COSMECEUTICALS 2024
CHANGING THE FACE OF BEAUTY

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Ablon
Skin Institute & Research Center
For Dermatology and Laser Rejuvenation

Disclosures

none

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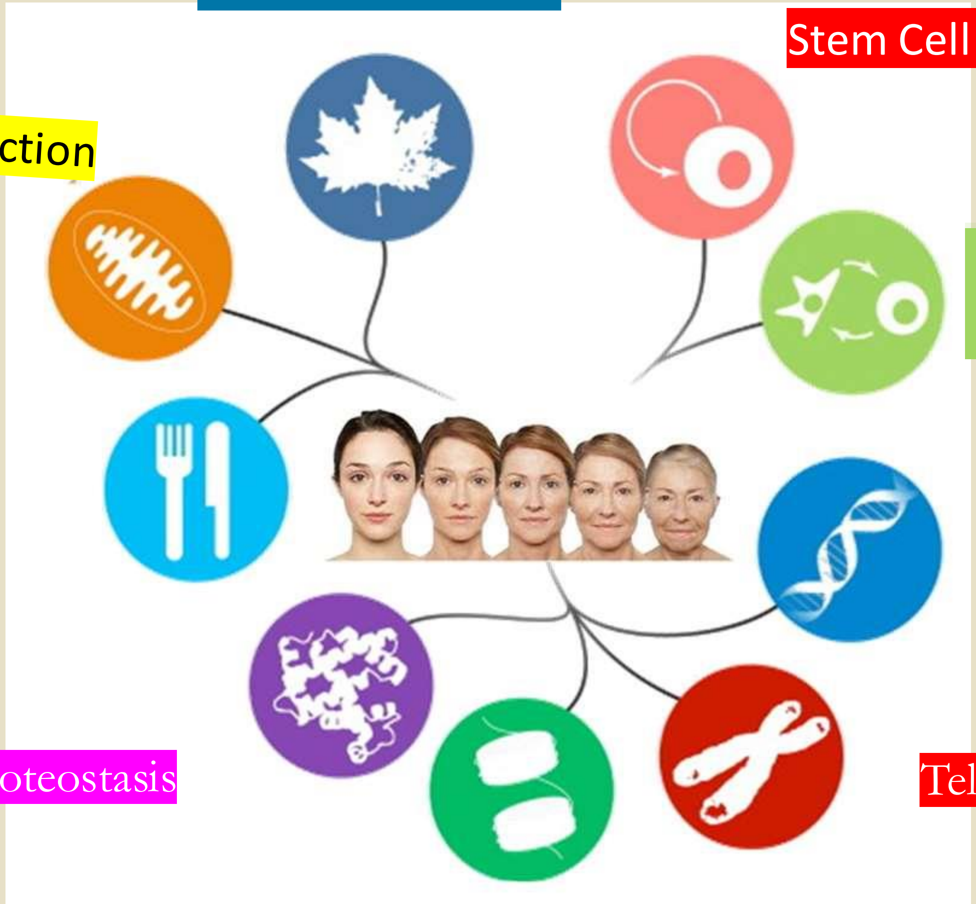
Cellular Senescence

Stem Cell Exhaustion

Mitochondrial Dysfunction

Altered Intercellular communication



Deregulated Nutrient Sensing

Genomic Instability

Loss of Proteostasis

Telomere Attrition

Epigenetic Alteration

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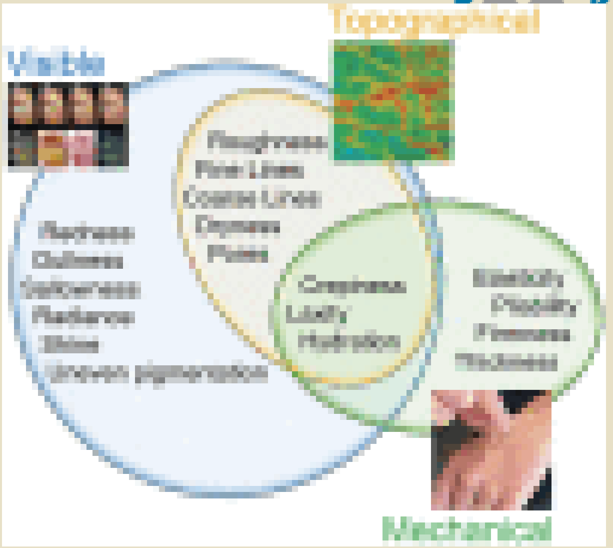
A. Expectations of Skin Care: Skin Quality Goals:



Visible

- Redness
- Dullness
- Sallowness
- Radiance
- Shine Uneven Pigmentation

Topographical

- Roughness
- Fine lines
- Coarse lines
- Dryness
- Pores
- Crepiness
- Laxity
- hydration

Mechanical

- Elasticity
- Pliability
- Firmness
- thickness

Humphreys et al. Defining Skin Quality: Clinical Relevance, Terminology And Assessment. *Derm Surg.* 2021 July;47(7):974-81

B. Back To Basics: Trends- Skinimalism

- Buying less, wearing less, using less
- Less makeup, cover up and more beneficial skincare for real change
- Embracing skin's appearance and enhancing it
- Using fewer products with multi-tasking ingredients
- Antioxidants, AHAs, botanicals, niacinamide, azelaic acid, retinol
- Hybrid products : sunscreens with AOXs, antiaging, skin lightening, prebiotics
- More sustainability, less waste
- Skincare specific for men

C. Top Global Concerns of Consumers: Avg monthly searches

Environmentally friendly	2,881,613
Reusable	5,314,973
Sustainable	22.098,457
Cruelty Free	1,130,325
Veganism	26,777,879

Kantar Report 2022 Beauty Trends

D. Solutions for Sustainability

- Reusable packaging
- Less plastic, use algae, bamboo
- Smaller packages, less paper packaging, no plastic wrap
- Safe and sustainable formulas, no sulfates, parabens, phthalates (clean beauty)
- Substitute single use products for multi use versions
- Anhydrous products less water, higher potency, longer shelflife, use less bulky packaging
- Multi-tasking ingredients: botanicals and marine algae
- Historical treatments like Aryveda

E. Focus on Ingredients: Multi tasking products

Spot & local Tx for acne, rosacea PIH

- Water,
- azelaic acid,
- salicylic acid,
- kaolin clay

Exfoliating, lightening serum

*Glycolic, lqctic and salicylic acid

*Mushroom extract

*arbutin

Sunscreen w/ AOXs & skin lighteners

- Niacinamide
- Ceramide
- prebiotics
- Sena alta leaf extract
- Thermal spring water
- Sunscreen ingred

Multi-Ingred Crm for photo-aged skin

- Retinol.
- B. Pilosa extract
- arbutin, TXA, olive leaves extract,
- ECM tripeptide,
- oligo galactomanmas
- sodium PCA,
- tocopheryl acetate

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F.Scientific Basis of Skincare:

- Growth Factors
- Peptides
- Antioxidants
- Mushroom Tyrosinase
- Cannabidiol
- Tretinoin/Retinoids
- Retinol/Retinaldehyde
- Exosomes
- Novel sunscreen

- FDA regulates products which alter structure and/or fn of skin; the CTFA [Cosmetic, Toiletry, & Fragrance Assoc] regulates marketing of things which improve appearance of skin, Revised 2022
- Fine balancing act between enough active ingred to work, but not to catch eye of stricter regulation
- More clinical trials being performed to show penetration of skincare, safety and efficacy

Growth Factors

- Naturally secreted cell-signaling proteins
- Interact with specific receptors on surface of skin cells
- Work locally to regulate cell activity for optimal tissue structure and fn
- Important in skin repair and remodeling
- Work synergistically within a complex network
- Production and level of GF decrease with age

Examples

- **Recombinant human growth hormone**
  - Mitogenic effect on keratinocytes and fibroblasts; increases insulin growth factor-1 and sebum prod. Cutaneous wound healing properties
- **Transforming growth factor α and β** :
  - GFs reversibly inhibit keratinocyte and leucocyte growth, promote keratinocyte migration, chemotactic for macrophages and fibroblasts. TGF-α has the highest human keratinocyte pro-motility activity, reach 80% activity in serum
- **PSP** (Skin-Cell Proteins):
  - Proprietary GFr and cytokine mixture extracted from cultured first trimester fetal human dermal fibroblasts in a moisturizing cream.
- **HSP70**(heat shock protein 70)
  - Protective effects against UV, apoptosis and ischemia; recommended for wound healing and anti-aging; inhibit aggregation and assist in the refolding of denatured proteins;reduce cellular damage by retaining the damaged proteins in soluble form, and binding to unfolded or misfolded proteins to assist in their proper refolding
- **Keratin**: major protein in structure of hair and skin; extracted from human hair or sheep's wool. Keratin's topical application can improve hydration and elasticity of the skin and hair.

Mori et al., Arch Dermatol Res 1998;290(3):158-162

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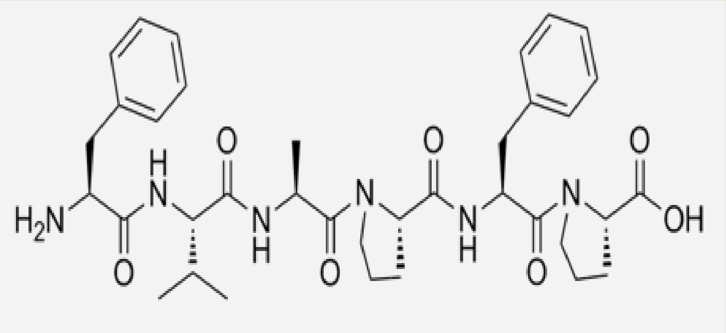
Peptides



- Peptides= 2-50 chains of Amino acids
- “500 Dalton Rule” <molecular weight needed to penetrate skin surface
- needed to make up proteins like collagen
- Derived from yeast, oat kernals, wheat, shellfish, eggs
  - Signal peptides
    - Stimulate matirix protein prod in general and collagen synthesis, stimul growth of skin cells and skin firbrolabasts
    - Increase elastin proteoglycan, GAGs and fibronectic
  - Enzyme inhibitor peptides(directly or indirectly inhib an enzyme)
    - Soybein protein, rice peptides
    - Slow collagen loss, moisturize
  - Carrier peptides-deliver Cu and Mn for woulnd healing and enzymatic process(matrixyl, copper peptides)
    - Facilitete delivery of bioactive moloecules into skin:
      - Support wound healing
      - Promote fibroblast growth, reduce wrinkles
  - Neurotransmitter-inhibitor peptides:
    - Inhib Ach release, pentapeptides 18 mimics catecholamine relaesae
    - Tripeptide mimics venom of temple viper (reduce muscle contraction by 82% after 2 hours of treatment)

Draelos. Cosmeceuticals: What's Real, What's Not. Dermatol Clin. 2019 Jan;37(1):107-115.
Skilirou. Hexapeptide-11 is a novel modulator of the proteostasis network in human diploid fibroblasts. *Redox Biol* 2015 Aug;5:205-15

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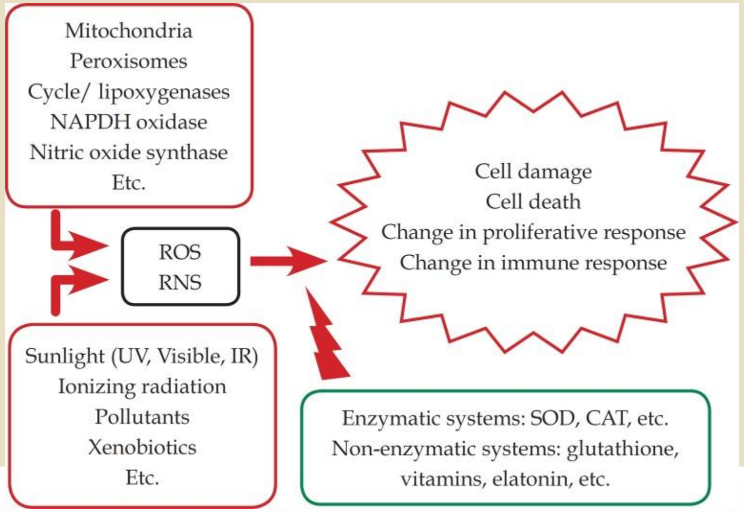
AntiOXidants

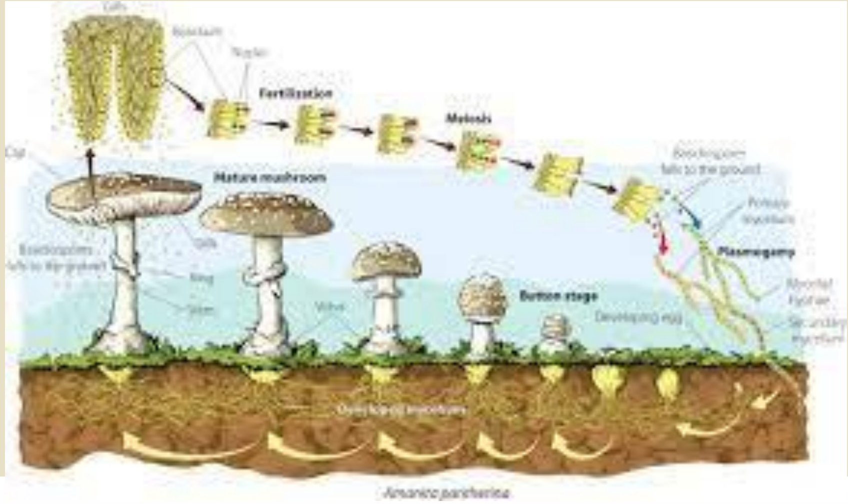
- Protect skin's surface from oxidative damage caused by free radicals, environmental aggressors (UV and pollution)
- Body's chemical rxns generate ROS(molecules that alter cutaneous homeostasis
- AOX neutralize these ROS or free radicals
- Polypodium leucotomas
- Vitamin C,E and ferulic=greater photoprotection against UV together
  - Reduce UV-induced cytokine mRNA expression
  - Added to sunscreen reduces upregulation of MMP-1 mRNA expression
  - Mix with chelating agents for more protection
- Resveratrol
- Co Q 10



Sunder. Relevant Topical **Skin Care Products** for Prevention and Treatment of Aging **Skin.**Sunder S.Facial Plast Surg Clin North Am. 2019 Aug;27(3):413-418.
Addor. Antioxidants in dermatology. *An Bras Dermtol.* 2017 May;92(3):356-62
Farris, Valacchi. UV light protection: Is it really enough? *Antioxidants* 2022 Aug;11(8): 1484

Mushroom tyrosinase

- Whitening agent
- Hard to reproduce activity in vivo
- Polyphenol oxidase, copper containing enzyme
- Reduce melanin content and production
- Replacement for hydroquinone



*Mann et al. Inhibition of Human Tyrosinase Requires Molecular Motifs Distinctively Different from Mushroom Tyrosinase. J Invest Dermatol. 2018 Jul;138(7):1601-8
*Lee et al. Glucose Exerts an Anti-Melanogenic Effect by Indirect Inactivation of **Tyrosinase** in Melanocytes and a Human **Skin** Equivalent. Int J Mol Sci. 2020 Mar 3;21(5):1736

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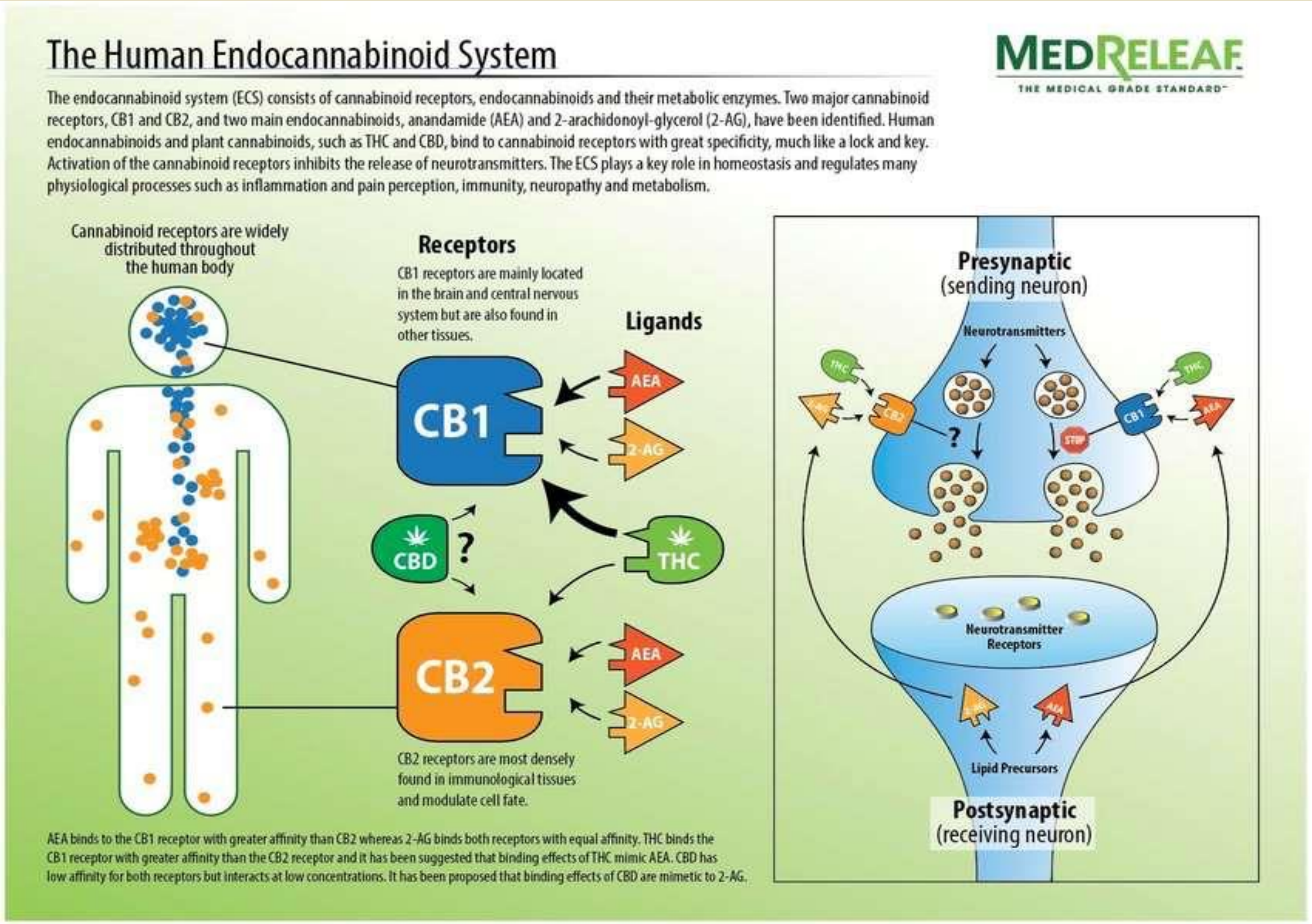
CBD:Cannabidiol

- Derived from medical marijuana or hemp
  - THC in marijuana is the chemical that causes psychoactive effects
- Antiinflammatory effects mediated through CB1 and CB2 rec: help repair UVA damage
- Cannabinoids are pharmacologically active compounds structurally similar to the psychoactive compound extracted from Cannabis sativa
- There are three primary cannabinoids
  - Endogenous cannabinoids (endocannabinoids) are made in the bodies of humans and animals, the two primary being arachidonoyl ethanolamide (anandamide or AEA) and 2-arachidonoyl glycerol (2-AG)
  - Phytocannabinoids are derived from plants
  - Synthetic cannabinoids are made in laboratories and are structurally akin to endocannabinoids and phytocannabinoids

Mounessa et al. The Role of Cannabinoids in Dermatology. *JAAD* July 2017; 77(1):188-90
Eagleston, et al.Cannabinoids in Dermatoloty: a Scoping Review. *Derm Online J*. June 2018; 24(6):1
McCormack, Bierman, Friedman et al. Topical Nanoencapsulated Cannabidiol Cream as an Innovative Strategy Combatting UVA Induced Nuclar and Mitochondrial DNA injury: A Pilot Randomized Clinical Study. *JAAD* July 2024

Potential Cannabinoids for Skin Dz



- Psoriasis-phase 1 trial
- Atopic Derm-pilot study
- Acme-trial
- Scleroderma-trial
- GVHD-ttial
- Dermatomysitis-phase 2 trial
- Epidermolysis Bullosa-case studies
- Pyoderma Gangrenosum-case studies
- Melanoma/NMSC-no humans studies

Friedman, A. Are Cannabinoids the future of Dermatology? Dermatologist. Feb. 2019.

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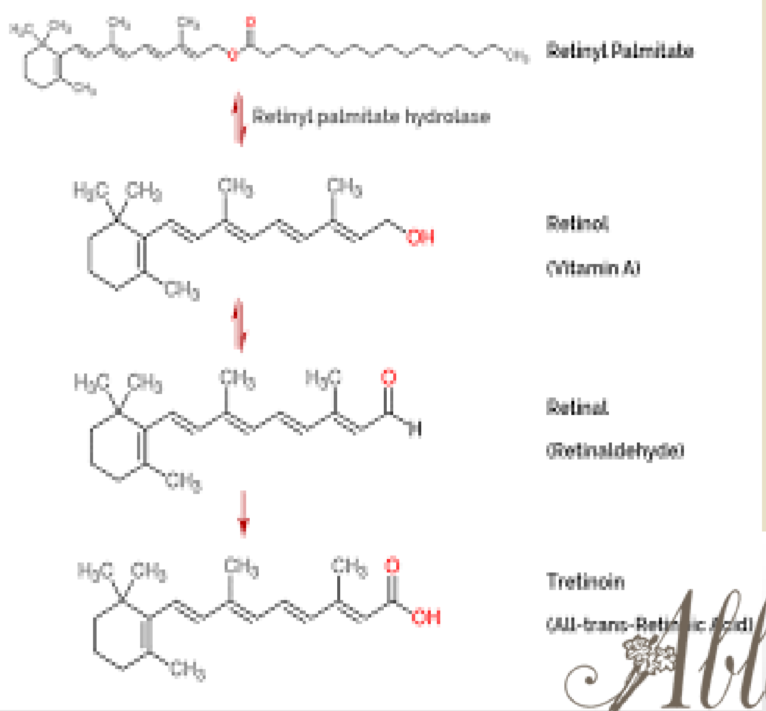
Tretinoin/Retinoids

- In 1980s Kligman first presented data on retinoids to a sceptism
- Now now retinoids stimulate fibroblasts in skin to prod more collagen and fibrillin, proteins in ECM that gives youthful plump look
- Adhere to retinoic receptors Tretinoin 0.025 (differin 0.1 does same thing)
- Can be irritating and difficult for sensitive skin types
- Adapalene: less irritation, antiinflam
- Tretinoin: prescription strength
- Retinoic acid: breakdown of Vitamin A, collagen and elastin hyperpigmentation reduction



Kligman A. The future of cosmeceuticals: an interview with Albert Kligman, MD, PhD. Interview by Zoe Diana Draelos. Dermatol Surg. 2005 Jul;31(7 Pt 2):890-1
Szymański et al.**Retinoic Acid and Its Derivatives in Skin.** Cells. 2020 Dec 11;9(12):2660

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Retinol/Retinaldehyde

- Like retinoids restore fibrillin fibrils that act like "tent pegs" and fix skin to ECM
- Plant based
- Improves cell turnover
- Neutralizes free radicals
- Stimulates collagen and elastin to help wrinkles, pore size
- Balances skin hydration by exfoliating dead skin cells
- Can still irritate sensitive skin
- Can start with retinols, increasing concentrations, then move up to retinoids, mixed in sunscreens

Draelos et al. A Double-Blind, Comparative Clinical Study of Newly Formulated **Retinol** Serums **vs** Tretinoin Cream in Escalating Doses: A Method for Rapid Retinization With Minimized Irritation. *JDD.* 2020 Jun 1;19(6):625-631.

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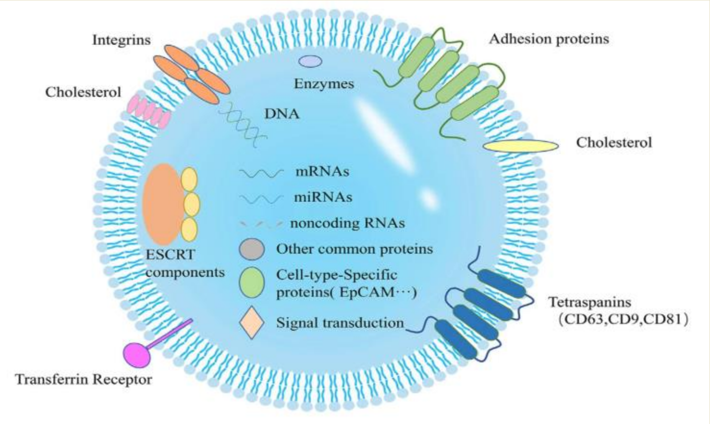
“Cosme”Exo”ceuticals”: Where we are headed…



- Companies are making topical skin care with exosomes, challenging to formulate
- Remember cosmetic vehicles must contain preservatives and emulsifiers that can destroy the exosomes
  - pH and osmotic concentration can also damage the exosomes present
- Exosomes produced by mesenchymal stem cells in culture, then culture media collected and differentially centrifuged high speeds and placed into cosmetic skin care products(meaning even cultured media can contain actual exosomes)
- Some from adipose stromal stem cells of healthy donors 20-40 years old
- Some from human donor blood platelets
- Remember we can find exosomes anywhere so many companies using exosomes from many different sources including plants
- Most current studies are in vitro and animal models(and usually done by injecting or open wound not applying topically)
  - Need large scale, double blind placebo controlled human studies to validate cosmetic products for:
    - Increase in skin cell proliferations
    - Reduce inflammation and modulate inflammatory response
    - Induce collagen and fibrinogen production
    - Accelerate wound healing
    - Combat UV damage with IL-8 and TNF productions inhibition

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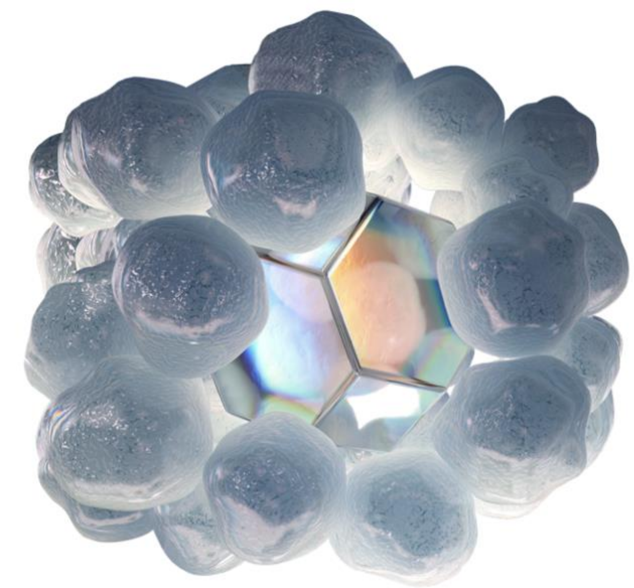
Novel Sunscreen: putting it all together

- Reverses skin again and regenerates by targeting core cellular skin aging mechanisms
  - Diamondcore technology
    - Eradicates ROS scavengind and neurtralizing 80% of ROS
    - Stimulates fibroblasts
    - Improves bioactibe delivery
    - Maximizes light defense providing 5x better broadspectrum defense against UVA, UVB and HEVL light
    - Bioactives:
      - Tranexamic acid
      - Pynogenol
      - Astaxanthin
      - Nicatinamide
      - Licorice root extract
      - Bisabolol
      - Squalene
      - Hyaluronic acid



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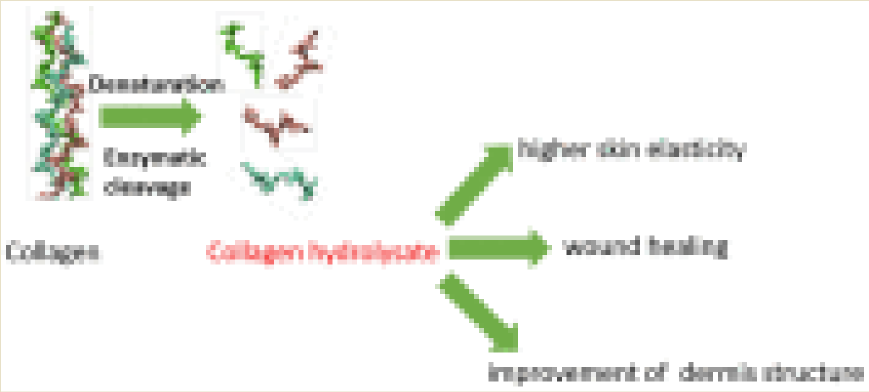
G. Adjuvant Medical Nutrition Therapy

- **Organic Flax seeds:** Essential Fatty Acids
- **Phytonutrients:** enhance photoprotection
- **Curcumin**:AOX, proteins help delay cellular senescence and promote longevity
- **Polyphenol**: Epigallocatechin gallate (EGCG)in green tea, reduce cancer, heart dz, promote longevity by restoring mitochondrial fn in cells
- **CoQ10**:reduce oxidative stress, help heart health, lower bp, and chol plaques
- **Astragalus:** stress-reducing herb used in traditional Chinese medicine reduce oxid stress, promote immune function, preventing cellular damage, and activating telomerase (enzyme that maintains telomere length)
- **Resveratrol:**polyphenol antioxidant found in grapes, berries, peanuts, and red wine,promote longevity by activating certain enzymes called sirtuins.

Cartwright, Graber, Stein Gold.The Role of Medical Nutrition Therapy in Dermatology and **Skin** Aesthetics: A Review. *JDD* 2020 Jan 1;19(1):12-18.

Collagen Supplement: Hip or Hype

- Bioactive peptides, such as collagen hydrolysate, most used ingredients for the development of nutraceuticals
- peptides resulted from ingestion of hydrolysate collagen and detected in the blood stream have chemotactic properties for skin fibroblasts, helping the skin restoration process
- Metanalysis of 19 studies from Brazil**
  - 90 days effective in reducing skin aging (reduces wrinkles, improves skin elasticity, and hydration)
- Consider organic bone broth



Lupu et al.Beneficial effects of food **supplements** based on hydrolyzed collagen for **skin care** .Exp Ther Med. 2020 Jul;20(1):12-17(Romania)

**Miranda et al.Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis..*Int J Dermatol.* 2021 Dec;60(12):1449-1461.

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You are what you eat!!!

- **Vitamin A :** cod liver oil, liver, egg yolks
  - promoting epidermal differentiation, modulate dermal growth factors, inhibit sebaceous gland activity, suppress androgen formation.
- **Zinc :**Kidney, liver, shellfish,pumpkin seeds
  - Necessary regulation gene expression,role in immune function, protein synthesis, wound healing, DNA synthesis, and cell division. structure of skin proteins and cell membranes, improves wound healing, anti-inflammatory effects, protects against UV radiation.
- **Magnesium:**Epson salts
  - required by at least 700 enzymes in the body, including those involved with DNA replication and repai,reduces oxidative stress, dampens inflammation, and inhibits the expression of histamine.
- **Vitamin C :**bell peppers, guava, dark leafy greens, broccoli, brussels sprouts, kiwi, citrus fruits, and strawberries
  - required by at least 700 enzymes in the body, including those involved with DNA replication and repair
- **Vitamin D :**
  - Support prod new skin cells, suppresses expression skin tumors, regulates growth of mature hair follicles, protects against damage caused sun exposure, supports would healing/ scar formation
- **Omega-3 Fatty Acids:**sardines, salmon, mackerel, tuna, anchovies, and black cod
  - Antiinflamm. Wound healing
- **Biotin:**egg yolks, liver, Swiss chard, romaine lettuce, almonds, and walnuts
  - essential cofactor for enzymes that regulate fatty acid metabolism
- **Sulfur:**egg yolks, meat, poultry, and fish, garlic, onions, brussels sprouts, asparagus, kale. Fermentation makes sulfur more bioavailable like sauerkraut
  - Synthesis of collagen and glutathione(an AOX)

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Nutrition Cont.

- **Silica:**water-soluble silica from volcanic rock (Hawaiian water)
  - maintain health of connective tissues with formation of GAGs, collagen
- **Niacin(vit B3):**meat, poultry, tuna , salmon, and seeds. Milk, green leafy vegetables, coffee, and tea
  - coenzyme in breakdown of carbohydrates, fats, and proteins, and anabolic reactions such as fatty acid and cholesterol synthesis.
- **Vitamin K2 :**dairy products from grass-fed cows, egg yolks, liver, natto, ferrmented foods (sauerkraut)
  - Protect from heart disease, formstrong bones, promotebrain fn, support growth and dev, prevent cancer , prevent calcif of elastin
- **Probiotics:** Skin-gut-brain connection(Saurerkraut)
  - influence systemic inflammation, oxidative stress, glycemic control, and tissue lipid content
- **Selenium:**Brazil nuts,cod, tuna, halibut, sardines, salmon, liver, beef, turkey, and lamb.
  - component of glutathione peroxidase, an enzyme necessary for antioxidant fn of glutathione.
- **Vitamin E :**spinach, turnip greens, chard, sunflower seeds, almonds, bell peppers, asparagus, collards, kale, broccoli, and brussels sprouts. Olive oil
  - anti-inflammatory agent, defending the skin against free radicals and ROS , immune function, cell signaling, regulation of gene expression
- **Pantothenic Acid (vitamin B5):**liver and kidney, egg yolk, and broccoli. Fish, shellfish, chicken, dairy products, mushrooms, avocado, and sweet potatoes
  - Promote wound healing, promote growth and differentiation of keratinocytes
- **Mushrooms:**Chaga for anticancer, reishi, shitake,
  - anti-inflammatory ,anti-oxidant,protect skin against damage UV light

Summary

- Skincare is under the dermatologist umbrella, easy addition to your practice
- As derms we need to look at the Science/data
- Patients looking for complementary alternative medicine in all aspects of their healthcare
- Supplements are a natural extension of look into skincare, as is nutrition
- Everyone can benefit from looking at "we are what we eat!"
- Healthy nutrition links to healthy body and skin.

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