AESTHETIC APLICATIONS

A.   HAIR LOSS

Alopecia or loss of hair has many causes and patterns. Androgenetic alopecia (AGA) is the most common type of hair loss and features progressive miniaturization of hair follicles. Although the occurrence of AGA has been thought to be driven by genetic and androgen predisposition, increasingly studies proposed AGA and elevated senescent cell burden, androgen and oxidative stress-induced senescence mechanisms in ageing are closely linked. Therefore, potential therapeutic strategies for improving cellular senescence may be initial targets to improve AGA.

Alopecia areata is a non- scarring condition, most commonly appearing on the scalp. This condition presents as sharply defined non-inflamed bald patches. During the active stage of hair loss pathognomonic, 'exclamation mark' hairs are seen (broken- off hairs of 3-4 mm long, which taper off towards the scalp). The condition may also affect the eyebrows, eyelashes, and beard. Patient's hair usually re-grows spontaneously in small bald patches.

Causes of Alopecia:

Administration of chemotherapeutic agents, medications (valproic acid), endocrine / autoimmune disorders, infection, nutritional deficiencies, mineral deficiencies (Zinc), excessive Vitamin A, heavy metal poisoning, hair shaft abnormalities, and rare dermatologic conditions.

Alopecia Areata

is associated with hypothyroidism, autoimmune disorders, atopy, and Down's syndrome. There are three main types of Alopecia: Alopecia Areata, Alopecia Areata Totalis, and Alopecia Areata Universalis. Most patients have small, localized patches, and some have widespread involvement. This condition has a risk for chronicity, in which factors include extensive skin involvement, onset before adolescence, and ophiasis (involvement of the peripheral scalp).

Androgenic alopecia

Male pattern baldness is physiological in men over 20 years old, though rarely it may be extensive and develop at an alarming pace in the late teens. It also occurs in females, usually post-menopause. The well-known distribution (bitemporal recession and then crown involvement) is described as 'male-pattern' but this type of hair loss in females is often diffuse.

Senescent Cells and Hair Loss

Senescence can be a cell state that secretes a group of cytokines and chemokines, known as the senescence-associated secretory phenotype (SASP). SASP factors create a local inflammatory environment and if senescent cells are not efficiently cleared, the accumulation of the SASP leads to pathologic dysfunction of nearby non-senescent cells, including tissue stem cells, which then contribute age-related degenerative phenotypes.

Recently, it was reported that the Dermal Papilla (DP) exhibits senescent like characteristics and expresses the SASP in aged tissue. Cellular senescence in the DP is associated with progressive dysfunction within the mesenchymal stem cell pool of the hair follicles (HFs). The inability to clear senescent stem cells from tissues has emerged as a direct contributor to aging and tissue degeneration in many tissues. These findings suggested that depletion of senescent cells can restore tissue homeostasis within the HFs and promote hair growth.

Senescent Cells and Alopecia

Androgen receptor (AR) overexpression in Dermal Papilla Cells (DPCs) from balding areas has been associated with increased cellular senescence markers, further supporting the link between androgen signaling, senescence, and hair loss. The accumulation of senescent cells in AGA disrupts the hair follicle microenvironment, leading to impaired stem cell function, follicular shrinkage, and hair loss. Understanding these mechanisms suggests that targeting senescence and oxidative stress could be a promising approach to managing AGA.

ASSESMENT OPTIONS:

Successful treatment of hair loss and alopecia is difficult, and management of these patients includes support and reassurance. Any underlying condition should be treated.

1. SENESCENCE BIOMARKERS

    helps to assess the current inflammatory, senescent situation and how its impact hair loss. This analyzes specific biomarkers using a highly sensitive method based in flow cytometry and genotoxicity test that provides high specificity and sensitivity measures of specific molecules such as FGF21, GFAP, NFL, GDF15 and 8-OHdG.

2. Interleukins

    Senescent cells that have escaped immunosurveillance have also been associated with enhanced chronic inflammation and influences immune reactions. Aging is marked by the decline of tissues and organs, with a rise in pro-inflammatory cytokines (like IL-6, IL-17A, IFN-γ, TNF-α, and CRP) and a drop in anti-inflammatory ones (IL-2, IL-4, IL-12). This imbalance promotes chronic inflammation, accelerating AGA and hair loss. With CYTOBALANCE it is possible to monitor the pro-inflammatory cytokine levels and control inflammation.

PRODUCT TREATMENT OPTION:

Concentrated human stem cell and exosomes product comprised of Adipose Derived Mesenchymal Stem Cells, donated or autologous, that has been expanded, processed, and banked through a validated pharmacological grade and strict quality control.

A. Objective: mesenchymal cells layer or exosomes injection utilizes biologic products that express immuno-modulatory and anti-inflammatory properties to help mitigate the impairment to the hair follicles.

B. Mesenchymal Stem Cell therapy for Hair Loss:

C. Exosomes therapy for Hair Loss:

D. Patient management:

- *Initial patient evaluation*: Reviews the medical information, lab work, and diagnostic imaging (if available) provided by the patient to determine the stage of the medical condition and any other secondary conditions.

- *Patient consultation:* Assessment of the nature of hair loss, the patient's medical history (including medication and supplement use), the patient's hair care practices, and the patient's family history as it relates to hair loss and potential causes of alopecia. Informed consent is obtained from all patients and medical records are updated, including patient's most recent physical exam, most up-to-date lab results. Internationally recognized tests for monitoring alopecia include:

- Complete Blood Count
- Androgen biomarkers
- Application of Ludwig Scale for female patients and Norwood scale for males (attached)
- Thyroid hormones: thyroxine (T4), triiodothyronine (T3) and thyroid stimulating hormone (TSH).
- Trichoscopy - Hair Pull Test.

- Treatment day:

- Swab the outside of the vial with alcohol, then remove the sterile cover and draw the contents into a syringe using aseptic technique.

- Injection will perform using sterile technique, per specific protocol consistent with the condition to be treated. Sample should be injected within 2 hours of thawing.

- *-Procedure for application of local scalp injections:* Using aseptic technique, a 1 cc syringe, and a 30 G needle administer 0.1 cc of cell mixture via subcutaneous injections to affected areas of scalp, each approximately a half inch apart. Take good care not to apply extra pressure to the syringe when administering the injection.

- Product should not be mixed with any other biologic compound.

E. Risks: There are possibilities for unwanted effects related to the injection of stem cells. Even with the most established protocol, adequate technique, and careful administration; a medical team may encounter uncontrollable events. Although there is no guarantee of perfect results, excellent results can be attained. The risks of complications with the administration of cord blood products are very low. Possible risks include but are not limited to:

- Pain at site of injections
- Malaise
- Fever
- Allergic reaction

F. Outcomes   :
Clinical response after 6 weeks, showing increased activity of hair growth and a higher number of active hair follicles is expected. Increased activity of follicles and changes to scalp will provide evidence of repair after stem cell graft.

G. Follow Up Plan:

- Pre-implant: Clinical evaluation of symptoms, use of Ludwig scale for female patients and Norwood scale for male patients. Photograph the area that was treated.

- 3 months after implant: Clinical evaluation of symptoms, use of Ludwig scale for female patients and Norwood scale for male patients. Photograph the area that was treated.

- 6 months implant: Clinical evaluation of symptoms, use of Ludwig scale for female patients and Norwood scale for male patients. Photograph the area that was treated.

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ALOPECIA– Ludwig Scale (Female Patients)

Physician (name & clinic): _____

Patient (name & age): _____

Treatment (include date): _____

Please Select a Grade Per Column (Pre-Treatment, Month 3, & Month 6)

Ludwig Scale	Pre Treatment	3 Month	6 Month
Grade I: Perceptible thinning of the hair on the crown, limited in the front by a line situated 1-3 cm behind the front hair line.			
Grade II: Pronounced rarefaction of the hair on the crown within the area seen in Grade I.			
Grade III: Full baldness (total denudation) within the area seen in Grades I and II.			

Dinh, Quan Q, and Sinclair, Rodney. "Female pattern hair loss: Current treatment concepts." Clinical Interventions in Aging (June 2007): Page 2. Web. 12/10/13.

The treatments described in this manual are considered experimental and have not been evaluated or approved by the FDA.
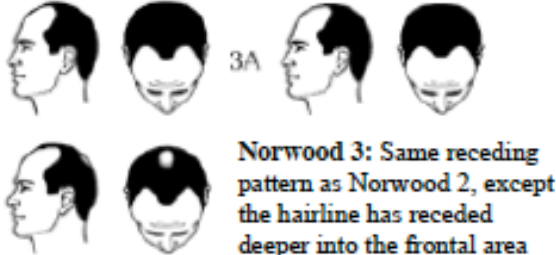
ALOPECIA – Norwood Scale (Male Patients)

Physician (name & clinic): _____

Patient (name & age): _____

Treatment (include date): _____

Please Select a Grade Per Column (Pre-Treatment, Month 3, & Month 6)

Norwood Scale	Pre Treatment	3 Month	6 Month
Norwood 1: Normal head of hair - no visible hair loss.			
Norwood 2: Hair is receding in a wedge-shaped pattern.			
Norwood 3: Same receding pattern as Norwood 2, except the hairline has receded deeper into the frontal area and the temporal area.			
Norwood 4: Hairline has receded more dramatically in the frontal region and temporal area than Norwood 3 and there is the start of a bald spot at the back of the head.			
Norwood 5: Same pattern as Norwood 4 but much reduced hair density.			
Norwood 6: The strip of hair connecting the two sides of the head that existed in Norwood 4 & 5 no longer exists in Norwood 6.			
Norwood 7: Norwood 7 shows hair receding all the way back to the base of the head and the sides just above the ears.			

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