, 2017



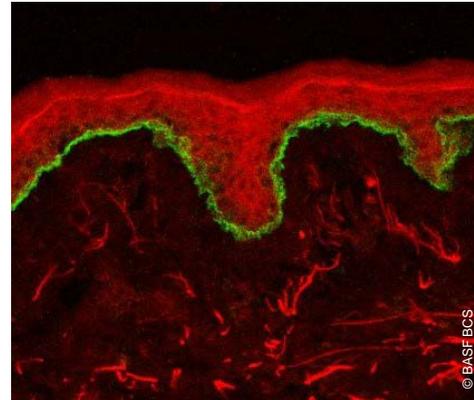
The structural integrity of the DEJ decreases, resulting in increased skin fragility.

A multi-pronged approach to address skin aging

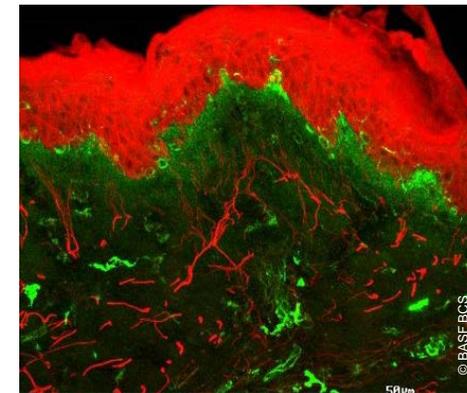
Syndecan-1 in Epidermis



Collagen XVII in Dermal-epidermal junction



Lumican in Dermis

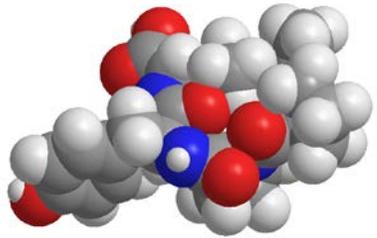


For a firmer, wrinkle-free skin with refined texture

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Replexium®



N-Acetyl-Pro-Pro-Tyr-Leu
MW: 530.6 g/mol

Skin Bioavailable Peptide Complex

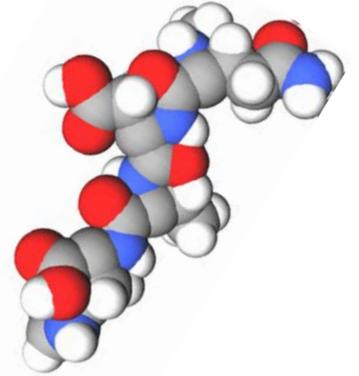
Dimethyl Isosorbide + Polysorbate 20

Acetyl Tetrapeptide-11

+

Acetyl Tetrapeptide-9

for quick and visible wrinkle reduction and skin firming

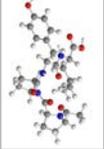


N-Acetyl-Gln-Asp-Val-His
MW: 539.5 g/mol

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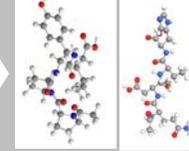
Replexium® *In vitro* efficacy tests - Summary



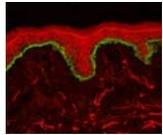
Acetyl Tetrapeptide-11



Acetyl Tetrapeptide-9

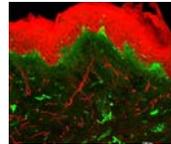


Acetyl Tetrapeptide-11
& Acetyl Tetrapeptide-9



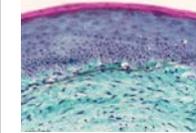
EPIDERMIS & DEJ

Syndecan-1 synthesis
Collagen XVII synthesis



DERMIS

Lumican synthesis
Collagen production



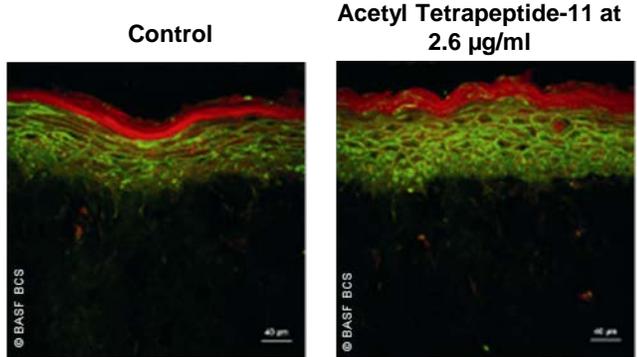
3D SKIN MODEL

Extracellular matrix network
on a 3D Bioprinted skin

**Stimulation of key dermal and epidermal components
by these 2 peptides**

Effect of Acetyl Tetrapeptide-11

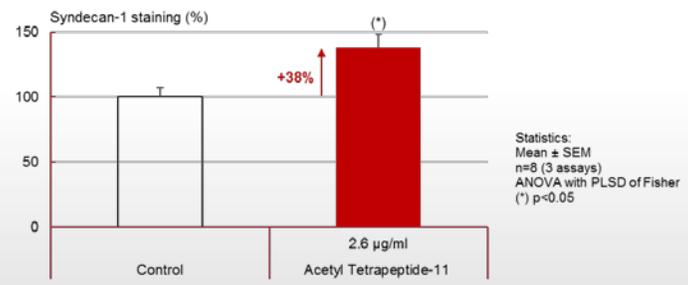
Syndecan 1



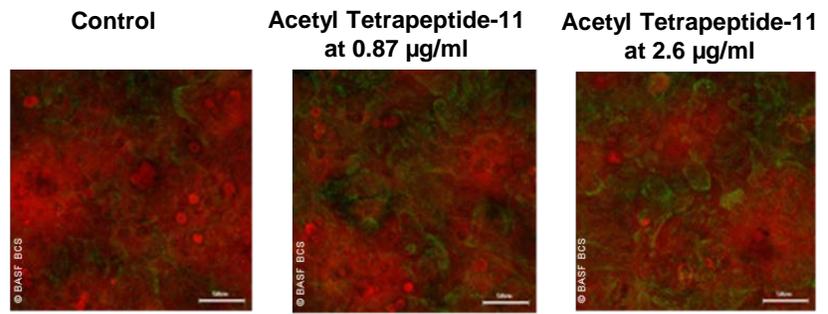
Syndecan-1 revealed in green

Method

Reconstructed full thickness skin
↓ 1 day
Acetyl Tetrapeptide-11
↓ 9 days
Cross-sections, then quantification of Syndecan-1 by IHC and image analysis



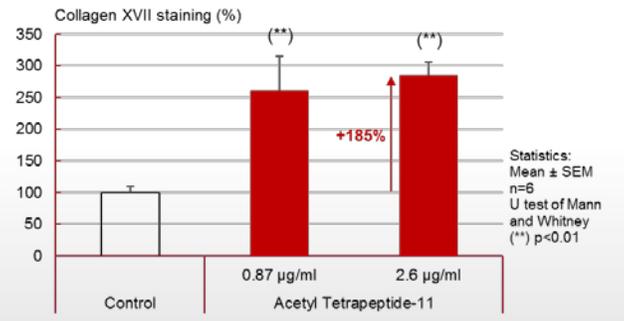
Collagen XVII



Collagen XVII revealed in green

Method

Seeding of human epidermal keratinocytes
↓ 2 days
Acetyl Tetrapeptide-11
↓ 3 days
Quantification of collagen XVII by ICC and image analysis



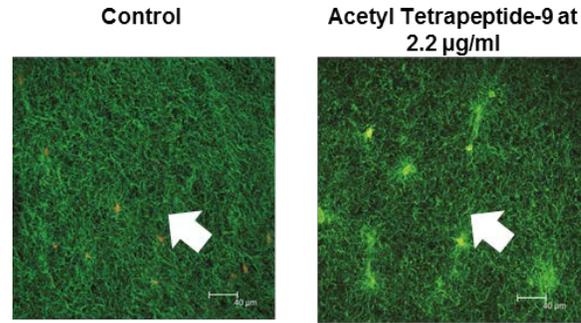
Acetyl Tetrapeptide-11 increases Syndecan-1 and Collagen XVII synthesis in reconstructed skin and keratinocytes, respectively.

Effect of Acetyl Tetrapeptide-9

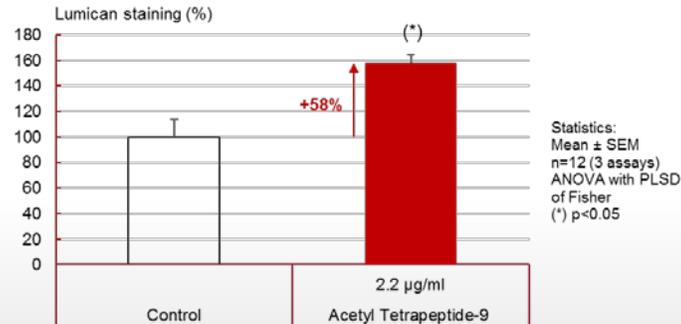
Lumican

Method

Pseudo dermis (fibroblasts in collagen lattices)
In vitro induced fibroblast aging (>15 passages) + Collagen I + Acetyl Tetrapeptide-9
↓ 6 days
Cross-sections, then quantification of Lumican by ICC and image analysis



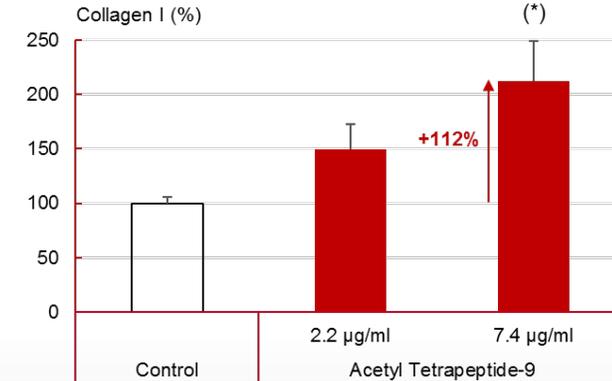
Lumican revealed in green



Collagen I

Method

Seeding of human fibroblasts
↓ 3 days
Acetyl Tetrapeptide-9
↓ 4 days
Quantification of Collagen I by DOT-BLOT



Statistics:
Mean ± SEM
n=3 (3 assays in triplicate)
Student t test
(*) p<0.05

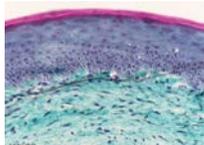
Acetyl Tetrapeptide-9 increases Lumican and Collagen I synthesis in pseudo-dermis and fibroblasts, respectively.

Effect of the Complex of the 2 Peptides Extracellular Collagen Fiber Network



Method

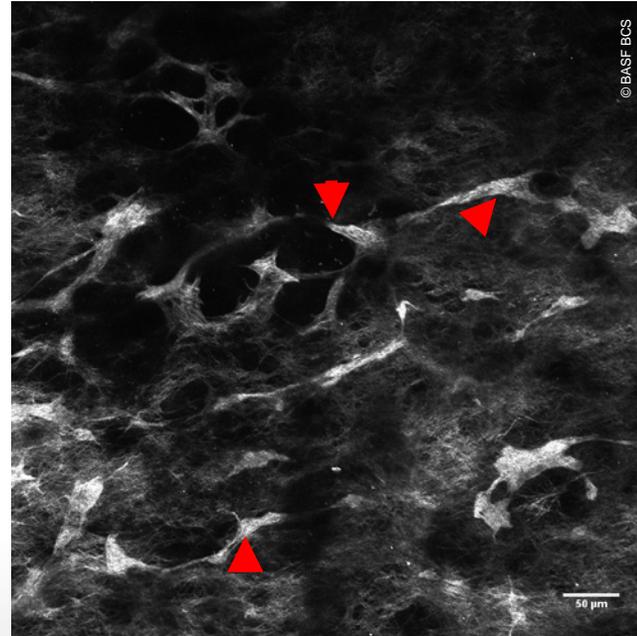
Reconstructed 3D bioprinted skin



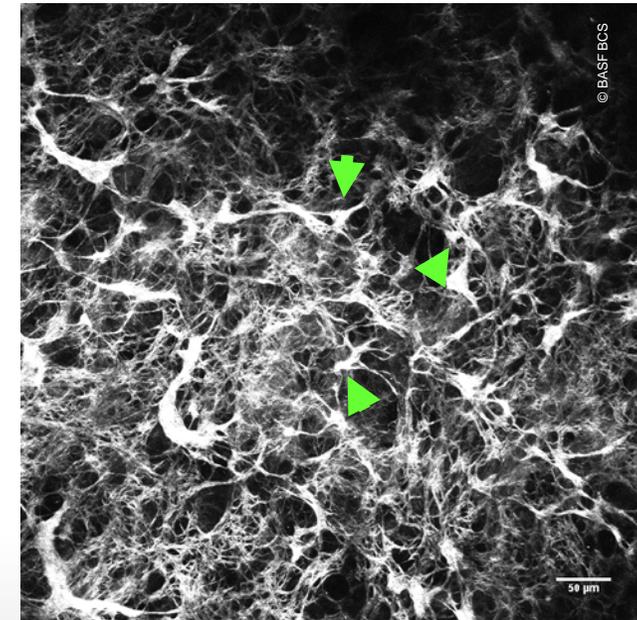
Daily treatment
15 days

Confocal microscopy associated with a multiphoton laser to generate a 2nd harmonic signal specific to fibrillar collagen

Image acquisition in depth to create a 3D stack (10 planes) of the upper part of dermis



Control



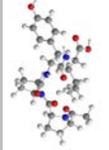
Acetyl Tetrapeptide-9 (7.3 μg/ml) and
Acetyl Tetrapeptide-11 (9.8 μg/ml)

The peptide complex improves the density and organization of the extracellular collagen fibers in the dermis of 3D bioprinted skin

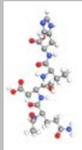
In the untreated control condition, the fibers are small and not well-defined, with a blurry network (red arrows).
When treated with the two peptides, the network is well-defined and very intense collagen fibers (green arrows).

Replexium®

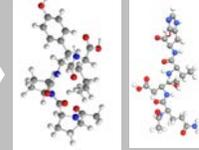
In vitro key results - Summary



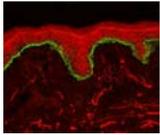
Acetyl Tetrapeptide-11



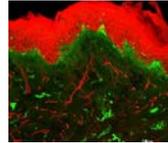
Acetyl Tetrapeptide-9



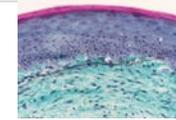
Acetyl Tetrapeptide-11
& Acetyl Tetrapeptide-9



- **38%** increase in **syndecan-1** levels in reconstructed skin
- **185%** increase in **collagen XVII** levels in keratinocyte cultures



- **58%** increase in **lumican** levels in pseudo-dermis
- **112%** increase in **collagen I** levels in fibroblast cultures



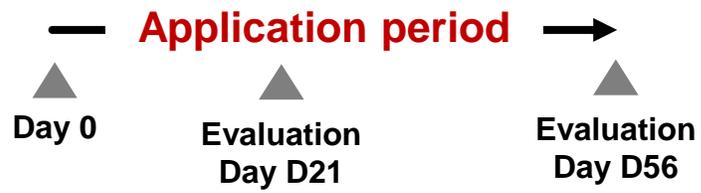
- Improves the **density** and **organization** of the extracellular collagen **fibers** in 3D bioprinted skin

Stimulation of key dermal and epidermal components by the 2 peptides

Replexium® Clinical Study Design



Replexium® at 2%  Peptide-blend benchmark at 3%



Method

Volunteer panel:

- Female volunteers, Fitzpatrick skin types I, II, III
- 45-65 years old
- Visible crow's feet and forehead wrinkles, nasolabial folds
- Low dermal density and considering themselves to have lost skin elasticity and firmness

Test products*:

- Emulsion with **2% Replexium®**
- Emulsion with **3% Peptide-benchmark**

*Content in DMI and Polysorbate 20 has been adjusted between the 2 formulations.

Application:

- Randomized, split face, twice daily for 56 days

Time points:

- D0, D21, D56

Evaluation:

- Wrinkle ranking from Visia images
- Dermal density by ultrasounds on the cheeks

DAY 0

DAY 21

DAY 56

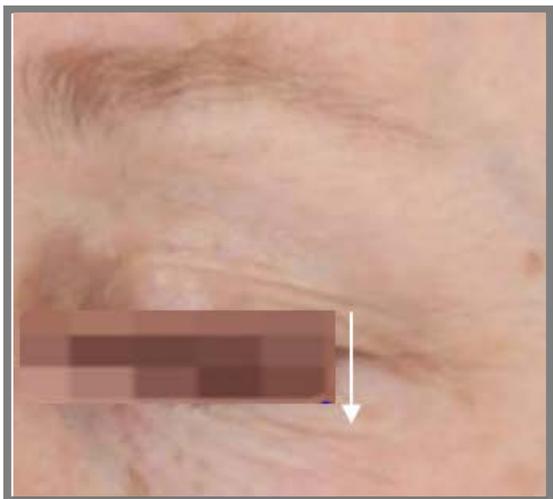


FOREHEAD



Panelist 1

CROW'S FEET



Panelist 2

NASOLABIAL

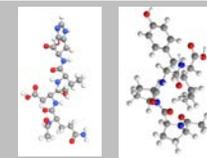


Panelist 3

Visible efficacy on wrinkles within 21 days, with improvement at 56 days

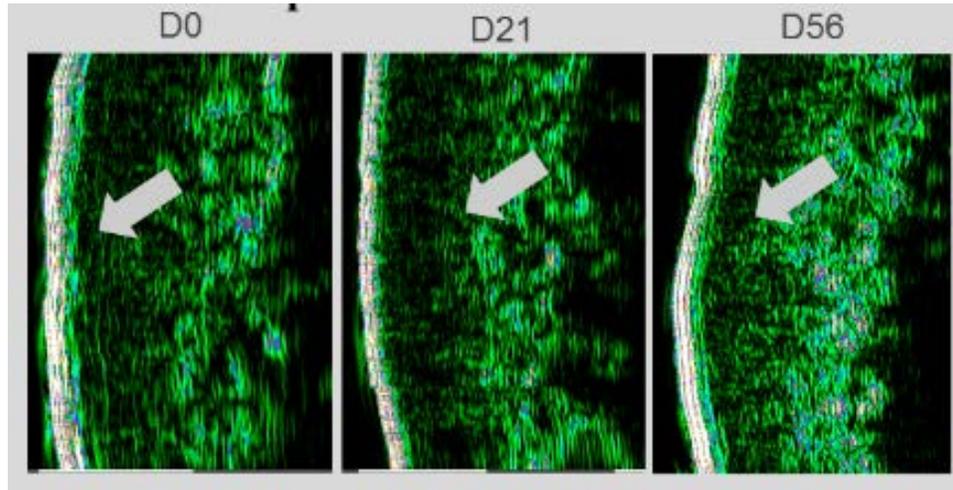
- Efficacy as early as day 21 (-11%) and improves over time (-23% at D56)
- As good as the Peptide-blend benchmark

Replexium® Impact on Dermal Density

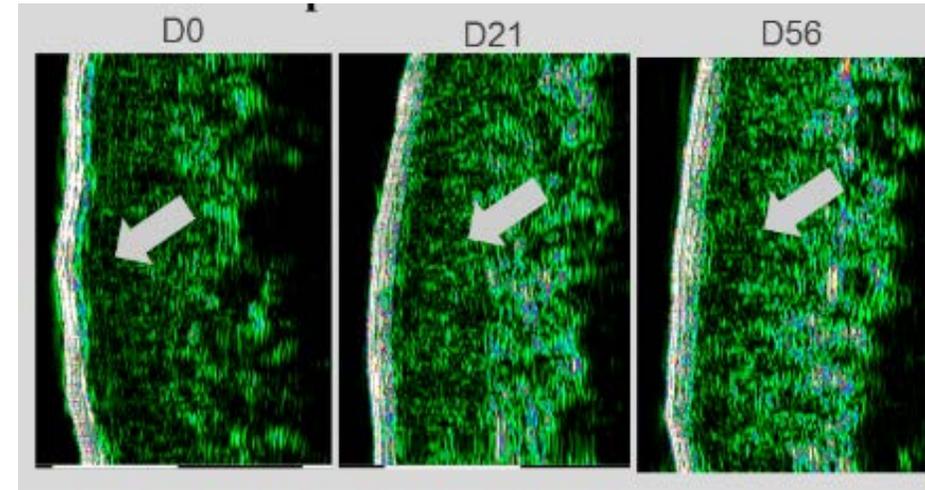


Replexium®

Peptide-blend benchmark



Replexium®

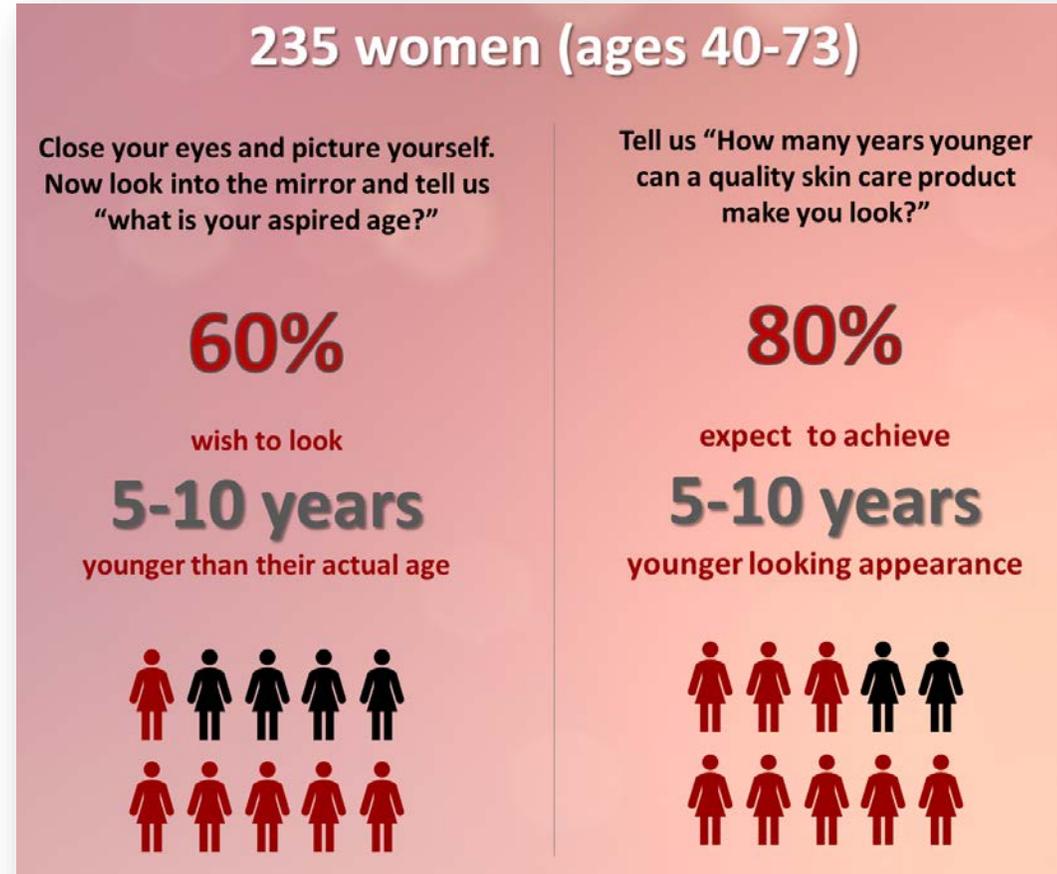


Changes in dermal density (green pixels) over time

- **Faster firming effect in 21 days with Replexium® not observed with Peptide-blend benchmark**
- **Estimated from evaluation of influence of age on dermal density, 21% improvement within 3 weeks with Replexium® corresponds to 7 years firmer skin in 21 days**

Consumers have high expectation from quality skincare products

Replexium®
**Gain 7 years*
younger, firmer skin
in 3 weeks**



BASF Consumer survey

Meet Consumer Expectations with Replexium®

* Dermal density gain at D21 comparable to a 7 years younger and firmer skin estimated from the evaluation of influence of age on dermal density

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Replexium® Achieve your beauty aspiration

IN VITRO STUDIES

- + 38%** Syndecan levels in reconstructed skin
- + 185%** Collagen XVII increase by keratinocytes
- + 58%** Lumican levels in pseudo dermis
- + + +** Collagen I increase in reconstructed bioprinted skin

IN VIVO STUDIES

- 11%** Wrinkle reduction at day 21
- 23%** Wrinkle reduction at day 56
- + 21%** Fast skin firming at day 21
(Faster than peptide benchmark)



Gain 7 years* firmer skin in 21 days with visible wrinkle reduction

* Estimated from the evaluation of influence of age on dermal density

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Replexium® key claims

**Gain 7 years of
firmer younger
skin in 21 days**

**Skin
Bioavailable
peptide
complex**

**Visible
reduction of
wrinkles in 21
days**

**Skin firming
faster than
peptide
benchmark**

**Active for high
performance
dermocosmetic**

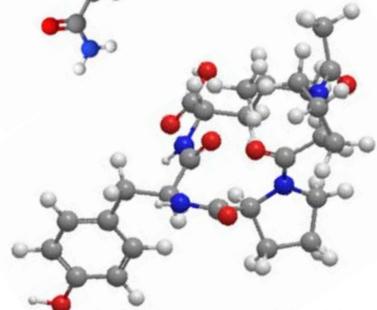
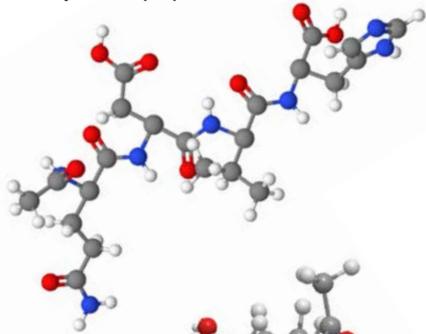
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Replexium® BC10091

Acetyl tetrapeptide-9



Acetyl tetrapeptide-11

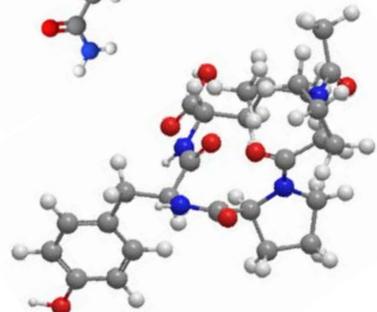
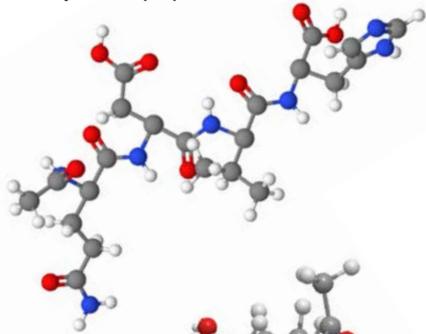
Replexium® peptides

Replexium®	BC10091												
Description	Skin-bioavailable synergistic complex of 2 peptides												
INCI	Dimethyl Isosorbide (and) Polysorbate 20 (and) Water (and) Acetyl Tetrapeptide-11 (and) Acetyl Tetrapeptide-9												
CAS No.	5306-85-4; 9005-64-5; 7732-18-5; 928006-88-6; 928006-50-2												
Composition 100%	Dimethyl Isosorbide: 35-45%; Polysorbate 20: 35-45%; Acetyl Tetrapeptide-11: 525-825 ppm; Acetyl Tetrapeptide-9: 350-650 ppm; Water: sqf 100%												
Preservatives	none												
Appearance	Syrupy liquid from pale yellow to yellow, with characteristic odor.												
Solubility	Soluble in water, insoluble in oils and fats												
Use level	2%												
Regulatory data	<table border="1"> <thead> <tr> <th>PCPC</th> <th>IECSC</th> <th>IECIC 2015</th> <th>REACH</th> <th>JP cosmetics</th> <th>QD additive</th> </tr> </thead> <tbody> <tr> <td>✓</td> <td>On going</td> <td>✓</td> <td>✓</td> <td>✓</td> <td>X</td> </tr> </tbody> </table>	PCPC	IECSC	IECIC 2015	REACH	JP cosmetics	QD additive	✓	On going	✓	✓	✓	X
PCPC	IECSC	IECIC 2015	REACH	JP cosmetics	QD additive								
✓	On going	✓	✓	✓	X								



Replexium® PW BC10082

Acetyl tetrapeptide-9



Acetyl tetrapeptide-11

Replexium® peptides

Replexium®	PW BC10082												
Description	Synergistic complex of 2 peptides												
INCI	Mannitol (and) Acetyl Tetrapeptide-11 (and) Acetyl Tetrapeptide-9												
CAS No.	69-65-8; 928006-88-6; 928006-50-2												
Composition 100%	Acetyl Tetrapeptide-11: 1050-1650 ppm; Acetyl Tetrapeptide-9: 700-1300 ppm; Mannitol: sqf 100%												
Preservatives	none												
Appearance	White to off-white fine homogeneous powder, with characteristic odor.												
Solubility	Soluble in water, insoluble in oils and fats												
Use level	1%												
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Replexium®

Stability & Formulation



Storage conditions

Shelf life: **2 years**
Storage temperature:
10-30°C
Store protected from
heat and light



Formulation method

Add during the final
process **below 40°C**,
or at room
temperature for cold
processing.
(pH: **4-8**)



Replexium® BC10091
Replexium® BC10091 at 2% in a lotion
Replexium® BC10091 at 2% in cream

Use level: **2%**



Powder form
Replexium®
PW BC10082

Use level: **1%**



- SWOP® Treatment Formula Powered With Replexium®



- Correct + Protect Primer With Replexium®



- Rapid Wrinkle Repair Firming Cream With Replexium®

Replexium® and other BASF products

Information can be obtained on

- **BASF Product Finder (on carecreations.basf.com)**
- **UL prospector**

Contact us

Email: bioactives.northamerica@basf.com

Phone: +1 (800) 962 7831

Replexium®

ACHIEVE YOUR BEAUTY ASPIRATION

Fast-Acting, Bioavailable Peptide
Complex to Address Skin Aging



Regain 7 Years' Younger Skin

- Visible reduction of wrinkles at Day 21, with further improvement at Day 56
- Significant improvement in dermal density at day 21, much faster than peptide benchmark
- Corresponds to bringing 7 years of firmness back to your skin in 21 days

Learn more at [CareCreations.basf.com/Replexium](https://www.CareCreations.basf.com/Replexium)

 **BASF**
We create chemistry

Care
Creations™

Other BASF Launches at Supplier's Day

- Soul Beauty Compass - a revitalizing 12 step skin and hair regimen
- Style without guilt – a 3 formulation hair-care concept, focusing on healthy hair without any damage

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We create chemistry

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Creations™