



# SkinMedica: Bioengineering Heritage and Future of Ground Breaking Ingredients

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# TNS<sup>®</sup> Tissue Nutrient Solution



# What is TNS?

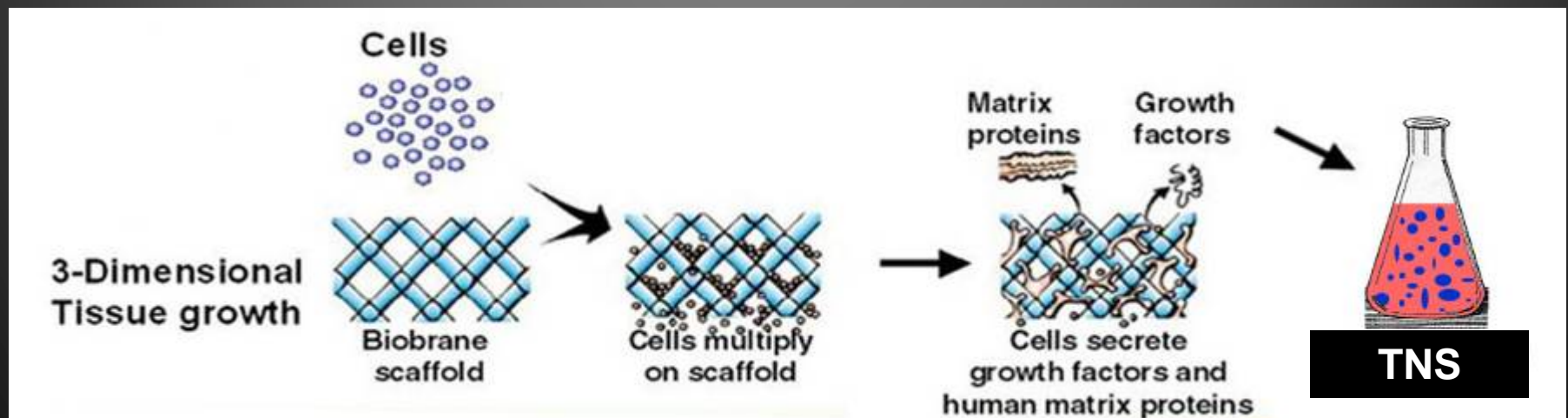
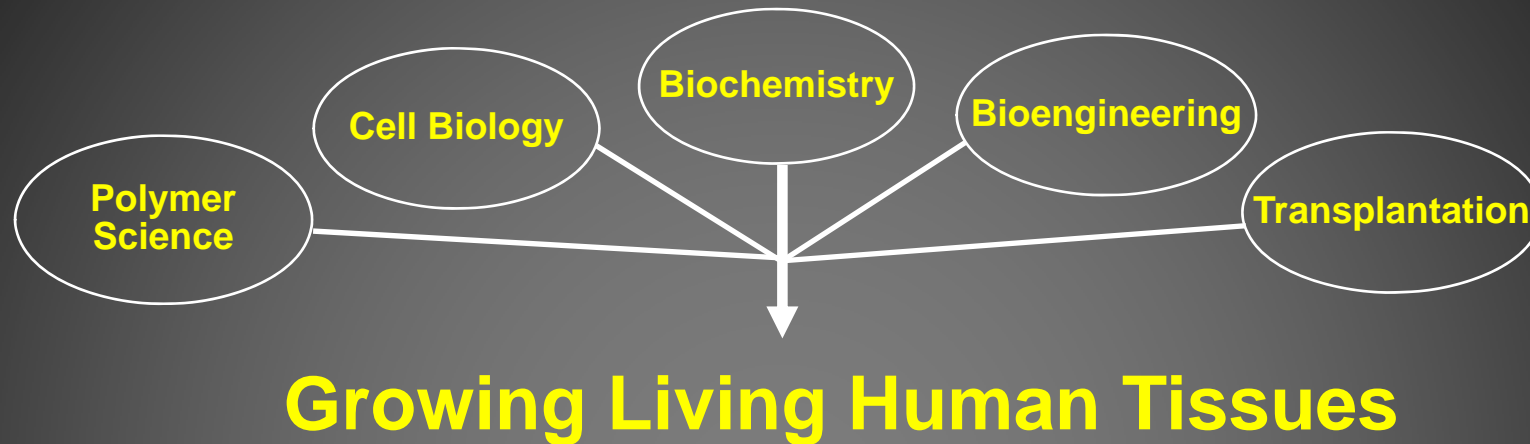
- ❖ INCI Registered Cosmetic Ingredient:  
**Human Fibroblast Conditioned Medium**
  
- ❖ Source: Neonatal foreskin fibroblasts cell bank
  - Single foreskin donation used to develop a cell banks used for commercialization of multiple FDA-approved products
  - TransCyte and Dermagraft wound-healing
  - Cosmoderm and Cosmoplast facial fillers
  
- ❖ Spent tissue culture medium used to grow fibroblast is collected and concentrated

# What makes TNS so valuable?

- ❖ TNS Recovery Complex
  - 93.6% TNS
  - Retail: \$172 / 0.65 Oz
- ❖ TNS Essential Serum
  - Side 1: 93.6% TNS
  - Side 2: Antioxidant blend
  - Retail: \$ 270 / 1.0 Oz
- ❖ Significant Revenue Contribution

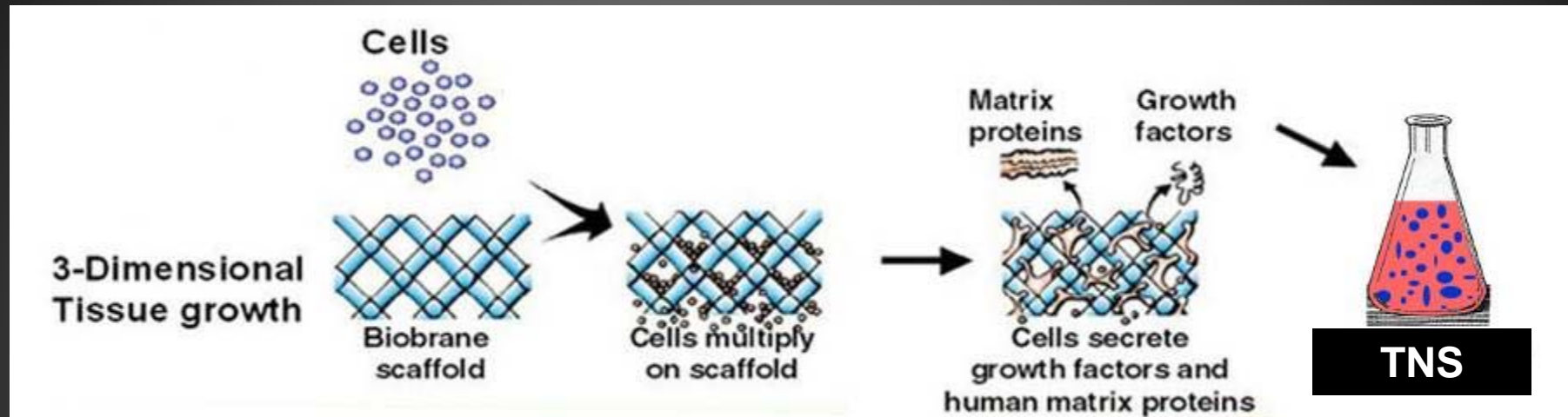


# TNS Manufacturing Process





# Manufacturing of TNS



- ❖ Cells from cell banks grow on a 3-dimensional scaffold
- ❖ Collagen and extra-cellular matrix are produced
- ❖ Growth factors and other essential proteins are secreted into medium.
- ❖ Growth factors levels are 4000 to 40000-fold higher than a 2-dimensional process
- ❖ Secreted growth factors are concentrated and stabilized to make TNS

# Physiologically Balanced Composition

❖ Optimal ratio and levels of fibroblast derived human growth factors for extracellular matrix production

❖ At least 110 growth factors, cytokines and other active proteins identified

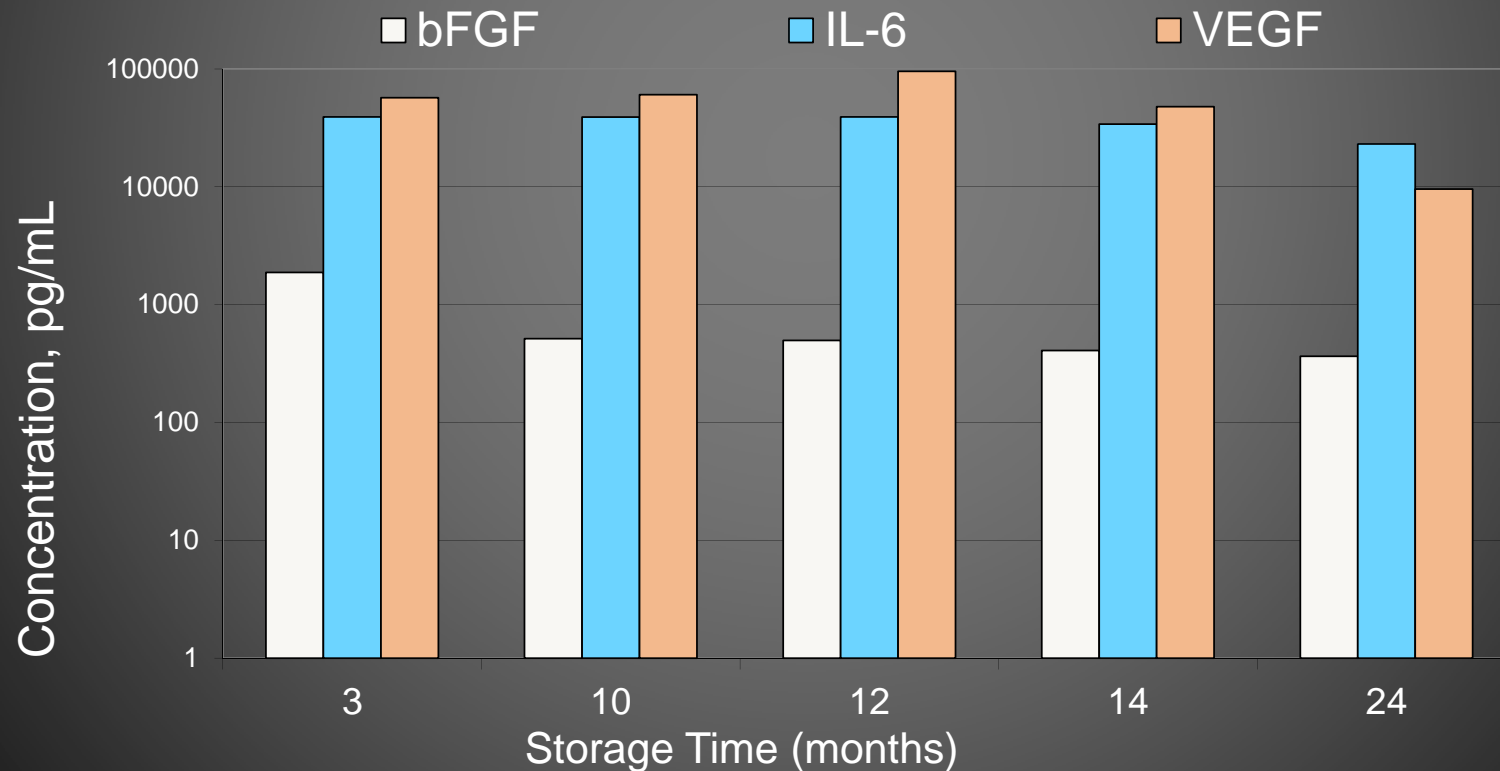
**TABLE 1.**

Partial list of growth factors and cytokines identified in active gel and their function in skin.

Ref	Growth Factor/Cytokine	Skin-related Functions
11	Fibroblast growth factors: bFGF (FGF-2), FGF-4, FGF-6, KGF (FGF-7), FGF-9	Angiogenic and fibroblast mitogen
12	Hepatocyte growth factor: HGF	Strong mitogenic activities; 3 dimensional tissue regeneration and wound healing
13	Platelet derived growth factors: PDGF AA, PDGF BB, PDGF Rb	Chemotactic for macrophages, fibroblasts; macrophage activation; fibroblast mitogen, and matrix production
14	Insulin-like growth factors: IGF1, IGFBP1, IGFBP2, IGFBP3, IGFBPw	Endothelial cell and fibroblast mitogen
15	Transforming growth factor: TGFβ1, TGFβ2, TGFβ3	Keratinocyte migration; chemotactic for macrophages and fibroblasts
16	Tissue inhibitor of metalloproteinases: TIMP1 (MPI1), TIMP2 (MPI2)	Prevent enzymatic degradation of collagen and hyaluronic acid
17	Vascular endothelial growth factor: VEGF	Influence vascular permeability and angiogenesis to improve tissue nutrition
18	Placenta growth factor: PLGF	Promote endothelial cell growth
19	Bone morphogenetic protein: BMP7	Promote development of nerve cells in developing tissue
20	Interleukins: IL-1α, IL-1β	Early activators of growth factor expression in macrophages, keratinocytes and fibroblasts
21	Interleukin: IL-2	Enhance epithelial wound healing
22	Interleukin: IL-6	Mediator of acute phase response to wound and has synergistic effect with IL-1
23	Interleukin: IL-10	Inhibits pro-inflammatory cytokines to reduce inflammation prevents scar formation
24	Interleukin: IL-4, IL-13	Stimulate production of IL-6
25	Interleukin: IL-3, IL-4, IL-5	Leukocyte maturation and degranulation during inflammatory phase
25	Interleukins: IL-7, IL-8, IL-15	Leukocyte activation and proliferation during inflammatory phase
26	Leptin	Epidermal keratinocyte proliferation during wound healing
27	Colony stimulating factors: G-CSF, GM-CSF, M-CSF	Stimulate the development of neutrophils and macrophages

# Stability of Growth Factors

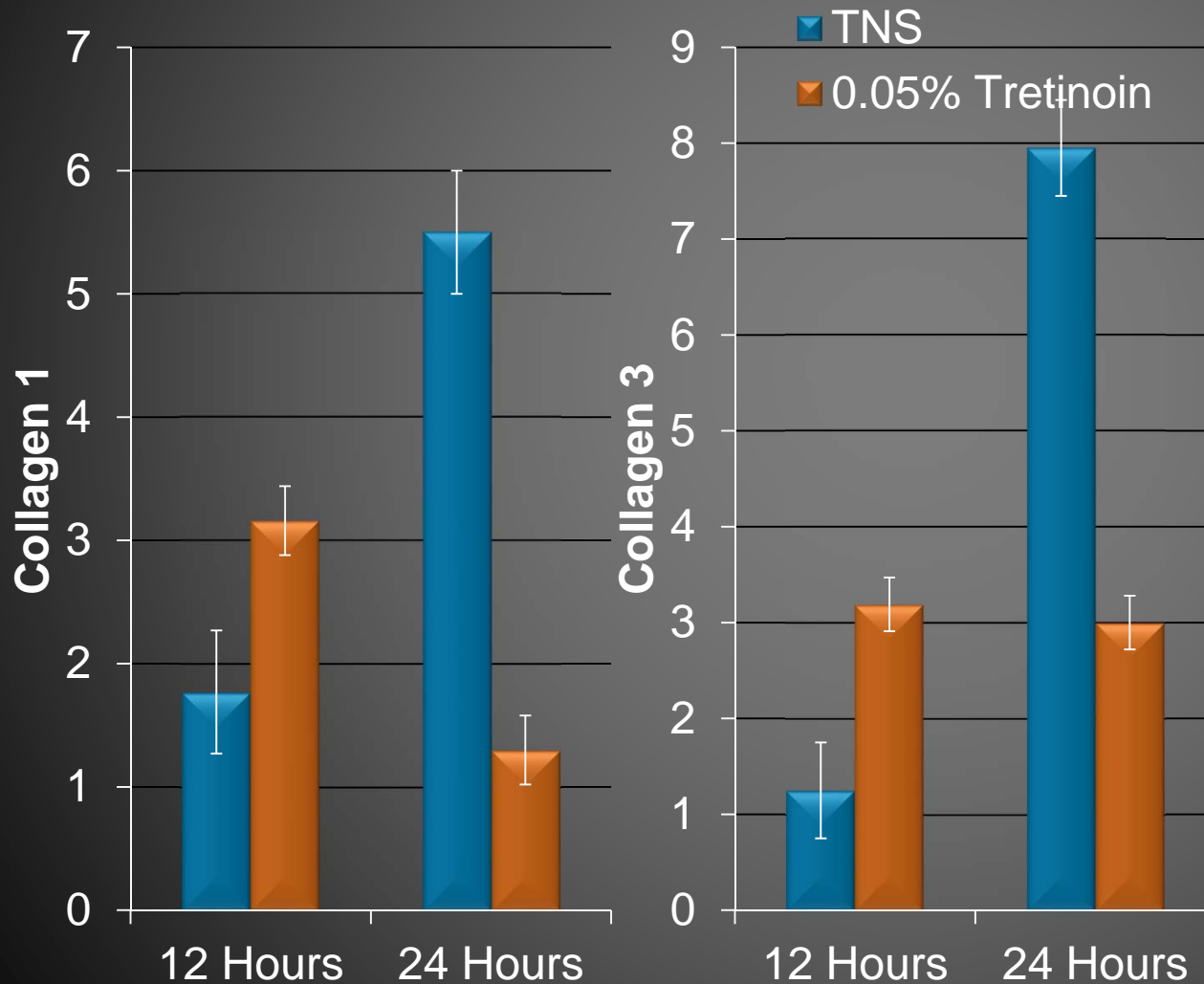
- ◇ ELISA assay shows that Growth Factors and Cytokines are present at high levels in TNS stored at room temperature for 24 months.





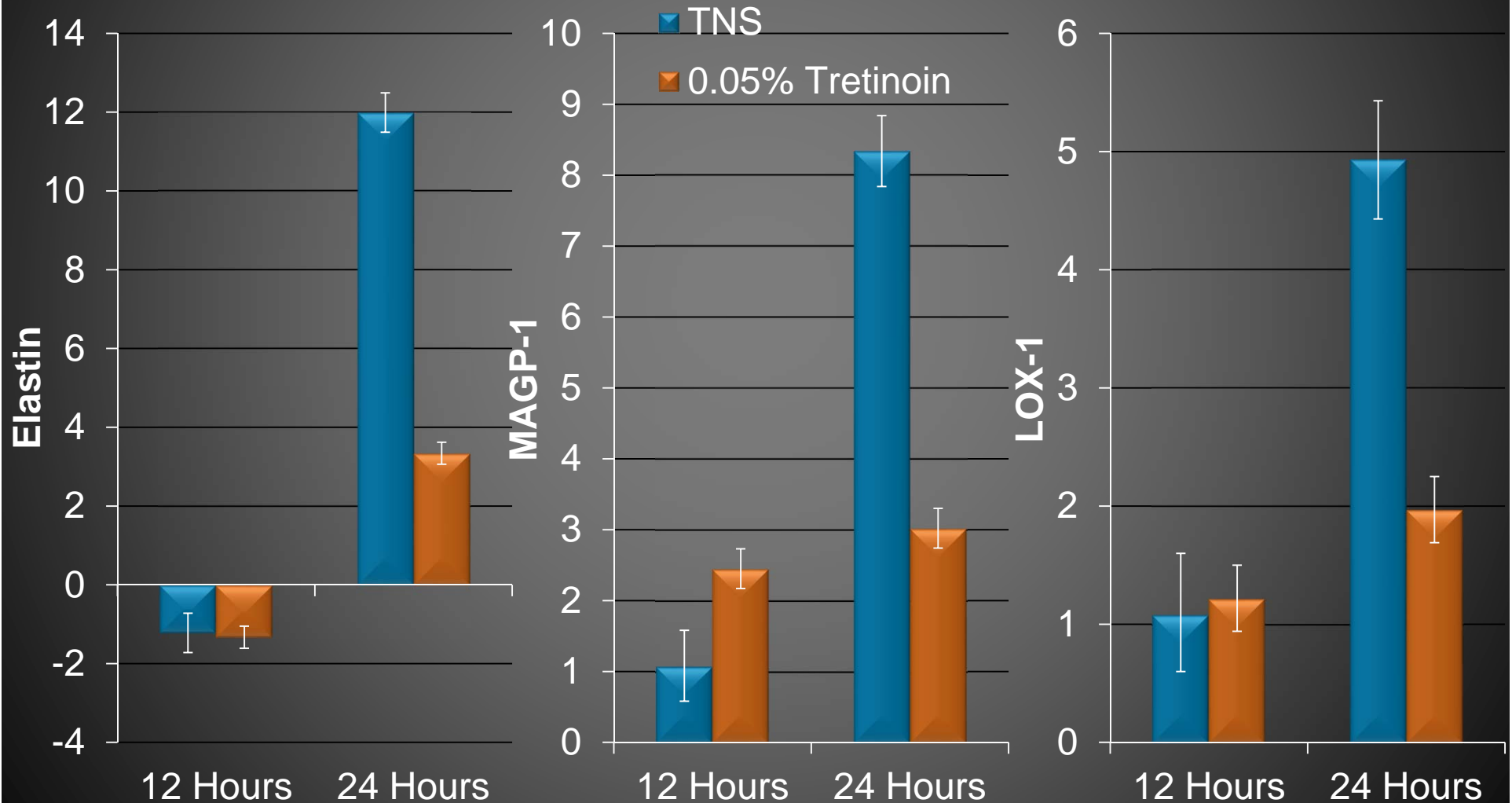
# Collagen 1 and 3: Gene Expression

## EpiDerm-FT Human Skin Model



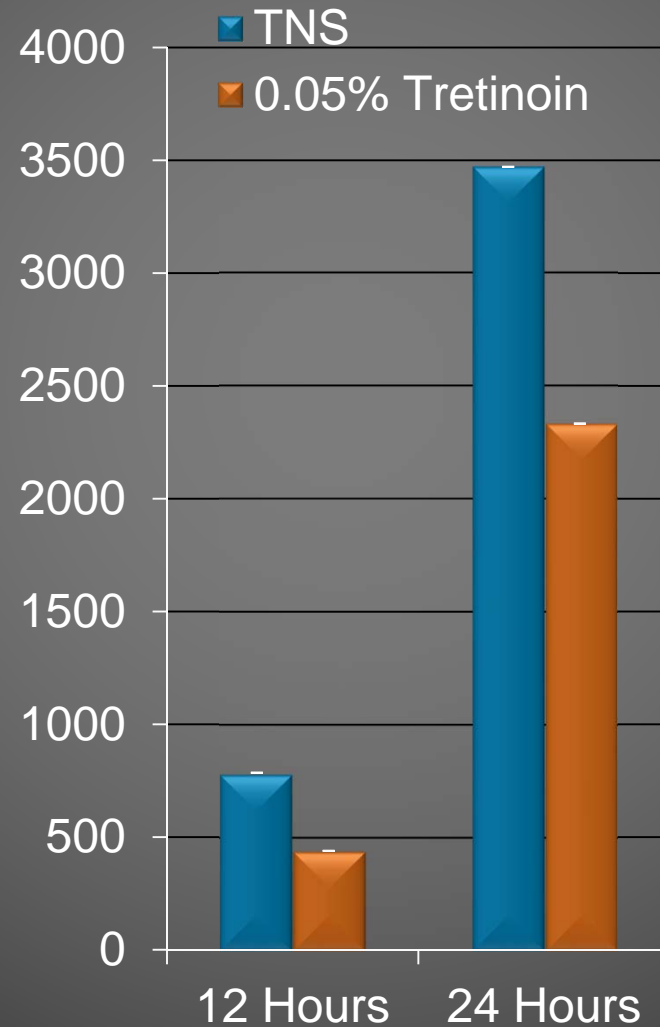
# Elsatin & Related Proteins: Gene Expression

## EpiDerm-FT Human Skin Model



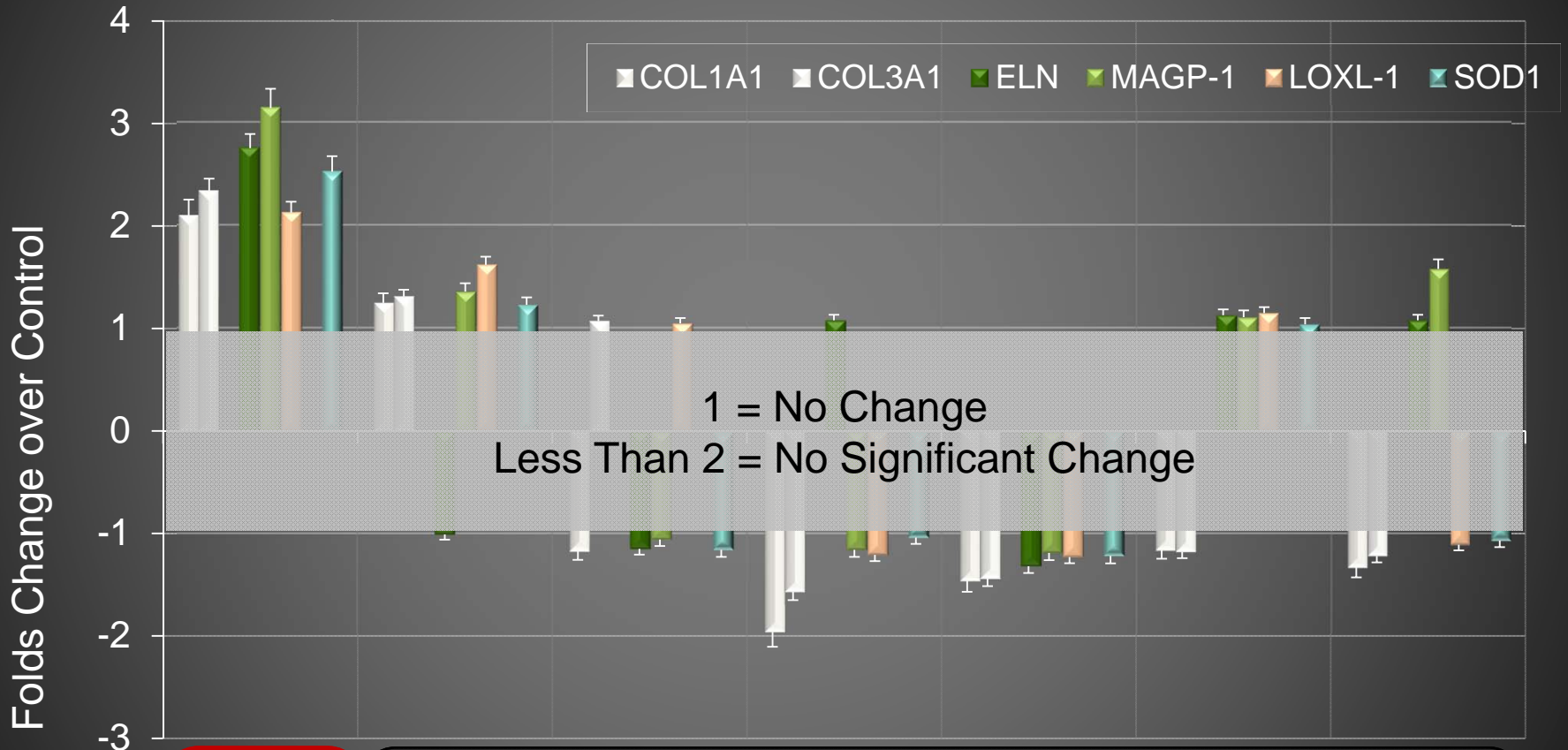
# Hyaluronic Acid: Concentration in Media

## EpiDerm-FT Human Skin Model



# Effect of “Growth Factors” Products on Aging Genes

## EpiDerm-FT Human Skin Model



**TNS  
Recovery  
Complex**

Neocutis Bioserum  
Obagi Regenica  
ZO Skin Health Ossential  
Jan Marini A. I. R. Booster  
Priori Cellular Recovery  
Peau Magnifique Youth Recruit

## Summary of Clinical Studies: TNS Recovery Complex

- ❖ Statistically significant improvements in multiple photodamage parameters
- ❖ Efficacy superior to placebo/vehicle and moisturizing skin care regimens
- ❖ Superior in subjective and objective evaluations
- ❖ Validated with positive structural changes in skin
- ❖ Excellent patient satisfaction: 93% desire to continue use

*Journal of Cosmetic  
and Laser Therapies*

Fitzpatrick and Rostan  
4:25-34, 2003

*Dermatologic Therapy*

Mehta and Fitzpatrick  
20:350-359, 2007

*Journal of Drugs in  
Dermatology*

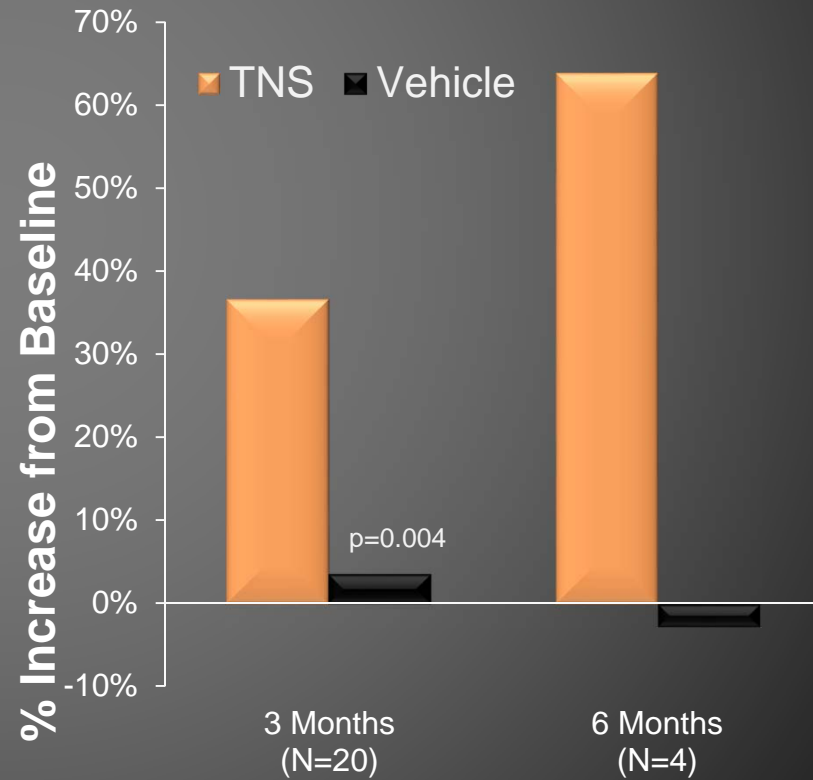
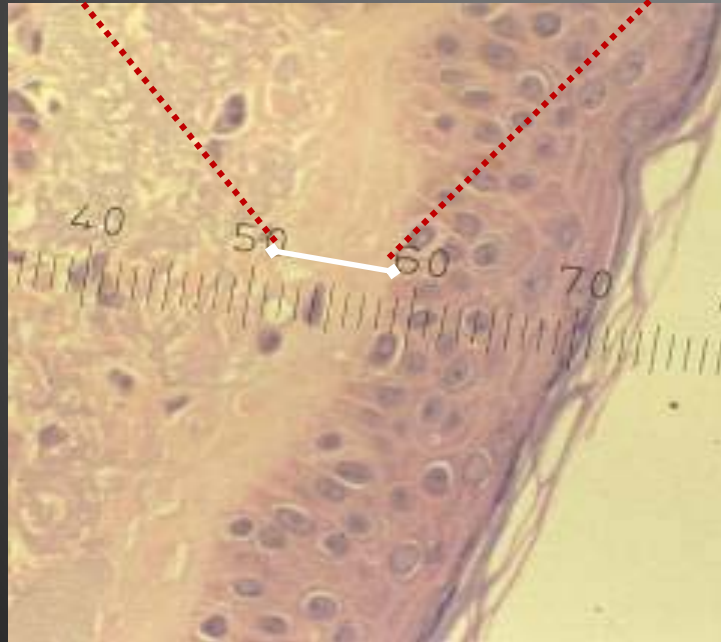
Mehta et al.  
7:864-871, 2008



# TNS<sup>®</sup> Increases Collagen Synthesis

## Thickness of Grenz Zone Collagen from Biopsy

**Grenz Zone: Outermost dermal layer where new collagen synthesis is first visible**



Fitzpatrick RE, Rostan EF. Reversal of photodamage with topical growth factors: a pilot study. *J Cosmet Laser Ther.* 2003;5(1):25-34.

Sundaram H, Mehta RC, Norine JA, et al. Topically applied physiologically balanced growth factors: a new paradigm of skin rejuvenation. *J Drugs Dermatol.* 2009;8(5SupplSkinRejuvenation): 4-13.

# Skin Surface Impression: Periorbital Area

**Baseline**



**6 Months**



**Female  
Age 63**

**Female  
Age 52**

**Female  
Age 62**

## Key Differentiating Benefit of Physiologically Balance Ingredients

- ❖ Provide all the necessary controlling functions for any given process instead of a single super-targeted function
- ❖ Consistent with how biological processes work through use of multiple redundant pathways of achieving same end-point
- ❖ Reduces need for identifying individual “actives” provided quality control can be achieved by other means
- ❖ Significantly lower carbon foot-print as extensive purification is eliminated

# Biometa™ – Working with Skin’s Own Actives



- ❖ In place of introducing external compounds to mask the signs of skin aging, Biometa Essential Serum™ unlocks one’s own anti aging potential.
- ❖ Biometa Complex™ has been shown to stimulate “key” proteins and genes within the skin that have been identified as being fundamental to the anti aging cascade; resulting in the improvement of all visible signs of aging

# What is Biometa™?

Starting  
Materials



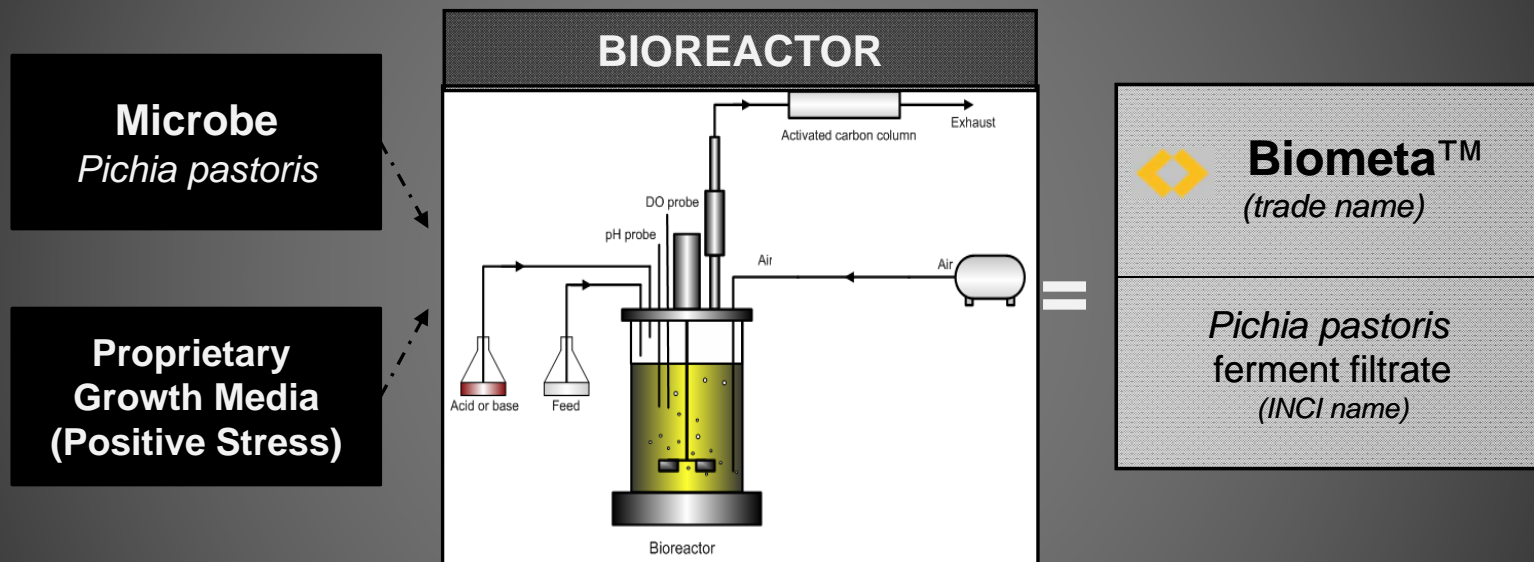
Proprietary  
Bio-Fermentation  
Process

*Pichia pastoris* fully  
metabolizes New Material



New Material

Synthesized  
NEW Ingredient



Using proprietary amino acids, proteins, vitamins and other key nutrients which induce a positive stress and metabolic energy to the *Pichia* to yield the ingredient; **Biometa™** (*Pichia pastoris* ferment filtrate).

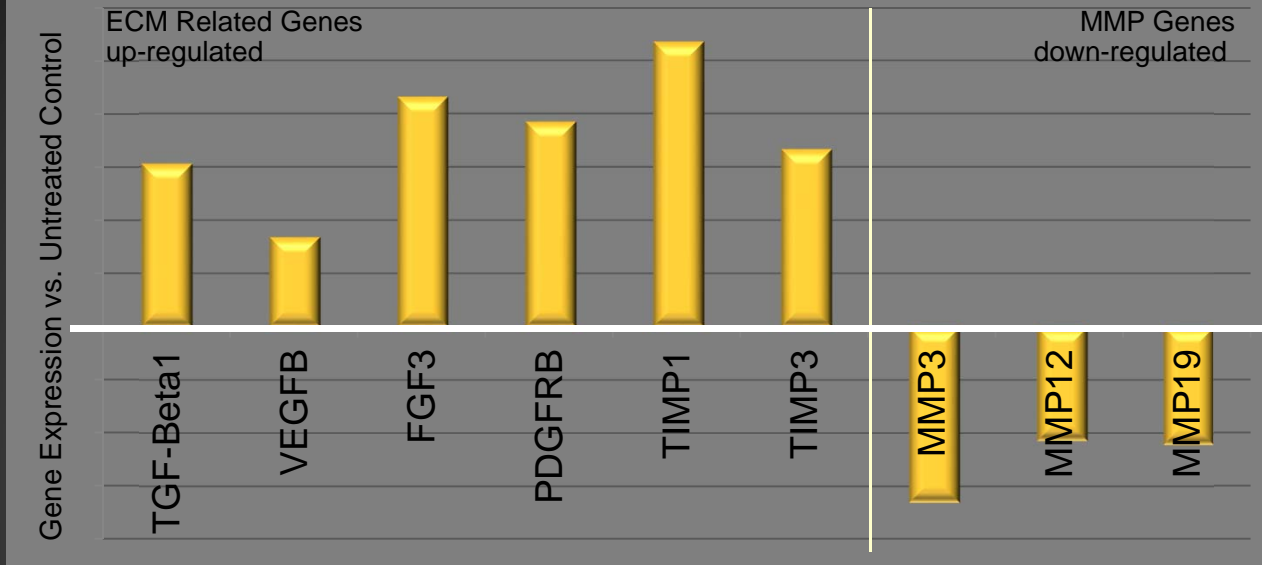


# How Does it Work?

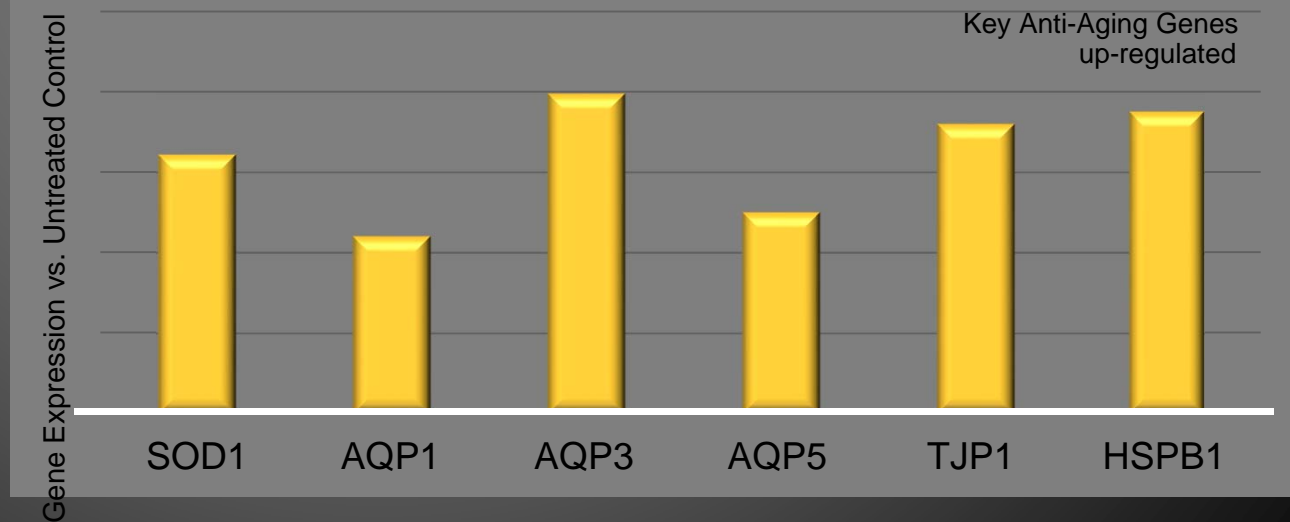
*In vitro* Gene Array: In cell culture, Biometax Complex modulates gene expression. Below are some of the key classes of genes that are up-regulated:

Gene	Function
AQP3	Hydration
COL12A1, COL15A1, Col 1A1, etc	Extracellular Matrix Proteins
TGF-Beta TIMP1 / TIMP3 VEGFA / VEGFb FGF3 PDGFRB IL10RB, IL11, IL8, etc.	Growth Factors and Cytokines involved in repair and ECM production
SOD1	Antioxidant
HSP	Anti-aging
TJP1/ ZO-1	Skin Barrier

### Biometa: Key ECM Genes



### Biometa: Other Key Genes



# Induction of Key ECM Proteins

Proprietary mixture shown to stimulate, express, and synthesize a number of “key” proteins (cytokines, growth factors, etc.) known to be involved in skin repair and remodeling including:

- ◆ bFGF: Fibroblast Growth Factor
- ◆ TIMP-1: Tissue Inhibitor of MetalloProteinases
- ◆ VEGF: Vascular Endothelial Growth Factor

Protein Array confirms gene expression data

## What's Next for SkinMedica?

- ❖ Greater need for multifunctional holistic ingredients that can only be derived from natural sources
- ❖ Fermentation with multiple micro-organism species to enhance “active” content
- ❖ Plant cell culture to improve supply stability and reduce environmental impact

Thank You!

