

New Techniques in Hair Restoration?

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Disclosures

Nutrafol: Research Grants

Church Dwight: Research Grants

Exocelcio: Advisory Board

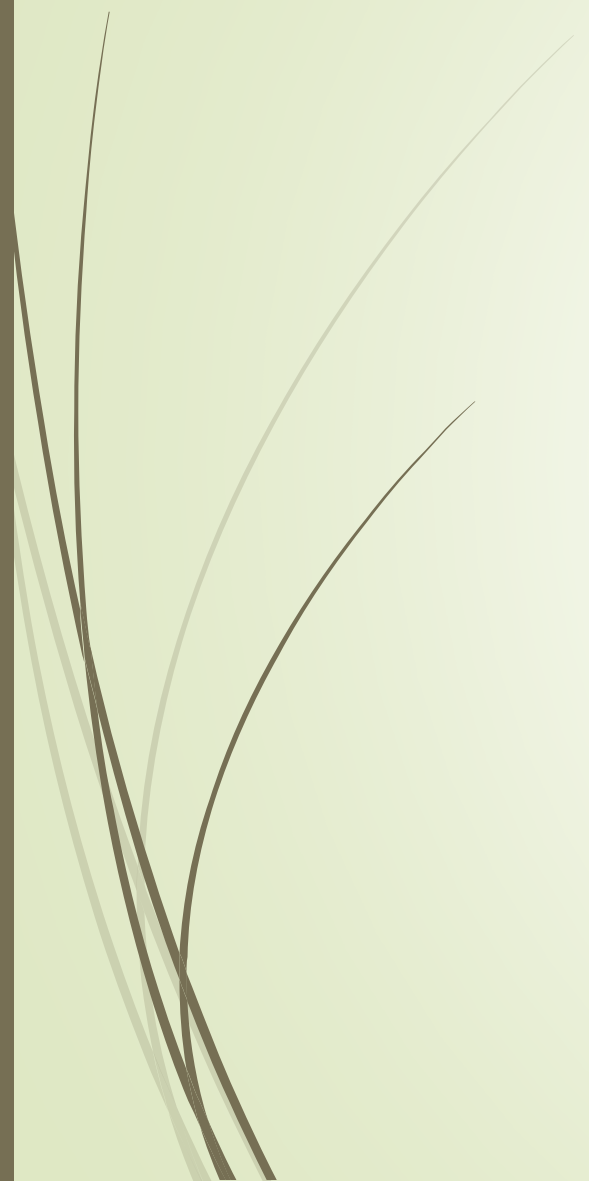
Sea Theory: Research Grants

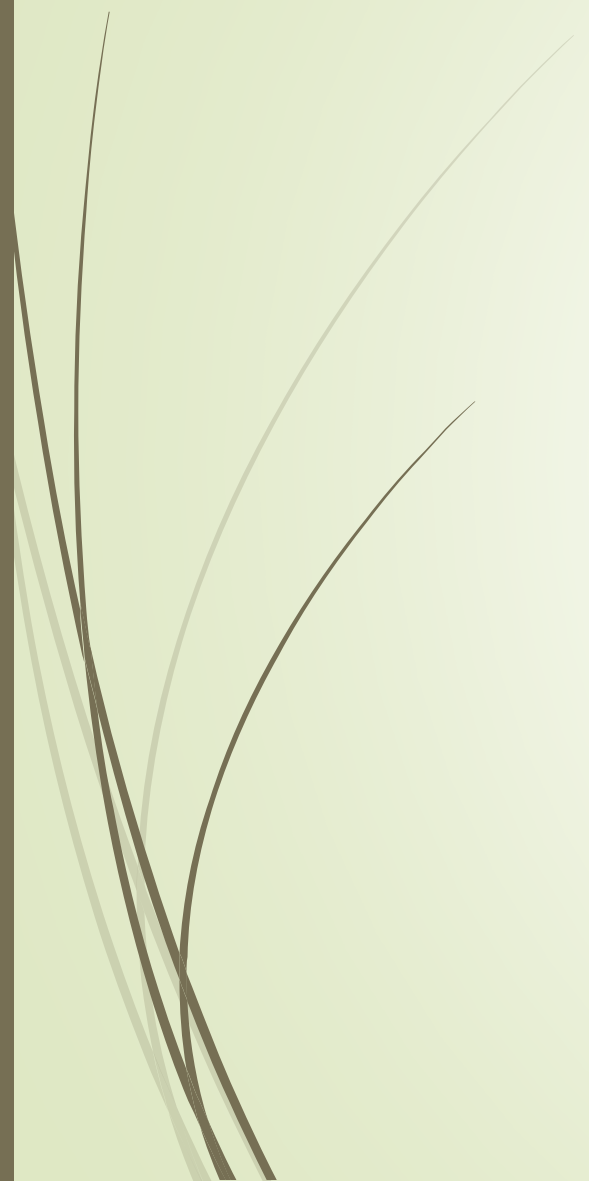


Why Discuss it?

Treatments for hair loss represent 2nd largest segment of aesthetic procedures performed in US

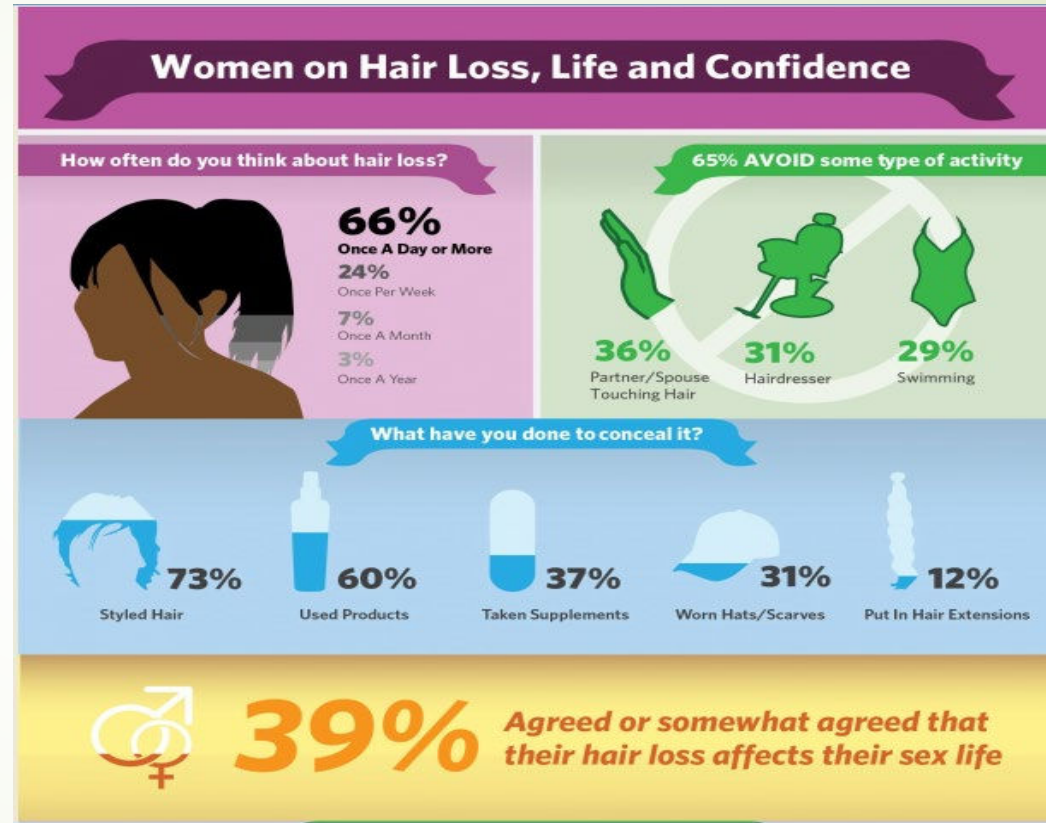
>70 million Americans suffer from hair loss (20 million are female)





Female Hair Loss – Psychological Impact

- 2000 women, ages 25-55
- 66 % suffering from hair loss think about their hair loss
- 39% hair loss affects their sex life
- 79% less happy, 9% said hair loss makes them depressed.
- 55% feel judged
- 86% envy thick hair.



2011 independent survey by Lab42



Etiology

Multifactorial Etiology of Hair Loss: multiple triggers and Inflammation



Genetics



Hormone



Health/Nutrition



Lifestyle: hair styles, products, alcohol consumption, tobacco, extreme exercise



Stress(neuroimmune inflammatory effects on follicle)



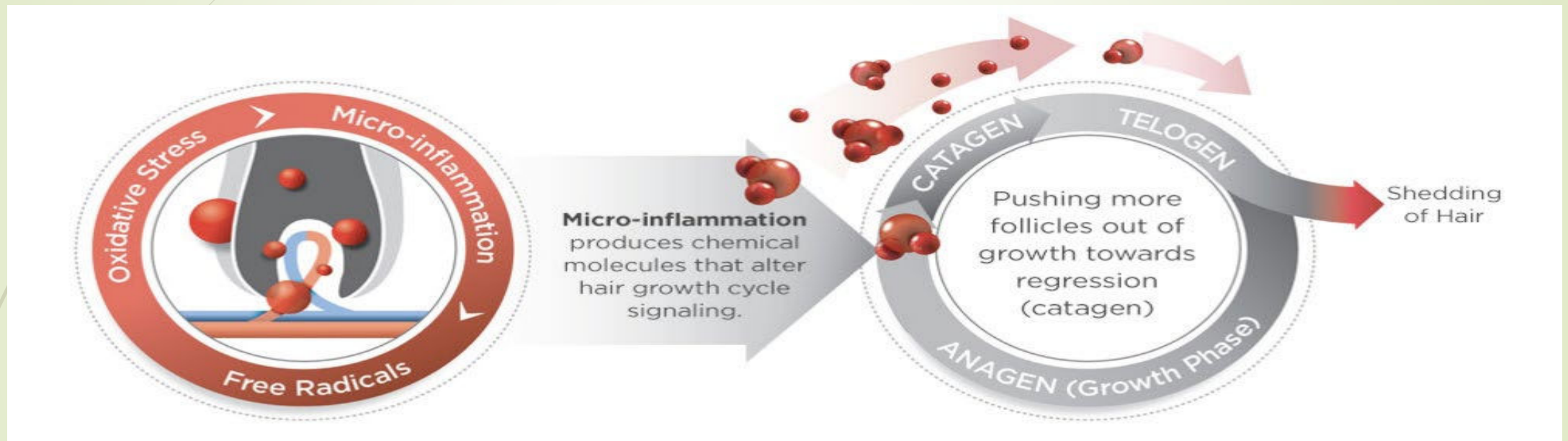
Environmental: pollution, UV



All TRIGGERS above lead to INFLAMMAGING: which creates**chronic microinflammation, free radicals,oxidative stress around follicle: multiple triggers throw the follicle out of balance

A NEW VIEW ON HAIR LOSS

INFLAMMATION LEADS TO DYSREGULATED SIGNALING


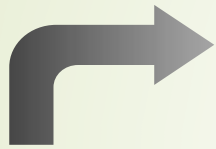


Excess inflammation, free radicals and generated cytokines **disrupt the normal signaling molecules** responsible for regulating the hair growth cycle and hair production – **tipping the scale towards regression**

Mahe et al. Androgenetic alopecia and microinflammation. *Int J Dermatol.* 2000;39(8):576-84



NEW NEUROLOGICAL, NEUROENDOCRINE & IMMUNE MECHANISMS BEHIND HOW
STRESS INHIBITS HAIR GROWTH



Peters et al. Probing the effects of stress mediators on the human hair follicle substance P holds central position. *Am J Pathol.*2007;17(6):1872-6

Non Scarring Alopecia DDx

- Androgenetic alopecia(hair out by roots): patterned hairloss
- Alopecia areata(hair out by roots): autoimmune dz, relapse frequent:
 - ILK 3mg/cc, tacrolimus bid, bimatoprost topically when inflammation under control, JAK inhib for AT or AU
 - Associated with Hashimoto's thyroiditis, pernicious anemia, vitiligo. Addison's dz so check labs
- Telogen effluvium: increase shedding, shift of hairs into telogen phase
 - Malnutrition
 - medication
 - Endocrine
 - stress
- Anagen Effluvium(hair breaks)
 - Anagen hairs receive toxic or inflammatory insult resulting in fracture of hair shaft
 - Chemo induced(antimetabolites, alkylating agents, mitotic inhibitors), heavy metals, cyclosporine, colchicine
- Polycystic ovary syndrome(hair out by roots)
- Associated with Systemic Syndromes:
 - Endocrine Diseases: hyper/hypothyroidism, hypo /hyperparathyroidism
 - Deficiency states (nutrition or metabolic): Kwashiorkor/marasmus, iron or zinc deficiency, AIDS
 - Drugs: Methotrexate, Cyclophosphamide, Colchicine, Prednisone, Heparin, Coumadin, Vitamin A, Propranolol, Levodopa, Thiouracil
 - Syphilis-hair out by roots
- Physical Alopecia-hair breaks
 - Traction alopecia-
 - Trichotillomania
- Hereditary Syndromes: congenital triangular alopecia, Ectodermal dysplasia, Progeria, Werner's Syndrome
- Tinea Capitis-hair breaks

Scarring Alopecia DDx

- ▶ Infection:
 - ▶ Bacterial, fungal(kerion), protozoan (leishmaniasis), viral
- ▶ Neoplasm:
 - ▶ BCC,SCC, adnexal tumors, mets
- ▶ Physical/chemical:
 - ▶ Burns, radiation, caustic agents, factitial
- ▶ Hereditary disorders:
 - ▶ Aplasia cutis congenita, epidermal nevi, Ichthyosis, EB(recessive/dystrophic)
- ▶ Other:
 - ▶ LPP/ Frontal Fibrosing Alopecia*
 - ▶ Central Centrifugal Cicatricial Alopecia*
 - ▶ Folliculitis Decalvans*
 - ▶ Acne Keloidalis
 - ▶ Dissecting Perifolliculitis of Scalp
 - ▶ Amyloidosis
 - ▶ Pseudopelade of Brocq
 - ▶ Lupus Erythematosus/DLE
 - ▶ Sarcoid
 - ▶ Morphea

It takes seeds and soil to make it grow!

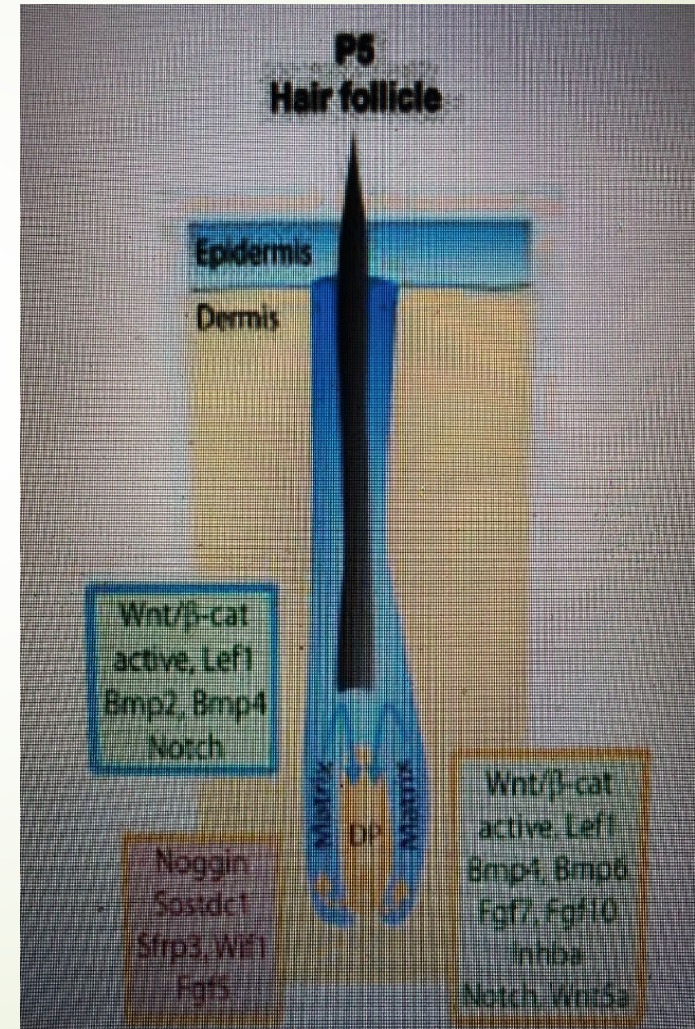
- ▶ Stem cells are the seeds (from which the hair grows)
- ▶ Microenvironment is the soil (blood vessels, nerves, adipocytes) informs the stem cells where to go and what to do
- ▶ Hair is the model for all stem cell research and biology
- ▶ NEED TO DETERMINE WHERE THE PROBLEM LIES



Hair growth pathways

- Wnt Signaling*
- MAPK(mitogen activated Protein kinases) Signaling
- TGF beta Signaling
- Signaling between matrix and DP during hair follicle growth

Song et al. Regional Control of Hairless Vs Hair-Bearing Skin by *Dkk2*. *Cell Reports* 2018



449 Active Studies (recently completed or recruiting) for Hair loss 2023

- Hair Stimulating Complex (HSC) is derivative of hypoxia-induced multipotent cell conditioned media enriched key growth factors
- 15mg Chelate zinc supplement : additional to standard 5% minoxidil
- Herbal solution in Iran
- Botulinum toxin A
- Topical certrazine 1% vs Minoxidil 5%
- Drug: tetrapeptide aldehyde proteasome inhibitor (NEOSH101)- Germany
- Cold atmospheric pressure plasma
- Nitrous Oxide gel



Treatment Options

Treatment Options

- ▶ Treat the cause: Attempt to correct lab abnormalities first
- ▶ Start supplements depending on etiology
- ▶ Consider Topical biomimetic peptides or topical Finasteride/Minoxidil (with or without microneedling)
- ▶ Consider Low Level Light Laser Therapy, home units/LED
- ▶ Possible intralesional corticosteroid (3-5mg/cc) injections, donor bone marrow stem cells/exosomes, intradermal minoxidil (4), or PRP with or without microneedling
- ▶ Discuss prescription meds (oral minoxidil, oral finasteride, oral spironolactone). Side effects seen with oral meds (1,2,3), oral antibiotics
- ▶ Topical Tacrolimus immune modulator
- ▶ Jak inhib, methotrexate, oral meds, other depending on Dx
- ▶ Experimental Protein injections with Copper
- ▶ Talk nutrition and stress management
- ▶ Consider transplant
- ▶ Always discuss price, frequency of in office visits, and duration of treatment (ie AGA Treatment is forever)

1. Randolph, Tosti. Oral Minoxidil Treatment for Hair Loss: A review of Efficacy and Safety. *JAAD*. 2020 Jul(1): S0190-9622

2. Sanabria, Vanzela et al. Adverse Effects of Low-Dose Oral Minoxidil for Androgenetic Alopecia. *JAAD*. 2020 Nov

3. Sinclair. Female Pattern Hair loss: a Pilot Study Investigating Combination Therapy with Low-Dose Oral Minoxidil and Spironolactone. *Int J Dermatol*. 2018 Jan 57(1):104-9

4. Iamsung, et al. Finasteride and Its Potential for the Treatment of Female Pattern Hair Loss: Evidence to Date. *Drug Des Devel Ther*. 2020 Mar 2(14):951-9

5. Uzel et al. Intradermal Injections with 0.5% Minoxidil for the Treatment of Female Androgenetic Alopecia: A Randomized Placebo-controlled trial. *Derm Therapy* 2020 Dec

A. Medical Treatments: Oral meds

Oral Finasteride

- Inhibits conversion of testosterone into DHT (causes hair miniaturization)
- Binds to sensitive follicles and destroys them
- No proof it helps with frontal hair loss
- Not safe in women of child-bearing age
- Continuous Tx required with AGA

**** Arif, et al, "Dutasteride in Androgenetic Alopecia: An Update," *Curr. Clin. Pharmacol.*, 2017 (12): 31-5

Oral Minoxidil

- Vasodilator: opens K⁺ channels, promotes blood flow= hair growth (i> O₂)
- Prolongs anagen phase and increases hair follicle size
- Topical vs 0.25mg oral, or 2% soln (1 tsp in two cups H₂O, drink 1.25tsp qam)
- Start 1.25-2.5mg bid, up to 5mg bid in men
- Can cause unexpected hair growth in unwanted places
- Continual treatment required with AGA

* Vastarella, et al, "Efficacy and safety of oral minoxidil in female androgenetic alopecia," *Dermatol. Ther.*, Nov. 2020;33(6):14234

A. . Medical Treatments: Compounded prescription strength products

Topical Finoxidil

- ▶ Finasteride or Dutasteride /Minoxidil/Retinoic Acid/
- ▶ Adds penetration with retinoic acid
- ▶ Likely reduces side effects of oral finasteride (watch for sexual SE)
- ▶ No studies in women of child-bearing age
- ▶ New dutasteride topical even stronger than finasteride

Topical Minoxidil

- ▶ Similar side effects: hypertrichosis, unpleasant texture
- ▶ Strong evidence similar to oral minoxidil
- ▶ Best results with 5%,
- ▶ Safe on men and women

Ramos, et al. Minoxidil 1mg Oral vs Minoxidil 5% solution Topically for the Treatment of Female Pattern Hair Loss *JAAD* 2019 Aug

Rafi, Katz, "Pilot Study of 15 Patients Receiving a New Treatment Regimen for Androgenic Alopecia: The Effects of Atopy on AGA," *ISRN Dermatol.* Apr 2011 (2011):241953

B.Oral Hormonal Therapies

Spironolactone

- **Efficacy is** good, weak evidence
- **Side Effects:** rare, hypertension, irregular menses, increased urination, avoid with renal failure.
- Best for FPHL, but not for pregnant women or kidney dz
- Decreases testosterone production in adrenal gland affecting 17 alpha hydroxylase and desmolase, competitive inhibition of androgen receptor
- 100-200mg qd

R. Sinclair, et al "Treatment of female pattern hair loss with oral antiandrogens," *Br. J. Dermatol.* Mar 2005 (152): 466-73

Flutamide/Bicalutamide

- **Efficacy is** good, but weak evidence
- **Side Effects:** liver toxicity, hot flashes/Bicalutamide, lower toxicity for prostate cancer Tx, but GI complaints
- **Compliance:** Moderate for flutamide/high for bicalutamide
- Interacts with other meds, black box warning hepatic failure
- Antiandrogen
- 250mg qd

D. B. Johnson and S. Sonthalia, "Flutamide," in *StatPearls*, Treasure Island (FL): StatPearls Publishing, 2020.

C. Complimentary and Alternative Mgt: (I)Supplements

Nutraceutical Supplement with Standardized Botanical Extracts

- ▶ Different versions for women, men, postpartum, women's balance (menopause)
- ▶ Ashwaghandha: Stress adaptogen
- ▶ Biocurcumin: anti-inflammatory
- ▶ Tocotrienols: anti-oxidant
- ▶ Saw Palmetto: natural DHT-inhibitor
- ▶ Piperine: increase bioabsorption
- ▶ Different versions for women, men, postpartum, women's balance (menopause)

Deep Sea Marine Protein Supplement

- ▶ Amino Mar: 28% Marine Protein Complex: (ECM components of shark and mollusks)
- ▶ Vitamin C
- ▶ Horsetail extract, Flaxseed extract
- ▶ Biotin
- ▶ Fumed Silica
- ▶ Apple Extract

G. Ablon, "A 6-month, randomized, double-blind, placebo-controlled study evaluating the ability of a marine complex supplement to promote hair growth in men with thinning hair," *J. Cosmet. Dermatol.*, Dec. 2016.;15(4):358-66

Ablon, Kogan, "A Six-Month, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Safety and Efficacy of a Nutraceutical Supplement for Promoting Hair Growth in Women With Self-Perceived Thinning Hair," *JDD*, May 2018 17(5):558-65

C.CAM: (I)Supplements cont.

Serenoa Repens

- **Efficacy:** moderate, evidence weak
- **Side Effects:** rare
- Possibility of missing early prostate cancer detection
- Saw palmetto: inhib 5 alpha red'ase
- Best on vertex scalp hair growth

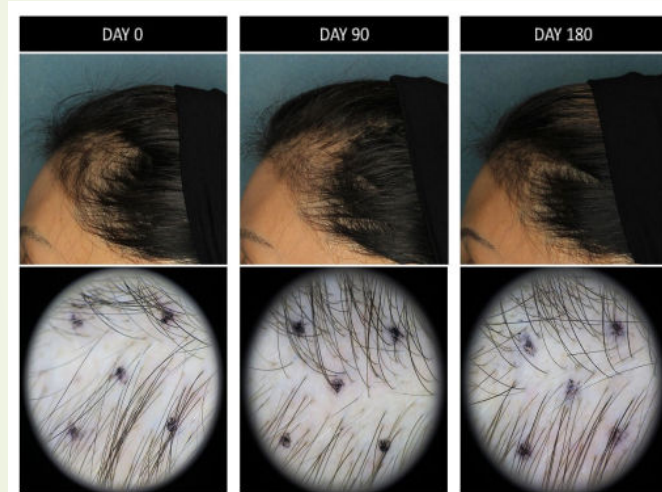
Murugusundram, "Serenoa Repens: Does It have Any Role in the Management of Androgenetic Alopecia?," *J. Cutan. Aesthet. Surg.*, Jan 2009 (2):31-2

Plant Based Oils

- **Efficacy:** unknown, need clin trials, anecdotal evidence
- **Side Effects:** SE GI discomfort, reduce PS
- **Compliance:** good
- **Cost:** affordable
- **Ethics:** need studies
- *Coconut oil, castor oil, amla oil, rosemary oil, tea tree oil, pumpkin seed oil*

Panahi, et al "Rosemary oil vs minoxidil 2% for the treatment of androgenetic alopecia: a randomized comparative trial," *Skinmed* Jan 2015 (13):15-21

Supplement Studies



Ablon, Kogan. **A Randomized, Double-blind, Placebo-controlled Study of a Nutraceutical Supplement for Promoting Hair Growth in Perimenopausal, Menopausal and Postmenopausal Women with Thinning Hair.** *JDD* Jan 2021 20(1):55-61



Burgess, Roberts, Downie, Kogan. **A Closer Look at Multi-Targeted Approach to Hair Loss in African American Women.** *JDD* Jan 2020: 19(1):95-98

D. Complimentary and Alternative Tx

(I) Devices: Low level laser Therapy



- **Clinical Evid:** strong, excellent efficacy
- **Side Effects:** none
- **Compliance:** moderate, need more studies for standardized protocols
- **Ethics:** best data of efficacy of all treatments, but expensive
- Energy Dispersed from Laser Array, Monochromatic (same wavelength) and Coherent Energy (NOT scattered) Red Spectrum (< 500 mW, no heat)
- BioStimulation Effect (hypothesis as mech unknown): decrease inflam, activate Wnt pathway, mitochondrial oxidative metabolism & stimulation of transcription factors promote blood flow by stim Nitric Oxide
- Stimulation of epidermal stem cells hypothesis, shifts follicle back into growth cycle:

D. Complimentary and Alternative Tx: (II) **Devices: Light Emitting Diodes**

- ▶ Clin Evid: moderate, Efficacy: good
- ▶ Home devices easier for pt access: dual band 620nm, 660nm
- ▶ Similar to LLLT promoting blood flow by stimulating nitrous oxide but also blocks DHT by downregulating 5-AR
- ▶ Noncoherent
- ▶ **Nitric Oxide:**
 - ▶ binds to free thiol in enzyme active site, stopping DHT production
 - ▶ enhances growth factors, reduces inflammation and increases blood flow to the hair follicle
 - ▶ Improves blood flow: increase cellular respiration, angiogenesis and vasodilation
- ▶ 10min qd



Before and 6 Months After LHG



Actual Patient of Dr Glynis Ablon

Before and 4 Months After LHG



Actual Patient of Dr Glynis Ablon

LED 6 month Daily Use



D. Complimentary and Alternative TX

(III) Devices: Microneedling

- Clin Evidence: weak to moderate, Efficacy: good
- Side Effects: rare, pain, bruising, folliculitis
- Works by releasing GF and dermal papilla assoc stem cells and activating wound regeneration mechanisms.
- Add GF topicals or topical OTC, PRP, exosomes

Neerja, "A study on the efficacy of microneedling with minoxidil solution versus microneedling with hair multivitamin solution for the treatment of androgenetic alopecia," *Int. j. dermatol. clin. res.*, Mar 2020(6):10-2

D. Complimentary and Alternative Therapy:

(IV) Platelet Rich Plasma

- Clinical evidence: strong, Efficacy: excellent
- Side Effects: scalp pain, HA, burn sensation
- deep dermis or subcutaneous injxn at a vol of 4-8 cc's/sessn, q mo, 3-4 sessions
- activated within 10 min, 95% secr by 1 hr
- 94% platelets: contain proteins, cytokines, bioactive factors
- Enhanced prolifer, differentiation and angiogenesis of dermal papillae and stem cells in bulge
- Usually injected but can be introduced by novel devices

Girijala, et al, "Platelet-rich plasma for androgenic alopecia treatment: A comprehensive review," *Dermatol. Online J.* Jul 2018(24)

*Gupta, Banimore. **Platelet-Rich Plasma Monotherapies for Androgenetic Alopecia: A Network Meta-Analysis and Meta-Regression Study.** JDD Sep 2022

Key Growth Factors



EGF

(Epidermal Growth Factor)

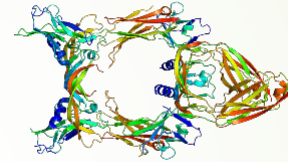
Promotion of epithelial cell growth, angiogenesis, promotion of wound healing



PDGF

(Platelet Derived Growth Factor)

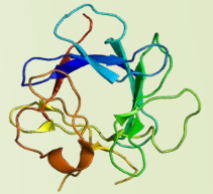
Cell growth, new generation and repair of blood vessels, collagen production



IGF

(Insulin-like Growth Factor)

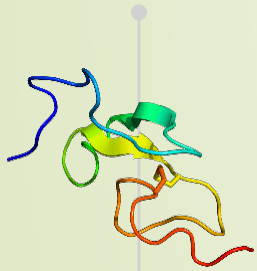
Induces anagen phase



FGF

(Fibroblast Growth Factor)

Tissue repair, cell growth, collagen production



VEGF

(Vascular Endothelial Growth Factor)

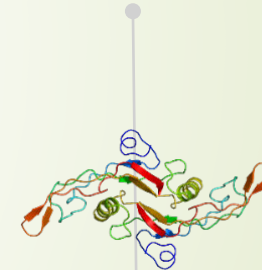
Growth and new generation of vascular endothelial cells



TGF- β 1

(Transforming Growth Factor)

Induces cell apoptosis



3 months after therapy(4 PRP sessions)



Property of Dr Glynis Ablon

[Tawfik, Osman.](#) The Effect of Autologous Activated Platelet-rich Plasma Injection on female pattern hair loss: A Randomized Placebo-controlled Study. *J of Cosmetic Derm* Feb 2018: 47-53

[Gupta, Versteeg, et al.](#) The Efficacy of Platelet-Rich Plasma in the Field of Hair Restoration and Facial Aesthetics-A Systematic Review and Meta-analysis. *J Cutan Med Surg.* 2019 Mar/Apr;23(2):185-203.

E. CAM: Other

Lanatoprost

- **Clinical Evidence:** weak, **Efficacy:** good
- **Side Effects:** rare pain, bruising, folliculitis, hypertrichosis
- Only tried in mild AGA
- Prostaglandin analog, orig to treat glaucoma
- Prolong anagen phase

Blume-Peytavi, "A randomized double-blind placebo-controlled pilot study to assess the efficacy of a 24-week topical treatment by latanoprost 0.1% on hair growth and pigmentation in healthy volunteers with androgenetic alopecia," *J.AAD*, May 2012 (66):794-800

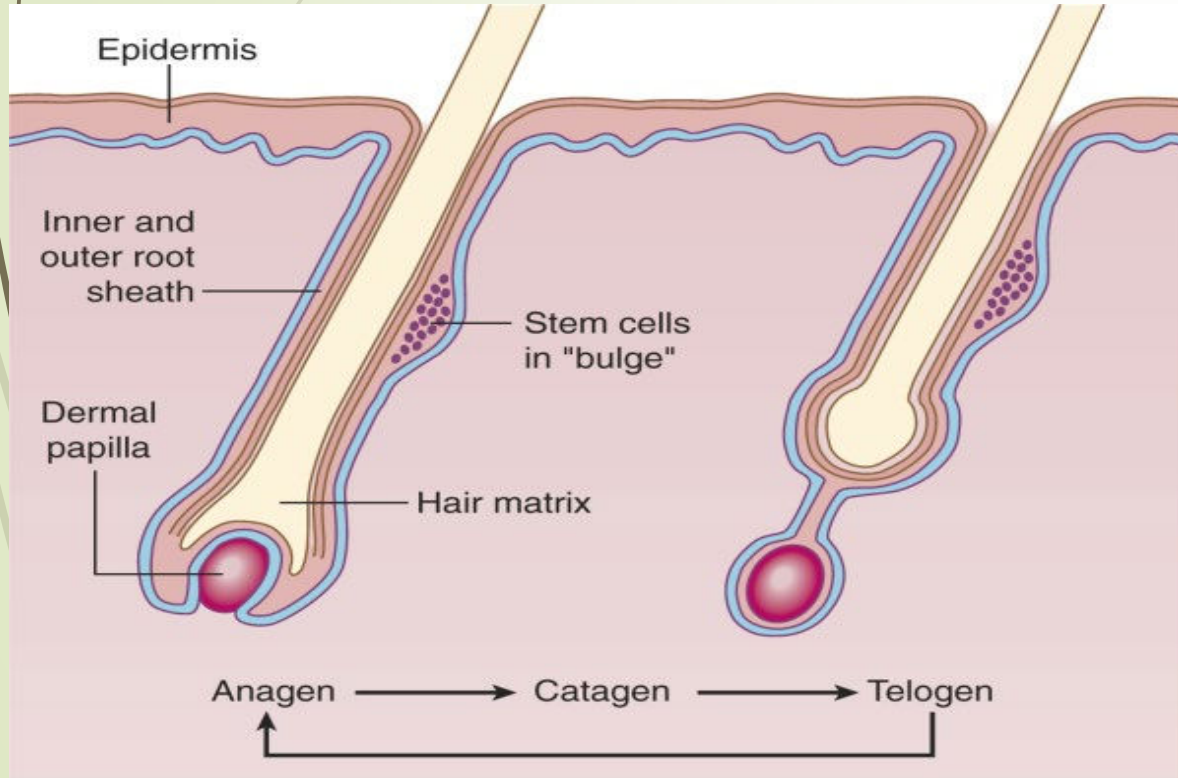
Bone Marrow Mesenchymal Stem Cells

- Sourced: regulated donor banks
- GF and cytokines filtered from stem cells to create conditioned media to coordinate repair
- Conditioned media primed with WNT pathway signaling growth factors delivered via nano lipid carriers (anti-inflam, no DNA)
- MRNAs stimulate good biosignals for hair growth
- Master regulator of biological fn, anti-inflammatory, pro-healing: 12 recombinant GF specific to follicle regeneration

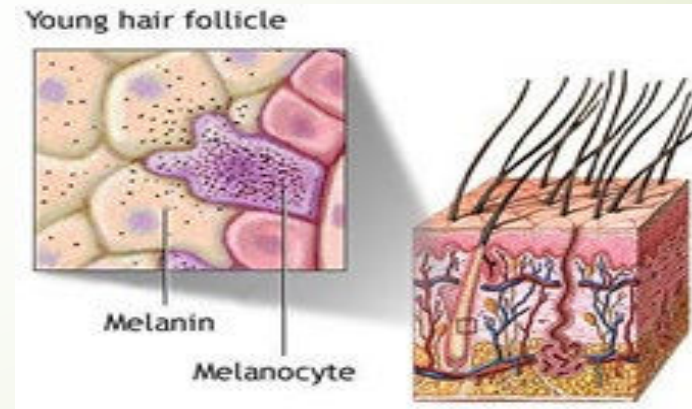
Hicok et al. Exosomes Origins: Why the Cell Source Matters. *Stem Cell & Regen Med* Dec 2019

Wnt Pathway Hair Regeneration

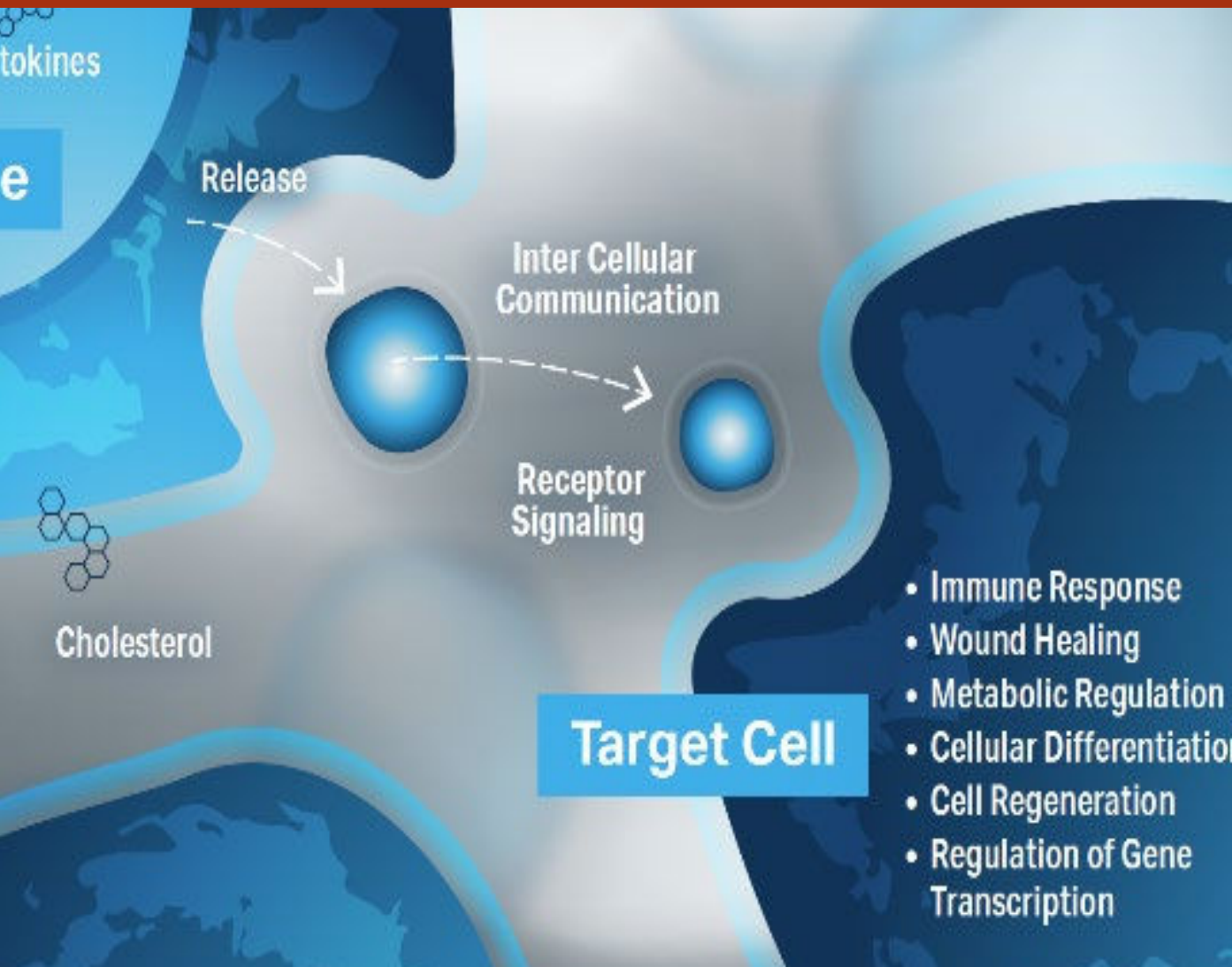
WNT Pathway regulates the growth and development of hair follicles.



- Treatment of MSCs with Wnt1a- conditioned medium activates DP cells and promotes hair follicle regrowth.



F. Exosomes

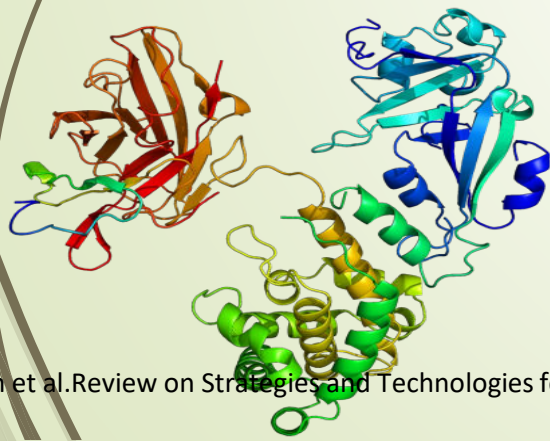


- ▶ **EXTRACELLULAR VESICLES (EVs)** LIPID BILAYER MEMBRANE MICRO-VESICLES SECRETED BY VARIOUS TYPES OF CELLS SUCH AS STEM CELLS THAT CARRIES GROWTH FACTORS
- **EVs target and repair damaged tissue** at sites of inflammation to transfer their content resulting in phenotypic functional changes
- **EVs contain growth factors**, mRNA and miRNA, lipids and cell-signaling proteins to repair and regenerate cells
- Reliable and **robust safety profile** and are acellular= **no DNA** or cellular material
- Source: Bone Marrow mesenchymal stem cells, Umbilical Cord Stem Cells, Plant Stem cells, Adipose Stem cells

Components of Exosomes

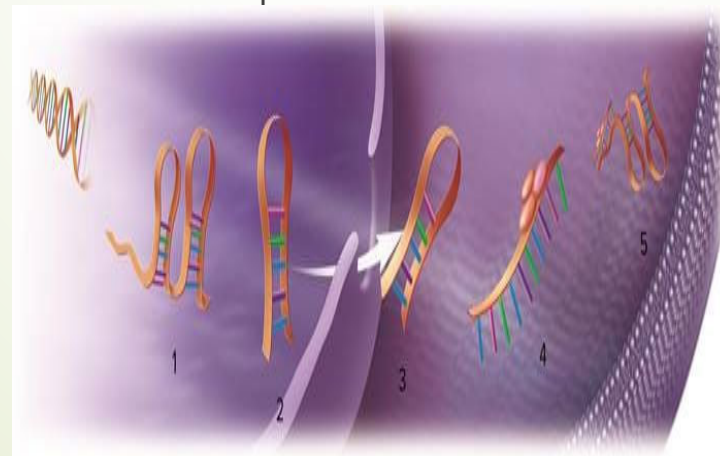
Growth Factors

- Stable protein bio-signals
- Manage inflammation and regeneration (enhance collagen and elastin synthesis)
- Used to enhance healing in aesthetic dermatological treatments



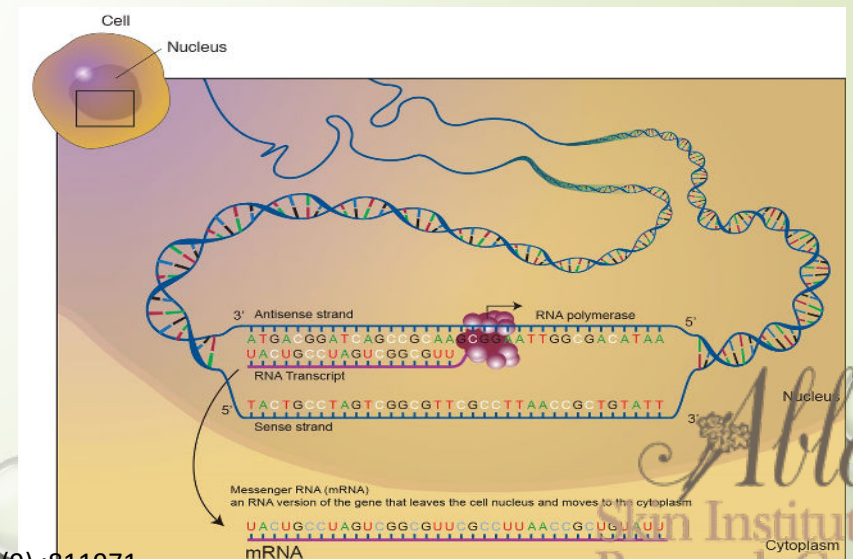
Micro RNA

- Regulate gene expression
- Promote keratinocyte migration
- Interact with messenger RNA
- Re-epithelialization of skin in



Messenger RNA

- Moderna COVID Vaccine
- Cancer Research
- Key component of Exosomes
- Natural vs. Synthetic



One session exosomes

before



6 wks after 1 session



Property of Dr Glynis Ablon

One year later



Single Exosome Treatment

Pre treatment



3 months after one session



Property of Dr Glynis Ablon

H. New and Upcoming Treatment Options

Clascoterone	Setipirprant	<u>Oral JAK inhib</u>
Antiandrogen (resembles DHT and spironolactone)	Oral CRTH2 antagonist: inhib proinflam effects in allergic response	AA =autoimmune attack on hair follicles with IL-15 production in response to interferon- γ secretion:
Antagonizing androgen rec on DP and inhib DHT on hair miniaturization and dermal inflam	Antagonist for Prostaglandin D2 receptor-blocks PGD2 mediated inflammation;CRTH2(chem oatractant receptor-homologous molecule expressed on Th2 cells	Mediated by JAK 1/2 and JAK 1/3 signaling in T cells via a positive feedback loop. JAK inhibitors disrupt this cycle and cause reentry of hair follicles into anagen phase, lead to hair growth.

Sun and Sebaratnam, "Clascoterone as a novel treatment for androgenetic alopecia," *Clinical and Experimental Dermatology*, 2020 (45): 913-4

"A Safety and Efficacy Study of Setipirprant Tablets in Androgenetic Alopecia in Males." <https://clinicaltrials.gov/ct2/show/results/NCT02781311> (accessed Feb. 16, 2021)

Yale, et al. "At the crossroads of 2 alopecias: Androgenetic alopecia pattern of hair regrowth in patients with alopecia areata treated with oral Janus kinase inhibitors," *JAAD Case Rep*, vol. 6, no. 5, pp. 444-446, May 2020. .



I. Others

- ▶ Synsapeum Seed Oil
 - ▶ Del Campo, Zhang, Wakeford. **Effect of Miracle Fruit Seed Oil on the Measurable Improvement of Hair Breakage in Women with Damaged Hair** *JCAD*. Nov 2017;10(11):39-48
- ▶ Change hair styles, products, blow dry low heat
- ▶ PDO threads, anecdotal
- ▶ Injectable peptides with Copper
- ▶ Estrogen Creams, anecdotal
- ▶ Scalp Tattooing
 - ▶ Park, Kim. **Effectiveness of Scalp Medical Tattoo Technique for the Treatment of Advanced Male Pattern Baldness.** *Int. J. Dermatol*; 2018 Nov
- ▶ Hair Transplant

My Approach to the Hair Challenged Patient

- Determine type of hair loss/etiology
 - Includes lab work:
 - free/total testosterone
 - DHEA-S
 - Prolactin
 - Thyroid function tests
 - Ferritin
 - ?ANA
 - Possible biopsy
 - Trichoscan
 - Micro/macrophotography
- Discuss treatment options:
 - Treat the cause
 - Start supplements, topical solutions(OTC or Compounded)
 - LLLT, LED
 - Possible intralesional corticosteroid injections/PRP
 - Topical biomimetic peptides, growth factors, exosomes with or without microneedling(or new delivery devices), especially if failed topicals
 - Discuss prescription meds
 - Consider hair transplant



Conclusion

- ▶ Take your time with patient:
 - ▶ review mechanism of hair loss
 - ▶ Work up causes of hair loss before starting treatments
 - ▶ Review all treatment options, including prices, time frame, frequency
- ▶ Indefinite use of any modality chosen for androgenic alopecia
- ▶ Combination works best: need combo studies
- ▶ Discuss hair thinning with all patients
- ▶ Address stress issues, nutrition, lifestyle

Nestor, Ablon, et al. Androgenic Alopecia: Efficacy and Ethics of Treatment. *JCD*. March 2023

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