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RATIONALE

SEFFIHAIR®

La **Terapia Rigenerativa** attraverso l'innesto di **stroma vascolare (SVF)** e **cellule mesenchimali staminali di origine adiposa (ADSCs)**

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RATIONALE

Il trattamento con il kit SEFFIHAIR® prevede l'innesto autologo e omologo della componente Vasculo Stromale (SVF) del tessuto adiposo selezionato con tecnica S.E.F.F.I. (Superficial Enhanced Fluid Fat Injection).

Numerosi lavori scientifici hanno dimostrato l'efficacia della terapia rigenerativa con SVF e ADSCs nel trattamento dell'alopecia androgenetica; recenti studi hanno dimostrato efficacia anche nell'alopecia areata.

INDICAZIONE

Il trattamento con il kit SEFFIHAIR® trova indicazione nelle seguenti condizioni:

- **alopecia androgenetica**

  Alcuni lavori internazionali riportano efficacia del trattamento con SVF anche nella:

- alopecia areata

Pertanto è di fondamentale importanza un'accurata diagnosi prima di intraprendere il trattamento.

ALOPECIA ANDROGENETICA

Interessa il 70% degli uomini e il 40% delle donne ad un certo stadio della loro vita. L'uomo tipicamente presenta una recessione dell'attaccatura alle tempie e perdita di capelli al vertice, mentre la donna normalmente ha un diradamento diffuso su tutta la parte alta dello scalpo.

La perdita di capelli androgenetica nell'uomo inizia sopra le tempie e al centro del cranio. Solitamente la striscia di capelli ai lati e posteriormente alla testa viene mantenuta.

L'alopecia androgenetica nella donna viene colloquialmente riferita come 'calvizie femminile', benché le sue caratteristiche possano verificarsi anche negli uomini. Causa di solito un diradamento diffuso senza recessione dell'attaccatura, e come la controparte maschile raramente porta a una perdita di capelli completa.

Per classificare i gradi di alopecia si utilizza la *Hamilton-Norwood Scale* per misurare il grado di calvizie nell'uomo e la *Ludwig Scale* per misurare il grado di calvizie nella donna.

FISIOPATOLOGIA

Nei soggetti geneticamente predisposti una delle cause dell'alopecia androgenetica è il diidrotestosterone (DHT); quest'ultimo deriva dal testosterone per azione della 5alfa-reduttasi.

La miniaturizzazione del bulbo avviene per effetto della trasformazione del testosterone nel suo metabolita più attivo, il diidrotestosterone (DHT); tale miniaturizzazione può portare fino alla morte definitiva del bulbo e la perdita irreversibile del capello. Il DHT promuove la crescita del pelo corporeo e della barba e può influenzare negativamente la prostata e anche i capelli.

Non c'è ancora l'assoluta certezza riguardo ai geni causanti l'alopecia androgenetica. Certamente sono responsabili i geni che controllano gli enzimi 5α-reduttasi: è stato dimostrato che la maggior parte dei geni coinvolti risiedono sul cromosoma X, ossia quello che la madre trasmette al figlio maschio, o che madre e padre trasmettono alla figlia femmina. L'ereditarietà verso un figlio maschio è maggiore secondo il cromosoma X che la madre ha ereditato dal padre, così la maggiore trasmissione avviene dal nonno materno al proprio nipote anziché da padre a figlio.

Il processo patologico fondamentale consiste nell'accelerazione, sotto stimolo androgenetico, della fase mitotica del ciclo pilare (*anagen I-V*) e nella conseguente riduzione della fase differenziativa, che è normalmente lunghissima. Essendo quest'ultima necessariamente incompleta, il fusto che ne deriverà sarà più sottile e corto (*vellus*).

Generalmente nell'uomo si assiste alla stempiatura, ossia nella parte frontale del capo i capelli diventano più fini e diradati. Successivamente lo stesso accade nel vertice. Infine la calvizie interessa tutta la parte superiore del capo. In età più avanzata si sovrappongono fenomeni atrofici del cuoio capelluto, che diventa sottile e lucido. In questa fase i *vellus* scompaiono. Un secondo processo patologico consiste nella perdita dell'individualità dei cicli papillari (caratteristica del cuoio capelluto adulto normale) e quindi della loro sincronizzazione. Questo fenomeno è dovuto alla riduzione della durata della fase di differenziamento. Un terzo fenomeno è l'aumento della *fase di kenogen*: quando il fusto del pelo si stacca alla fine del *telogen*, il follicolo è già occupato da un altro in *anagen* avanzato. Può comparire un intervallo tra la caduta del pelo in *telogen* e il suo rimpiazzo con il nuovo in *anagen*: durante tale intervallo fisiologico (*kenogen*), il follicolo rimane vuoto.

Nella calvizie androgenetica vengono persi soltanto i capelli nella regione frontale perché in questa zona l'alfa 5-reduttasi è più attiva, quindi vi si concentra una maggiore quantità di DHT.

Inoltre entra in gioco anche l'irrorazione sanguigna. Infatti la regione frontale è la parte più periferica della circolazione sanguigna del cuoio capelluto, e quindi quella che più va incontro all'atrofia dei vasi. A prescindere, il nutrimento dei bulbi è un fattore critico. Come suddetto, l'area più periferica della circolazione sanguigna è il cuoio capelluto.

Altra molecola favorente l'alopecia androgenetica in soggetti geneticamente predisposti è la prostaglandina D2 (PGD2), mediatore dell'infiammazione.

Naturalmente anche carenze di micronutrienti e stress possono favorire l'alopecia androgenetica nei soggetti geneticamente predisposti.

Patologie quali endocrinopatie (come carenza di GH, ipotiroidismo, menopausa, policistosi ovarica e tumori virilizzanti) possono causare calvizie.

MECCANISMO D'AZIONE

Molti studi hanno dimostrato l'efficacia e la sicurezza dell'innesto autologo di tessuto contenete SVF e ADSCs:

- SVF e pre adipociti hanno dimostrato un'importante azione favorente l'attivazione delle cellule staminali del follicolo attraverso la secrezione di numerosi e importanti Growth Factors, quali PDGF (dermal papillae growth factor), vascular endothelial growth factor (VEGF), insulin-like growth factors (binding protein IGFBP-1, and IGFBP-2).

Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling; DOI 10.1016/j.cell.2011.07.019 Eric Festa,Jackie Fretz, Ryan Berry, Barbara Schmidt, Matthew Rodeheffer, Mark Horowitz, and Valerie Horsley; Departments of Molecular, Cell, and Developmental Biology; Orthopædics and Rehabilitation Section of Comparative Medicine Yale Stem Cell Center; Molecular Cell Biology, Genetics, and Development Program Yale University, 219 Prospect St., New Haven, CT 06520, USA

Eplasty. 2015; 15: e10. Published online 2015 Mar 26 Hair Regeneration Treatment Using Adipose-Derived Stem Cell Conditioned Medium: Follow-up With Trichograms Hirotaro Fukuoka, MD, PhD and Hirotaka Suga, MD, PhD

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Stem Cell Res Ther. 2018; 9: 141 Published online 2018 May 15. doi: 10.1186/s13287-018-0889-y Cellular therapy with human autologous adipose-derived adult cells of stromal vascular fraction for alopecia areata Rami Anderi, Nehman Makdissy, Albert Azar, Francine Rizk and Aline Hamade.

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J Dermatolog Treat. 2018 Aug;29(5):431-440 Stem cell therapy as a novel therapeutic intervention for resistant cases of alopecia areata and androgenetic alopecia Elmaadawi IH, Mohamed BM, Ibrahim ZAS, Abdou SM, El Attar YA[1], Youssef A, Shamloula MM, Taha A, Metwally HG, El Afandy MM, Salem ML

Adipocyte Lineage Cells Contribute to the Skin Stem Cell Niche to Drive Hair Cycling DOI 10.1016/j.cell.2011.07.019 Eric Festa, Jackie Fretz, Ryan Berry, Barbara Schmidt, Matthew Rodeheffer,Mark Horowitz, and Valerie Horsley; Departments of Molecular, Cell, and Developmental Biology; Orthopædics and Rehabilitation Section of Comparative Medicine Yale Stem Cell Center; Molecular Cell Biology, Genetics, and Development Program Yale University, 219 Prospect St., New Haven, CT 06520, USA

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ESCLUSIONE AL TRATTAMENTO

- Infezioni in atto nella zona di prelievo o di innesto del tessuto.
- Presenza di neoplasie maligne nella zona di prelievo e innesto del tessuto.
- Gravidanza o allattamento.

- Terapia anticoagulante o grave disturbo della coagulazione.
- Allergia all'anestetico locale.
- Dismorfofobia.
- Terapie immunosoppressive in atto.
- Soggetti debilitati.
- Chemioterapia
- Trazione compulsiva dei capelli (tricotillomania)

POSSIBILI ASSOCIAZIONI TERAPEUTICHE

- Minoxidil (vasodilatatore)
- Finasteride (inibitore 5alfa-reduttasi)
- Carbossiterapia

  J Cosmet Dermatol. 2018 Dec;17(6):1275-1285 Study of the efficacy of carboxytherapy in alopecia. Doghaim NN, El-Tatawy RA, Neinaa YME, Abd El-Samd MM
- Innesto di capelli

Come in tutte le patologie multifattoriali, la combinazione terapeutica è quella che ottiene i migliori risultati.

La terapia rigenerativa trova indicazione in tutti gli stadi di alopecia androgenetica: sicuramente negli stadi avanzati (Scala di Norwood Hamilton V-VI-VII) è indicata in associazione con trapianto di capelli.

La terapia rigenerativa é consigliata in **preparazione** all'intervento e come **mantenimento** post-intervento.

PROCEDURA

Al fine di raggiungere il follicolo l'impianto deve essere eseguito con la metodica sotto descritta:

Siringa da 4ml luer lock (presente nel kit)

ago 27G 4mm (presente nel kit)

Iniezione perpendicolare allo scalpo alla distanza di 1 cm

circa 5 ml vengono somministrati in circa 10 spot

dopo somministrazione l'ago rimane viene mantenuto nello scalpo per circa 2 sec.

CONSIGLI POST-TRATTAMENTO

Solitamente non viene prescritta terapia anti-infiammatoria e/o antibiotica;

evitare doccia per 24 ore;

evitare esposizione solare per 1 settimana;

attività lavorativa immediata.

I risultati saranno apprezzabili dopo 4-6 mesi.

CELLULARITÀ / DOSE

Dai nostri studi (oggetto di prossima pubblicazione) la staminalità che si ottiene con la metodica SEFFIHAIR® è di circa 150.000 cell/ml.

Quindi considerando la somministrazione di 0.5 ml per punto di inoculo, innestiamo circa 75.000 cellule staminali per spot di inoculazione.

Considerando che somministriamo circa 10 -15 ml di tessuto, possiamo dire di avere innestato circa 1.500.000 - 2.250.000 cellule su una superficie dai 4x5 cm ai 5x6 cm.

ALOPECIA AREATA

L'alopecia areata è una patologia in cui la repentina caduta dei capelli, o di altri peli del corpo, si manifesta tipicamente a chiazze glabre o aeree.

Solitamente le prime chiazze si manifestano nel cuoio capelluto e, nella maggior parte dei casi, si risolvono spontaneamente, senza mostrare segni di cicatrici.

Nell'1% circa dei casi la patologia può estendersi all'intero cuoio capelluto (alopecia totale, AT) o a tutto il corpo (alopecia universale, AU) con la totale perdita di tutti i peli del corpo.

FISIOPATOLOGIA

Si tratterebbe di una componente immunopatologica (dovuta spesso all'attacco degli anticorpi IgE, quelli specifici allergici, o più generalmente degli antigeni dei leucociti umani di seconda classe e linfociti T; in sostanza si produrrebbe una reazione immunitaria anomala in grado di danneggiare, transitoriamente e localmente, i follicoli piliferi.

Inoltre si collegherebbe alla genetica, infatti tale condizione sembra colpire le persone che hanno una predisposizione a livello genetico.

Lo stress psicologico non è mai la causa ma, tuttalpiù, viene visto come un elemento che peggiora la patologia.

MECCANISMO D'AZIONE

Dati clinici hanno evidenziato che pazienti con Alopecia Areata (AA) hanno evidenziato crescita dei capelli dopo somministrazione di ADSCs. La citometria ha evidenziato l'effetto delle ADSCs nella regolazione delle citochine Th2 e del bilanciamento della produzione di citochine Th1/Th2/Th3.

Inoltre studi di immunoistochimica hanno evidenziato la creazione di un "anello di formazione di growth factor beta 1 (TGF-beta1)" intorno al follicolo, che sembra protegga il follicolo stesso dall'attacco autoimmune.

> *BMC Med. 2015; 13: 87 Published online 2015 Apr 20. doi: 10.1186/s12916-015-0331-6 Hair regrowth in alopecia areata patients following Stem Cell Educator therapy, Yanjia Li, Baoyong Yan, Hepeng Wang, Heng Li, Quanhai Li, Dong Zhao, Yana Chen, Ye Zhang, Wenxia Li, Jun Zhang, Shanfeng Wang, Jie Shen, Yunxiang Li, Edward Guindi, and Yong Zhao*
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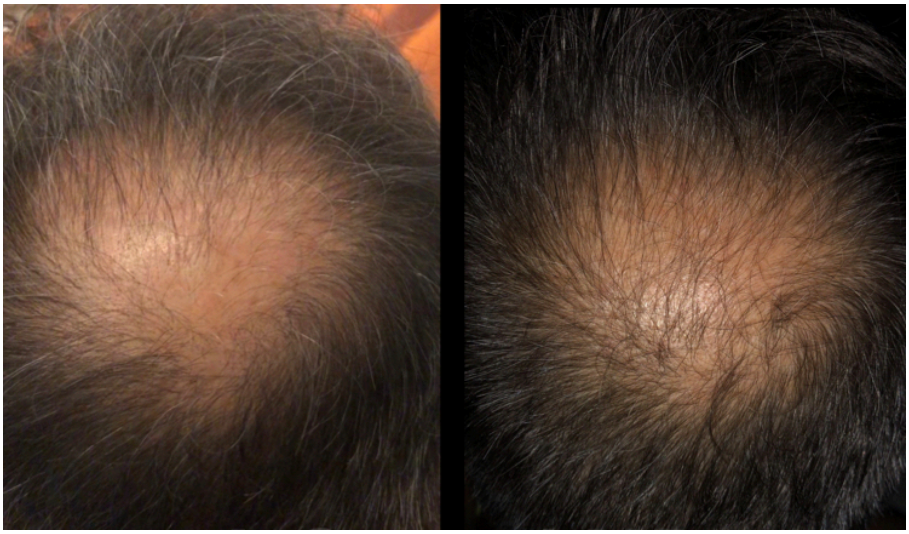
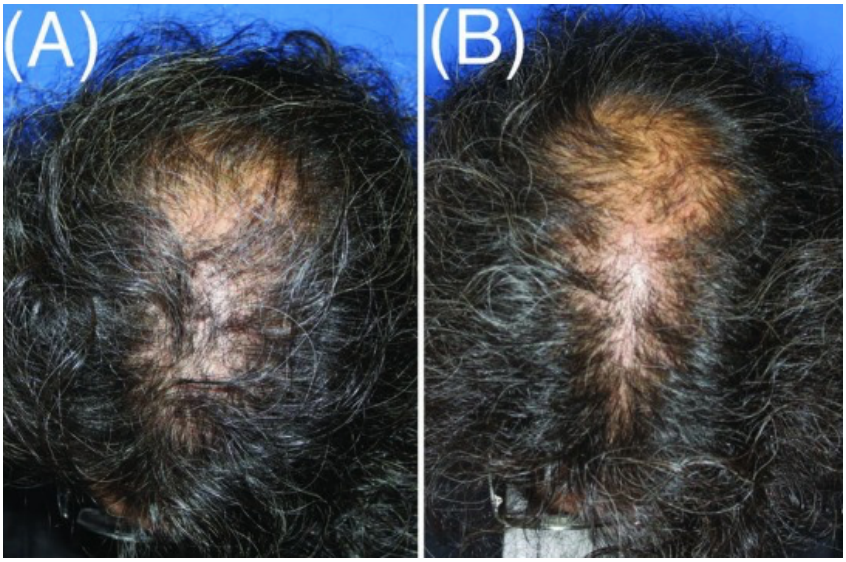
> *Stem Cell Res Ther. 2018; 9: 141 Published online 2018 May 15. doi: 10.1186/s13287-018-0889-y Cellular therapy with human autologous adipose-derived adult cells of stromal vascular fraction for alopecia areata, Rami Anderi, Nehman Makdissy, Albert Azar, Francine Rizk and Aline Hamade*

Altri studi hanno dimostrato l'importanza delle cellule Treg (Regulatory T cells, una linea eterogena di linfociti presenti anche nel tessuto adiposo) nella stimolazione del follicolo attraverso la stimolazione e proliferazione delle cellule staminali epiteliali. I Treg stimolano il follicolo (HF) attivando le cellule staminali follicolari (HFSC).

> *Cell 169, 1119–1129 June 1, 2017 Regulatory T Cells in Skin Facilitate Epithelial Stem Cell Differentiation; Niwa Ali, Bahar Zirak,Robert Sanchez Rodriguez, ..., George Cotsarelis, Abul K. Abbas, Michael D. Rosenblum*
>
> *PLoS One. 2019; 14(7): e0210308.Published online 2019 Jul 5. doi: 10.1371/journal.pone.0210308 Alopecia areata patients show deficiency of FOXP3+CD39+ T regulatory cells and clonotypic restriction of Treg TCRβ-chain, which highlights the immunopathological aspect of the disease, Fatma N. Hamed, Annika Åstrand, Marta Bertolini, Alfredo Rossi, Investigation,4 Afsaneh Maleki-Dizaji, Andrew G. Messenger,Andrew J. G. McDonagh, Rachid Tazi-Ahnini,*



CASISTICA da letteratura



post 4 mesi, A. Gennai

post 4 mesi, Fokura

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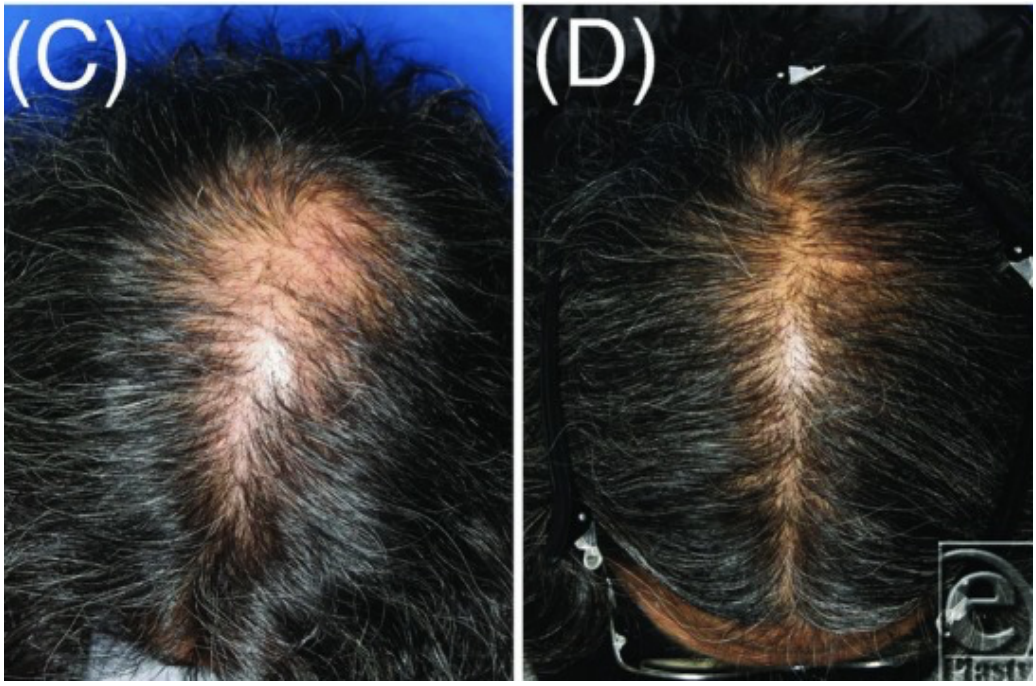
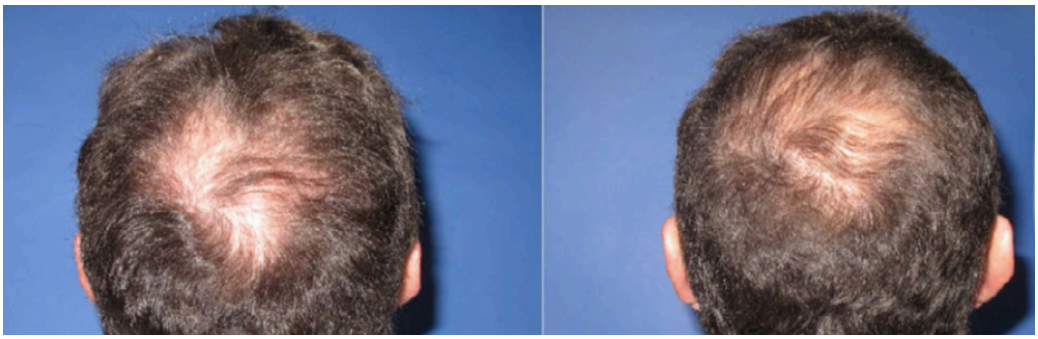


post 1 mese e 2 anni, Fokura



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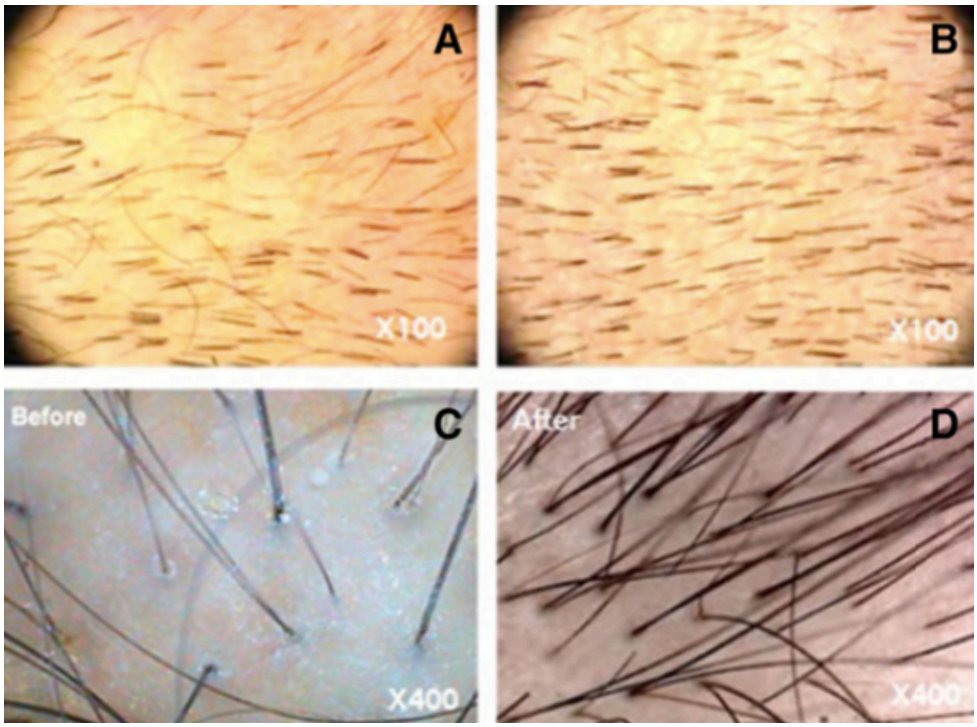

post 6 mesi, Perez - Meza

post 6 mesi, Rami Anderi

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Review focused on the effect of ADSCs and their secretory factors on the stimulation of hair growth in vitro, ex vivo and in vivo.
The conditioned media of ADSCs (ADSC-CM) increases the proliferation rate of human follicular cells. ADSCs-derived proteins improve hair growth and protect human dermal papilla cells against cytotoxic injury caused by androgen and reactive oxygen species.
ADSC-CM induces the anagen phase and promotes hair growth in mice, and enhances the elongation

of hair shafts in ex vivo human hair organ cultures.

9. Shin H, Won CH, Chung WK, Park BS; Up-to-date Clinical Trials of Hair Regeneration Using Conditioned Media of Adipose-Derived Stem Cells in Male and Female Pattern Hair Loss; Curr Stem Cell Res Ther. 2017;12(7):524-530.
   Review on the use of adipose-derived stem cells (ADSCs) on hair regeneration. Besides replacing degenerated cells in affected organs, ADSCs exhibit their beneficial effects through the paracrine actions of various cytokines and growth factors.
   Several laboratory experiments and animal studies have shown that ADSC-related proteins can stimulate hair growth. In addition, we introduce our clinical pilot studies using conditioned media of ADSCs for pattern hair loss in men and women, which shown to be a promising alternative therapeutic strategy for hair loss.

10. Shin H, Ryu HH, Kwon O, Park BS, Jo SJ; Clinical use of conditioned media of adipose tissue-derived stem cells in female pattern hair loss: a retrospective case series study; Int J Dermatol. 2015 Jun;54(6):730-5.
    Adipose tissue-derived stem cells (ADSCs) and conditioned media of ADSCs (ADSC-CM) are reported to promote hair growth in vitro.
    This study evaluates our clinical experience in the use of ADSC-CM for the treatment of FPHL. A retrospective, observational study of outcomes in 27 patients with FPHL treated with ADSC-CM
    The application of ADSC-CM showed efficacy in treating FPHL after 12 weeks of therapy. Hair density increased from 105.4 to 122.7 hairs/cm (2) ($P < 0.001$). Hair thickness increased from 57.5 µm to 64.0 µm ($P < 0.001$). None of the patients reported severe adverse reactions.

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15. Butt G, Hussain I, Ahmad FJ, Choudhery MS; Stromal vascular fraction-enriched platelet-rich plasma therapy rev.erses the effects of androgenetic alopecia; J Cosmet Dermatol. 2019 Sep 21. doi: 10.1111/jocd.13149. [Epub ahead of print]
Abstract
BACKGROUND: Since antiquity, humans have been trying to devise remedies to cure androgenetic alopecia (AGA). These efforts include use of oral and topical concoctions and hair transplant strategies. As AGA affects people of all colors and creed, there has been a continuous effort to find a magic bullet against AGA. Unfortunately, to date, all the strategies to negate AGA effects have limitations and thus require new treatment options.
AIM: To evaluate the efficacy of use of stromal vascular fraction (SVF) in androgenetic alopecia patients.
METHODS: Stromal vascular fraction was obtained by enzymatic digestion of autologous adipose tissue. The patients were divided into two groups, that is, platelet-rich plasma (PRP) group and SVF-PRP group. In PRP group, only PRP was injected, while in SVF-PRP group a mixture of PRP and SVF was injected in affected scalp areas. After two sessions (4 weeks apart), the patients in both groups were assessed and analyzed using various parameters.
RESULTS: Mean hair density in PRP group was increased from 52.44 hair/cm2 to 63.72 hair/cm2 (21.51% increase); while in SVF-PRP group, it was 37.66 hair/cm2 before treatment and 57.11 hair/cm2 after SVF-PRP therapy (51.64% increase). Percentage reduction in pull test was more significant in SVF-PRP group (80.78 ± 5.84) as compared to PRP group (34.01 ± 22.44). The physician and patient assessment scores also indicated a significant improvement in SVF-PRP group.
CONCLUSION: A combined SVF-PRP therapy reversed effects of AGA more efficiently as compared to PRP therapy alone.

16. Epstein GK, Epstein JS; Mesenchymal Stem Cells and Stromal Vascular Fraction for Hair Loss: Current Status; Facial Plast Surg Clin North Am. 2018 Nov;26(4):503-511. doi: 10.1016/j.fsc.2018.06.010. Epub 2018 Aug 16.
Abstract
The current state of the applicability of cell therapy for the treatment of various conditions of hair loss reveals a promising and potentially effective role. Further research, based on published work to date, is indicated to further explore the potential roles of autologous fat grafting, mesenchymal stem cells, and stromal vascular fraction therapy. The authors' evolving experience matches these promising scientific findings.

17. Stevens HP, Donners S, de Bruijn J.; Introducing Platelet-Rich Stroma: Platelet-Rich Plasma (PRP) and Stromal Vascular Fraction (SVF) Combined for the Treatment of Androgenetic Alopecia; Aesthet Surg J. 2018 Jul 13;38(8):811-822.

Abstract

BACKGROUND: Androgenetic alopecia (AGA) is characterized by miniaturization of the hair follicles gradually causing conversion of terminal hairs into vellus hairs, leading to progressive reduction of the density of hair on the scalp. Approved therapeutic options are limited and show side effects.

OBJECTIVES: To evaluate injections of stromal vascular fraction (SVF), which is rich in adipose-derived stromal cells (ASCs) in combination with platelet-rich plasma (PRP) in the upper scalp as a new autologous treatment option for AGA.

METHODS: Ten male patients (age range, 25-72 years), suffering from AGA at stage II to III according to the Norwood-Hamilton scale, have been treated with a single injection of autologous PRS (ACPSVF: combination of PRP and SVF) in the upper scalp. Preinjection and 6 and 12 weeks postinjection changes in hair density were assessed using ultra high-resolution photography (Fotofinder).

RESULTS: Hair density was significantly increased after 6 weeks and 12 weeks postinjection ($P = 0.013$ and $P < 0.001$). In hair-to-hair matching analyses, new hair grew from active follicles. Furhtermore nonfunctioning hair follicles filled with hyperkeartotic plugs, up to today assumed incapable of forming new hair, proved to grow new hair. No side effects were noted after treatment.

CONCLUSIONS: A single treatment of platelet-rich stroma injected in the scalp of patients with AGA significantly increased hair density within 6 to 12 weeks. Further research is required to determine the optimal treatment regimen. Preferred options to our opinion include the repetition of PRS or additional treatments with PRP.

18. Ziering Medical, Marbella, Spain; Ziering Medical, Los Angeles, CA, USA; The Hospital Group, Bromsgrove, Worcestershire, Ziering Medical, Birmingham, Ziering Medical, London, UK, Kerastem Technologies, San Diego, CA, USA; Hair follicle growth by stromal vascular fraction-enhanced adipose transplantation in baldness; Stem Cells Cloning. 2017 Jul 6;10:1-10. doi: 10.2147/SCCAA.S131431. eCollection 2017.

Abstract

Great interest remains in finding new and emerging therapies for the treatment of male and female pattern hair loss. The autologous fat grafting technique is >100 years old, with a recent and dramatic increase in clinical experience over the past 10-15 years. Recently, in 2001, Zuk et al published the presence of adipose-derived stem cells, and abundant research has shown that adipose is a complex, biological active, and important tissue. Festa et al, in 2011, reported that adipocyte lineage cells support the stem cell niche and help drive the complex hair growth cycle. Adipose-derived regenerative cells (also known as stromal vascular fraction [SVF]) is a heterogeneous group of noncultured cells that can be reliably extracted from adipose by using automated systems, and these cells work largely by paracrine mechanisms to support adipocyte viability. While, today, autologous fat is transplanted primarily for esthetic and reconstructive volume, surgeons have previously reported positive skin and hair changes post-transplantation. This follicular regenerative approach is intriguing and raises the possibility that one can drive or restore the hair cycle in male and female pattern baldness by stimulating the niche with autologous fat enriched with SVF. In this first of a kind patient series, the authors report on the safety, tolerability, and quantitative, as well as photographic changes, in a group of patients with early genetic alopecia treated with subcutaneous scalp injection of enriched adipose

tissue. The findings suggest that scalp stem cell-enriched fat grafting may represent a promising alternative approach to treating baldness in men and women.

19. Park BS, Kim WS, Choi JS, Kim HK, Won JH, Ohkubo F, Fukuoka; Hair growth stimulated by conditioned medium of adipose-derived stem cells is enhanced by hypoxia: evidence of increased growth factor secretion; H.Biomed Res. 2010 Feb;31(1):27-34.
Abstract
Adipose-derived stem cells (ADSCs) and their secretomes mediate diverse skin-regeneration effects, such as wound-healing and antioxidant protection, that are enhanced by hypoxia. We investigated the hair-growth-promoting effect of conditioned medium (CM) of ADSCs to determine if ADSCs and their secretomes regenerate hair and if hypoxia enhances hair regeneration. If so, we wanted to identify the factors responsible for hypoxia-enhanced hair-regeneration. We found that ADSC-CM administrated subcutaneously induced the anagen phase and increased hair regeneration in C(3)H/NeH mice. In addition, ADSC-CM increased the proliferation of human follicle dermal papilla cells (HFDPCs) and human epithelial keratinocytes (HEKs), which are derived from two major cell types present in hair follicles. We investigated the effect of hypoxia on ADSC function using the same animal model in which hypoxia increased hairregrowth. Forty-one growth factors in ADSC-CM from cells cultured under hypoxic or normoxic conditions were analyzed. The secretion of insulin-like growth factor binding protein (IGFBP)-1, IGFBP-2, macrophage colony-stimulating factor (M-CSF), M-CSF receptor, platelet-derived growth factor receptor-beta, and vascular endothelial growth factor was significantly increased by hypoxia, while the secretion of epithelial growth factor production was decreased. It is reasonable to conclude that ADSCs promote hair growth via a paracrine mechanism that is enhanced by hypoxia.

20. Batch JA, Mercuri FA, Werther GA; Identification and localization of insulin-like growth factor-binding protein (IGFBP) messenger RNAs in human hair follicle dermal papilla; J Invest Dermatol. 1996 Mar;106(3):471-5.
Abstract
The role of the insulin-like growth factors (IGFs) in hair follicle biology has recently been recognized, although their actions, sites of production, and modulation by the insulin-like growth factor-binding proteins (IGFBPs) have not to date been defined. IGF-I is essential for normal hair growth and development, and may be important in regulation of the hair growth cycle. In many culture systems, IGF-I actions are modulated by the IGFBPs. Thus, if IGFBPs are produced in the human hair follicle, they may play a role in targeting IGF-I to its receptor or may modulate IGF-I action by interaction with matrix proteins. We have used in situ hybridization to localize messenger RNA for the six IGFBPs in anagen hair follicles. Anti-sense and sense RNA probes for the IGFBPs (IGFBP-1 to -6) were produced, and 5-micrometer sections of adult facial skin were probed. Messenger RNA for IGFBP-3, -4, and -5 were identified, with predominantly IGFBP-3 and -5 mRNA found in the dermal papilla, and to a lesser extent IGFBP-4 mRNA. IGFBP-4 mRNA was also found at the dermal papilla/epithelial matrix border. Messenger RNAs for both IGFBP-4 and -5 were also demonstrated in the dermal sheath surrounding the hair follicle. Messenger RNAs for IGFBP-1, -2, and -6 were not identified. These studies demonstrate

specific localization of IGFBP mRNAs in hair follicles, suggesting that they each play specific roles in the local modulation of IGF action during the hair growth cycle.

21. Elmaadawi IH, Mohamed BM, Ibrahim ZAS, Abdou SM, El Attar YA, Youssef A, Shamloula MM, Taha A, Metwally HG, El Afandy MM, Salem ML; Stem cell therapy as a novel therapeutic intervention for resistant cases of alopecia areata and androgenetic alopecia; J Dermatolog Treat. 2018 Aug;29(5):431-440. doi: 10.1080/09546634.2016.1227419. Epub 2018 Mar 6.
ABSTRACT
BACKGROUND: Management of alopecia areata (AA) and androgenetic alopecia (AGA) is often challenging as patients may be resistant to currently available modalities of treatment. The use of stem cells may be a novel option for resistant cases.
OBJECTIVE: To evaluate the safety and efficacy of the use of autologous bone marrow derived mononuclear cells(including stem cells) as compared to follicular stems cells for the management of resistant cases of AA and AGA.
METHODS: This study included 40 patients (20 AA patients and 20 AGA patients), all patients were treated with a single session of intradermal injection of autologous stem cells (SCs) therapy. They were divided into four groups according to the applied modality [either autologous bone marrow derived mononuclear cells (bone marrow mononuclear cells [BMMCs] or autologous follicular stem cells [FSC]).
RESULTS: Six months after stem cell therapy (SCT) injection, there was a significant improvement, confirmed by immunostaining and digital dermoscopy. The mean improvement in all groups was "very good". There was no significant difference between both methods in either type of alopecia. No serious adverse events were reported.
CONCLUSION: Autologous BMMCs and FSC seem to be a safe tolerable and effective treatment for the management of both resistant AA and AGA.