

Trichoscan Update

Bimonthly Newsletter

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Dr. Kapil Dua is a consultant otolaryngologist and hair transplant surgeon. He is the founder and director of AK clinics. He holds more than 14 years of clinical and teaching experience. He is the Hony. Secretary & Founder Member of AHRS. He was the Finance secretary of NW Zone of Association of Otolaryngologists of India from 2008-2011. He has several publications to his credit in various national and international journals. He has actively participated in several conferences and workshops including 39th Annual National Conference of Indian Medical Association, Capacity Building workshop on HIV/AIDS held in DMC&H, and Microsurgery of the Ear workshop Cum Update in Otolaryngology in PGIMER, Chandigarh.

Signaling Pathways and their Importance in Hair Growth Therapy

Introduction

Hair follicle development and maintenance require precise reciprocal signaling interactions between the epithelium and underlying dermis. These signals belong mostly to four conserved families:

- Transforming growth factor β family (TGF β),
- Fibroblast growth factors (FGFs)
- Hedgehog family (HH) and
- WNT family

EDA/EDAR/NF- κ B signaling pathways

Ectodysplasin-A (EDA) /EDAR/NF- κ B signaling pathways play an important role in HF initiation and primary hair placodes maintenance. Wnt signaling proceeds through EDA/EDAR/NF- κ B signaling. Wnt/ β -catenin regulates expression of EDA as well as expression of its receptor EDAR. EDA pathway is downstream of the primary inductive signal required for placode initiation. EDAR signaling can refine Wnt/ β -catenin pattern during primary placodes induction and it also acts as a suppressor of BMP signals nulling the inhibitory effect on placode formation. NF- κ B refines pattern of placode borders and also helps further development of the placode. It also regulates expression of Dkk4 along with LEF/TCF/ β -catenin^{1,2}.

Wnt inhibitor : Dickkopf1 and 4 (Dkk1 and Dkk4) pathway

Dickkopfs (Dkks) belong to the family of secreted Wnt inhibitors. Dkks inhibit Wnt signaling by binding to the LRP5/6 co-receptors, resulting in their endocytosis and eventual degradation. Four Dkk family members are known (Dkk1–4), however, not all Dkks inhibit canonical Wnt signalling. Only Dkk1 and Dkk4 appreciably inhibit secondary axes formation by XWnt8. Dkk2 is a context-dependent Wnt inhibitor, and Dkk3 does not appear to inhibit Wnt signalling. Dkk1 is the most widely studied member of this family and exhibits the most potent Wnt inhibition. DKK1 expression reduces overall appendage density especially hair follicle development during embryogenesis and also inhibits melanocyte growth & function via the suppression of β -catenin & microphthalmia-associated transcription factor (MITF). Catagen promotion by DKK-1 is also partly due to a block in canonical Wnt/ β -catenin signaling in follicular keratinocytes. Dkk-4, is also a potential modulator of Wnt signaling in the placode during the morphogenesis of the hair follicle.¹



Hair matrix precursor cell proliferation and differentiation : Bone Morphogenetic Proteins (BMP) pathway

BMPs are secreted signaling molecules that belong to the TGF- β superfamily and exert their biological activity via interaction with specific BMP receptors. BMPs act as multifunctional regulators of vertebrate development, controlling cell proliferation, differentiation, and apoptosis in various organs including the skin. BMPs interact with Wnt, Shh, TGF- β , EGF, FGF, Notch and neurotrophins to control cell proliferation, differentiation, and apoptosis in the developing skin and its appendages.¹

BMP signaling also plays a role in hair follicle morphogenesis, postnatal regeneration and control of the hair follicle cycle through regulation of hair matrix precursor cell proliferation and differentiation. The two closely related genes, Bmp2 and Bmp4, are both activated in hair shaft precursors, while expression of Bmp4 is also found in the dermal papilla. Expression of Bmp7 has been reported in the IRS and outer root sheath (ORS) and the dermal papilla. BMPs exert their biological effects by means of binding to specific BMP receptors, which transduce the signal to the nucleus by recruiting the Smad1/5 transcriptional regulators or components of the mitogen-activated protein kinase pathway. Noggin is a BMP antagonist secreted by the mesenchyme, which prevents BMP-2/4/7 binding to BMP receptors and is critically important for proper orchestration of a large variety of developmental events, including induction of follicle morphogenesis in the embryo and promotion of new hair follicle growth (anagen) postnatally. A delicate balance between Noggin and Bmp2 and Bmp4 is important for the initial stages of hair follicle morphogenesis. Other BMP antagonists, including Gremlin and ecto-dysplasin, are made by the dermal papilla (DP) and, hence, are likely to play paracrine roles in stem cell activation^{1,3}.

Upon initiation embryonic hair follicle express BMP4 suggesting a negative feedback loop to prevent new hair follicle initiation in the vicinity. In adult follicle stem cells, Smad1 is phosphorylated and BMP6 levels are elevated, suggesting that BMP signaling is active in the bulge. BMP signaling is strongest in the cells that differentiate to produce the IRS and hair shaft. Hair follicle stem cells display signs of activated TGF- β and BMP signaling in vivo, and in vitro, and ablation of BMP signaling alone can disrupt the quiescent state of the hair follicle stem cell niche.¹ BMP signaling is specifically required for proper proliferation and differentiation during late morphogenesis of secondary hair follicles and that inhibition of this signaling pathway may be one of the triggers for the onset of catagen when the follicles are in anagen and the onset of anagen when the follicles are in telogen.⁶ BMP signaling also plays an important role in controlling hair pigmentation.³



Novel therapy in management of hair loss

Renocia is a unique formulation with high treatment efficacy in male & female pattern hair loss. It consists of patented biomimetic peptides which include -

- CG-WINT (Decapeptide-18)
 - Stimulator of hair placode formation
 - Generates de novo hair through activated catenin signal
- CG-Nokkin (Oligopeptide-54)
 - Strong BMP Blocker - promotes hair growth & inhibits depigmentation
 - Stimulates formation of healthier hair
 - Helps blood circulation in the scalp & revitalizes hair follicles
- CG-Keramin2 (Decapeptide-10)
 - Down regulates DKK-1
 - Promotes new hair cell proliferation & migration - induces strong hair follicles & hair shaft

Mechanism of action of these active biopeptides are summarized in Fig. 1

Other ingredients include retinyl palmitate which provides nutrition to the cortex as well as possesses strong anti-oxidant properties helping hair to recover its elasticity. Biotin improves blood flow leading to healthier hair & scalp. The natural plant extracts - *Serenoa serrulata* fruit extract blocks DHT; *Polygala tenuifolia* root extract prevents hair loss & stimulates new hair growth; *Portulaca oleracea* extract keeps scalp clean & healthy; *Thuja orientalis* extract prevents hair loss & strengthens hair follicle and *Gingko biloba* leaf extract cleans & soothes scalp further improving blood circulation.

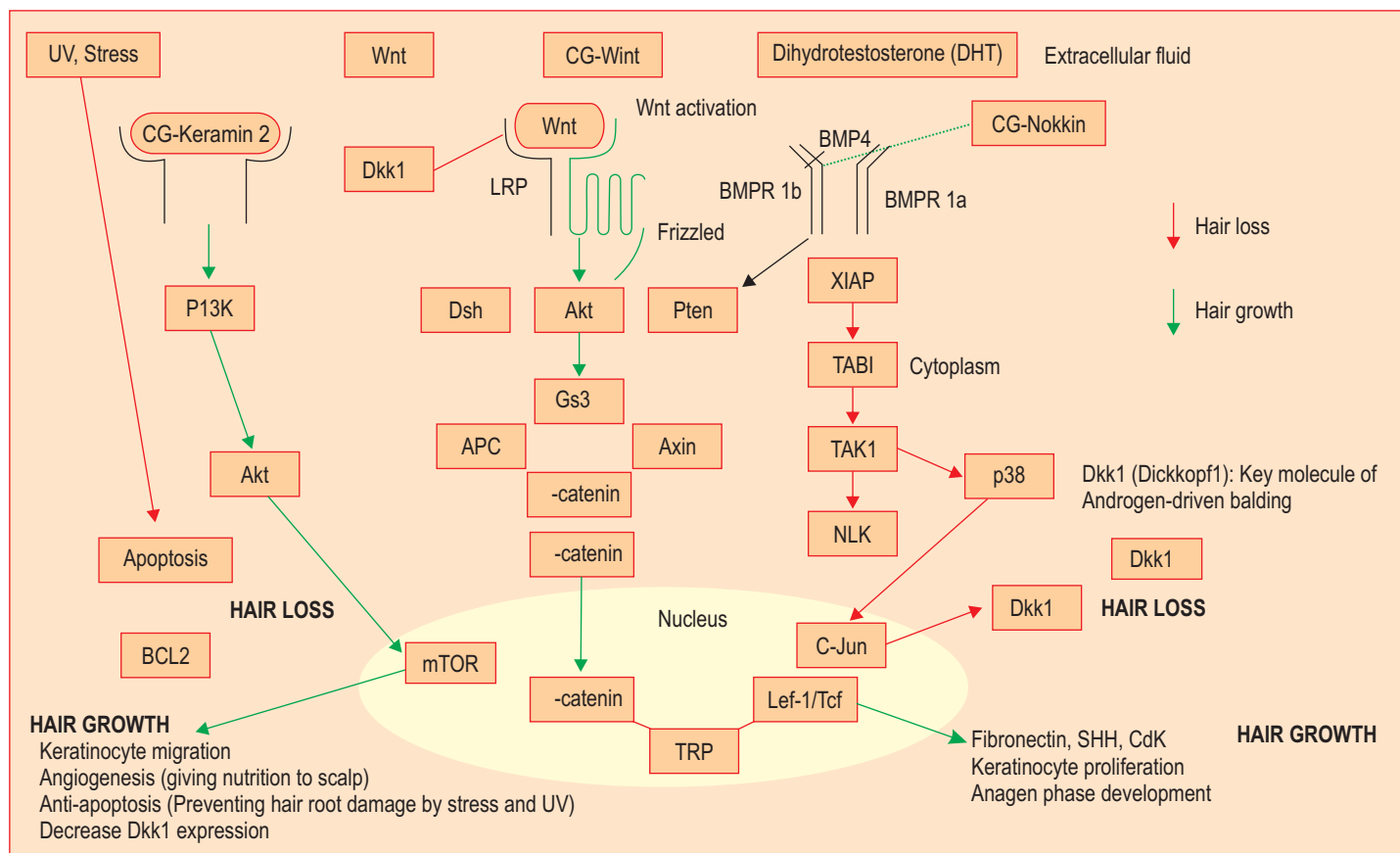


Fig. 1. Mechanism of action of bioactive peptides (CG-Wnt, CG Keramin 2 & CG Nokkin) of Renocia in management of hair loss

Preparation and usage:

- Renocia Hair Revitalizing Solution is to be applied on target area after using shampoo & conditioning hair. Gently massage with fingertips and leave it for at least 3 hours. Use twice-a-day in the morning & at night.
- Renocia Hair Revitalizing Shampoo & Renocia Hair Revitalizing Conditioner - Contain certain actives and further contribute to efficacy of Renocia Hair Revitalizing Solution.

Renocia hair revitalizing solution –

- **Blocks DHT-induced DKK1 binding to its receptor & down-regulates its transcriptional activity**
- **Antagonises BMP4 & increases angiogenesis**
- **Induces hair placode formation**
- **Demonstrates anti-hair loss & hair re-growth effect in vitro & in human clinical study**
- **Is safe and well tolerated by patients.**

References

1. Rishikaysh P, Dev K, Diaz D, et al. Signaling involved in hair follicle morphogenesis and development. *Int J Mol Sci*. 2014 Jan 22;15(1):1647-70.
2. Mustonen T1, Ilmonen M, Pummila M, et al. Ectodysplasin A1 promotes placodal cell fate during early morphogenesis of ectodermal appendages. *Development*. 2004 Oct;131(20):4907-19.
3. Sharov AA, Fessing M, Atoyan R, et al. Bone morphogenetic protein (BMP) signaling controls hair pigmentation by means of cross-talk with the melanocortin receptor-1 pathway. *Proc Natl Acad Sci U S A*. 2005 Jan 4;102(1):93-8.



Dr. Rajesh Rajput, M. Ch, ISHRS (USA), is a Founder Member and Vice President AHRS – India. He was the President at AHRS India during the year 2010-2011. His areas of special expertise are restoration of eyebrows, eyelashes, moustache, beard for patients with burns, Hanson's disease, trauma, cancer excision, cleft lip, etc. He is a member at International Society of Hair Restoration Surgery, ISHRS, USA. He is also a member at several other prominent professional organizations. He has pioneered "Hair Transplant Micrografting & Follicular Unit Transplants in India" and "Use of microsurgery instruments for delicate handling & minimizing injury to the follicles". He has received "Best Research Paper Award" from the Association of Plastic Surgeons of India in 1994. He has been invited for several lectures, symposium and workshops on plastic surgery and dermatology. He has also contributed in training several surgeons across India.



Dr. T. Salim. MD, DNB.

Dr.T.Salim is currently the Medical Director of Cutis Institute of Dermatology & Aesthetic Sciences, Calicut, India. He was formerly attached to Govt. Medical College, Calicut as Asst. Professor. He is trained in the field of Aesthetic Medicine and Dermatosurgery at various international centers. His areas of interest include Pigmentary Disorders, Dermatosurgery and Aesthetic Dermatology. He is one of the pioneers in Cellular grafting techniques for vitiligo in the country. He was invited faculty in many workshops in the field of Dermatosurgery and performed live workshops at several scientific meetings. He has chaired scientific sessions and was invited faculty in many international forums including International Society of Dermatosurgery and Asian Society of Pigment Cell Research. He has authored few chapters on dermatology. He is the co-ordinator of IADVL – SPG Dermatosurgery, Joint Secretary of Association of Cutaneous Surgeons (India).

Case studies

CASE 1

Patient complain

A 28-year-old man presented to the trichology centre with complaint of hair loss for the last 2years. He was quite concerned about his appearance and self image. The patient also complained of having suffered emotionally because of hair loss and avoided socializing.

Patient history

- Male / Single/ MBA/ Trainer with a MNC
- No history of Diabetes / Hypertension / Heart disease
- No history of major illness or surgery
- No known allergies

Personal history

- The patient was a non-vegetarian having erratic eating habits
- The patient's job was field based therefore had no regular meal timings and mostly binged on junk food
- H/o smoking- 1–2 Cigarettes/day; occasional intake of alcohol
- The patient had a stressful work life with no time for recreation and lacked adequate sleep
- The patient travelled mostly on bike and his job profile involved heavy travelling both within the city and elsewhere
- The patient was very concerned about his looks and had been quiet depressed about his appearance

Family history

- Father / 64y / history of baldness / No history of any other disease
- Mother / 60y / Diabetic / No hair complaints
- Brother / 32y / history of baldness/ No history of any other disease

General examination

- BMI – 26 kg/m²
- Vital signs – BP: 130/80 mm of Hg; Pulse: 78/min; Respiratory rate: 14 breaths/min
- Cardiovascular examination – Normal
- Respiratory examination – Normal

- Gastrointestinal examination – Normal
- Nails – normal

Local examination

- Receding hairline in the frontoparietal region
- Reduced hair density on the vertex
- The hair appeared short and frizzy
- Easy pluckability of hair
- Scalp appeared mildly inflamed

The patient was asked to undergo some basic laboratory investigations.



Laboratory investigations

- CBC – Normal
- FBS – 93 mg/dL
- Thyroid function tests - Normal

Diagnosis: Androgenic Alopecia

Management

- Peptide therapy: The patient was advised to apply a solution containing Decapeptide-10, Oligopeptide-54 and Decapeptide-18 two times a day with regular follow ups every month
- The patient was counseled for his diet and was instructed to have a well balanced diet with adequate intake of fresh fruits and vegetables
- The patient was prescribed a multivitamin supplement for one month

On follow up after 4 months, the patient showed considerable improvement with reduction in hair loss. The vertex area also showed some improvement in hair density.



CASE 2

Patient complain

A 25-year-old woman presented to her dermatologist with the complain of excessive hair fall for the last few months. The hair loss had been progressive and interfered with her quality of life and emotional well being. She also mentioned of having tried various oils for hair growth but all her efforts were in vain.

Patient history

- Female / Single/ M.A/ Journalist
- No history of Diabetes / Hypertension / Heart disease
- Normal menstrual history
- No history of major illness or surgery
- No known allergies

Personal history

- The patient was a vegetarian having a balanced diet
- The patient's job involved interacting with different people on a daily basis. However, her hair loss affected her image and affected her professional life
- No h/o of smoking; occasional intake of alcohol
- The patient had a stressful work life and involved outdoor projects
- The patient was also being pressurized by her parents for marriage; however, her looks made her feel sad and depressed

Family history

- Father / 58y / No history of baldness / No history of any other disease
- Mother / 55y / No hair complaints

General examination

- BMI – 27.3 kg/m²
- Vital signs – BP: 120/80 mm of Hg; Pulse: 79/min; Respiratory rate: 12 breaths/min
- Cardiovascular examination – Normal
- Respiratory examination – Normal
- Gastrointestinal examination – Normal
- Nails – Normal

Local examination

- Diffuse reduction of hair density over the crown
- Near complete preservation of frontal hair line
- The hair appeared short and dry
- Widening of the central hair parting
- Easy pluckability of hair
- Scalp appeared normal



The patient was asked to undergo some basic laboratory investigations.

Laboratory investigations

- CBC – Normal
- FBS – 80 mg/dL • Thyroid function tests - Normal

Diagnosis: Female pattern hair loss

Management

- Peptide therapy: The patient was advised to apply a solution containing Decapeptide-10, Oligopeptide-54 and Decapeptide-18 two times a day with regular follow ups every month
- The patient was counseled for her diet and was instructed to include adequate intake of fresh fruits and vegetables

On follow up after 4 months, the patient showed considerable improvement with reduction in hair loss. The crown area showed improvement in hair density.



Patented & Safe Hair Growth Biomimetic Peptides

For Men and Women
A Hair Revitalizing Program
Prevents Hair Loss,
Re-Growth of New Hair,
With No Side Effects

- CG-Nokkin (Oligopeptide-54)
- CG-WINT (Decapeptide-18)
- CG-Keramain 2 (Decapeptide-10)

In All Types of Non-Scarring Alopecia

R
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Hair Revitalizing Therapy

Advanced & Safe Hair Regrowth Therapy

