



Redefining Regenerative Medicine

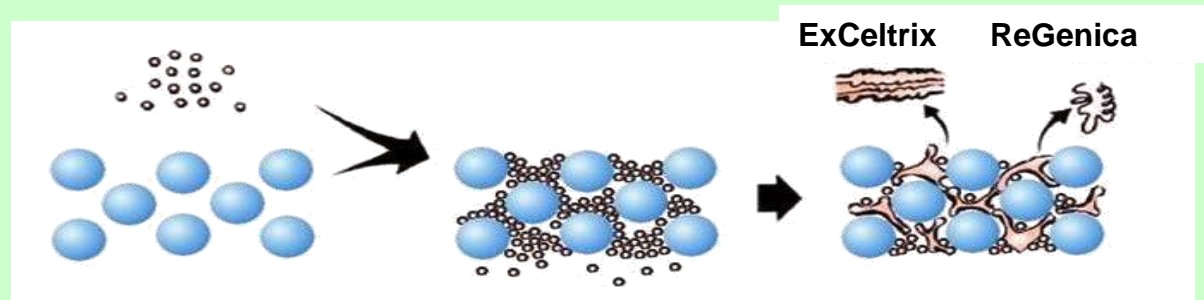
**A Novel Business Model for Regenerative
Medicine: Skin and Hair Aesthetics**

February 17,2008

Stem Cell Summit

Company Overview

- Regenerative medicine company
- Avoids controversial issues and problems
- One technology – Two outputs – Many products
- Initial business focus: aesthetic medicine with no reimbursement issues and clear regulatory paths

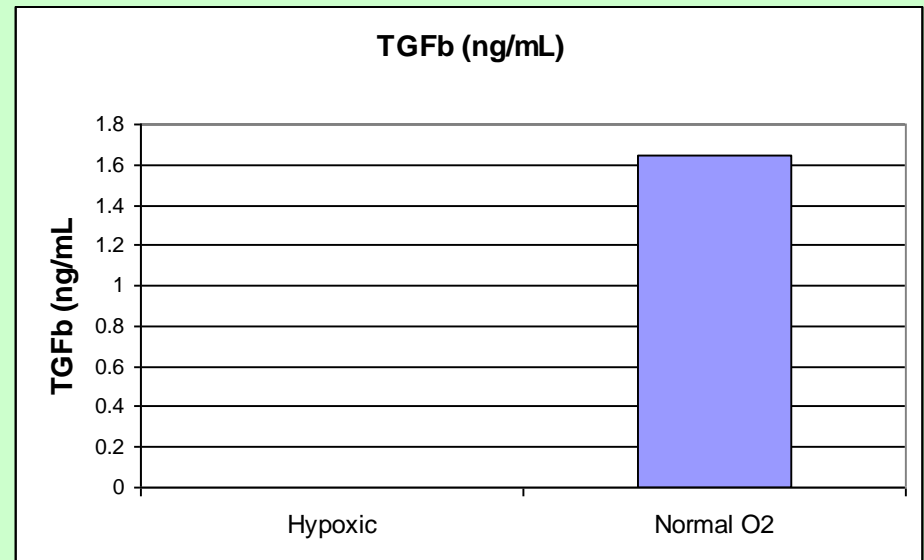
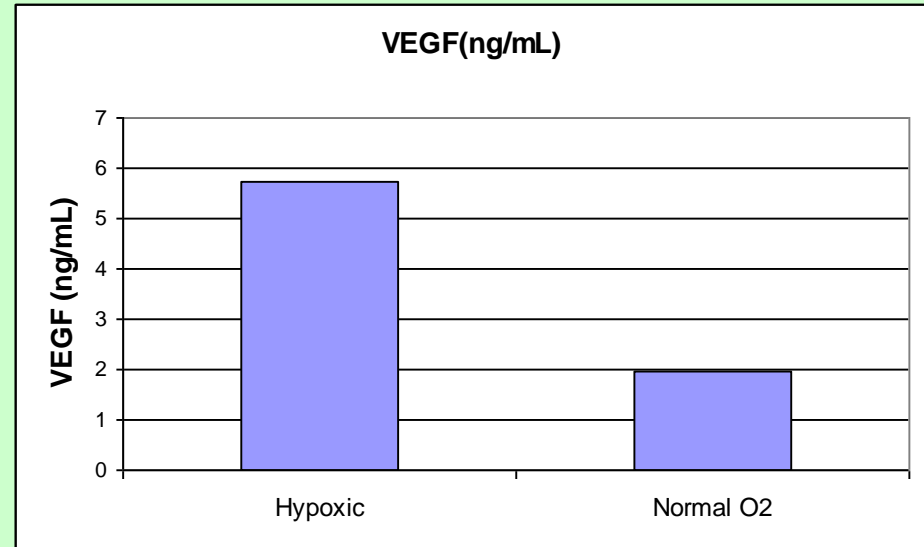


Hypoxia-induced Products

- **Embryonic extracellular matrix (ECM) creates an environment conducive to rapid cell proliferation and healing without the formation of scars or adhesions (similar to fetal mesenchymal tissue)**
- **Hypoxic (1-5% oxygen) and low gravity conditions stimulated cells to make embryonic matrix**
- **Gene chip array analysis showed the differential expression of over 5000 genes under the hypoxic versus traditional tissue culture conditions.**
- **Hypoxia up-regulates soluble factors, including growth factors and wnt proteins**

Effects of Hypoxia on Gene Expression

GENE	FOLD INC.	FOLD DEC.
Hypoxia-Inducible Factor (HIF1A)	14.78	
Hypoxia-Inducible Factor Inhibitor (HIF1AN)		4.9
VEGFB	4.33	
VEGFC	3.84	
TGFb1		3.9
TGFb2		6.7
KGF	11.51	



Products for Facial Aesthetic Market: 3 clinicals completed

ReGenica Facial Rejuvenation Complex: Post Resurfacing

-49 subjects 40-60 years – Double blinded, randomized

-41 subjects 40-60 years – Double blinded, randomized, LF/RT

- Clinical photography (3 blinded evaluations- dermatologists)
- TEWL (transepidermal water loss)
- Punch biopsy

ReGenica Advanced Rejuvenation Repair : Anti-aging

-26 subjects, 40-65 years – Double blinded , randomized

- Study duration - 10 weeks
- 2x day topical ReGenica Tx, or vehicle w/o ReGenica for 10 weeks
- Clinical photography (2 blinded cosmetic dermatologists)
- Corneometer-surface hydration
- Cutometer-elasticity
- Punch biopsy

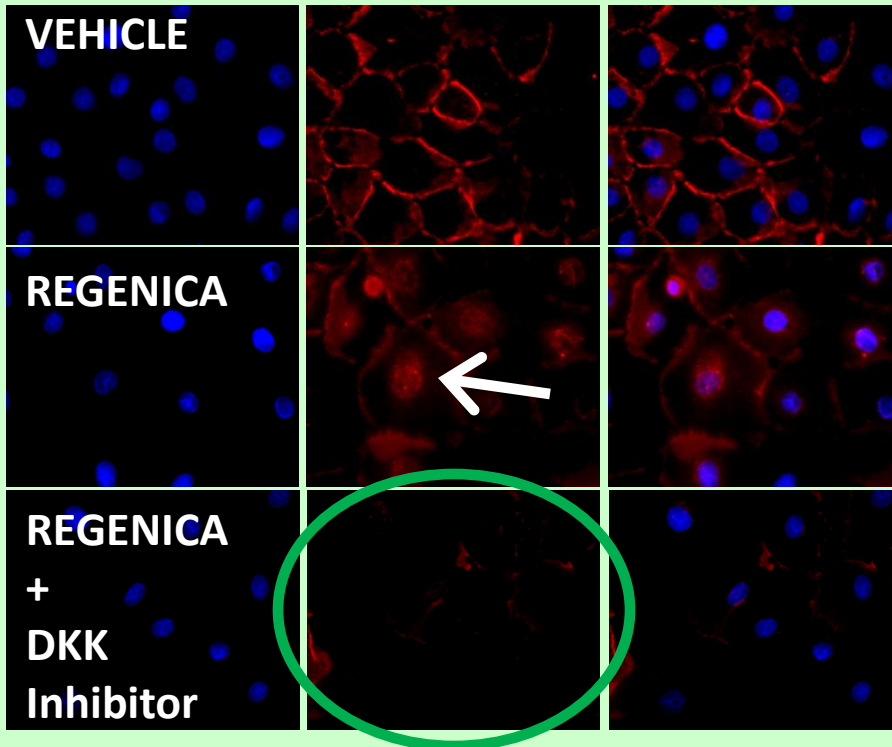
Affects of Hypoxia and 3D Culture on Gene Expression

GENE	FOLD INCREASE	FOLD DECREASE
COL4A1	17.2	
COL20A1	6.88	
COL19A1	5.22	
COL9A1	4.81	
COL10A1	4.45	
COL6A3	3.48	
COL9A2	2.48	
COL14A1	2	
SPARC	2.74	
COL1A2		3.45
COL13A1		4
COL18A1		4.76
COL1A2		7.14

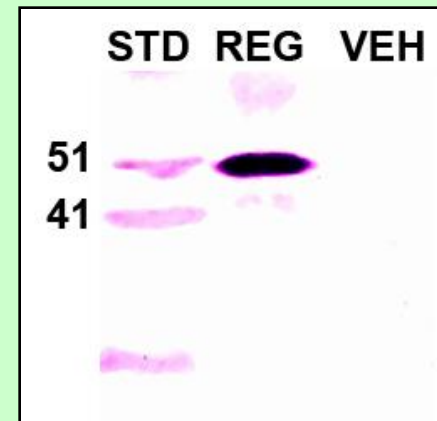
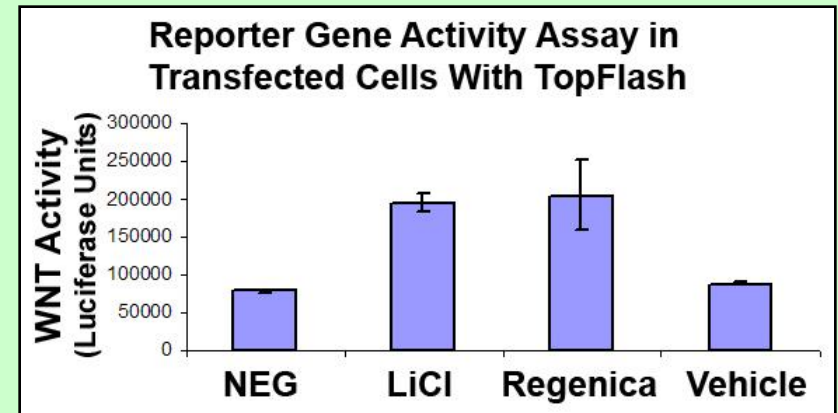
GENE	FOLD INCREASE	FOLD DECREASE
WNT4	5.94	
WNT7a	5.43	
WNT 7b	4.05	
WNT 2b	3.95	
WNT 10a	3.86	
WNT 8b	3.48	
WNT 6	3.36	
WNT 3a	3.19	
WNT 9b	3.06	
WNT 9a	3.02	
WNT 11	2.89	
WNT 5a		8.33
WNT 2		7.14
WNT 5b		5.26

Regenica Delivers Active Human WNT Proteins: Summary of Biochemical Characterization In Vitro

Nuclear beta-catenin localization and
Specific Inhibition with DKK1



Downstream Signaling of WNT-Responsive
TCF/Lef Promoter



Western Blotting for
human WNT7a
Protein in Regenica

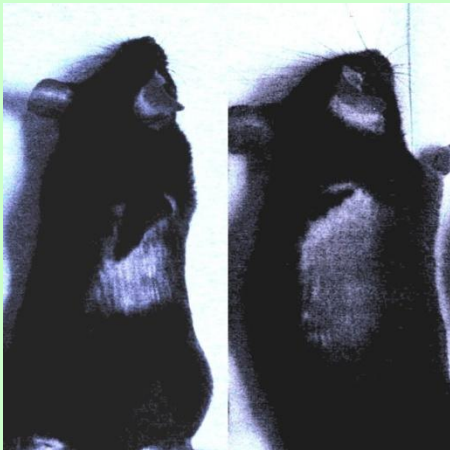
Potential Applications of Soluble Wnts

- Hair
 - *Wnt signalling maintains the hair inducing activity of dermal papilla, Kishimoto, Burgeson, and Morgan, Genes Dev 2000*
- Brain
 - *Axonal remodeling and synaptic differentiation in the cerebellum is regulated by Wnt-7a signalling, Hall, Lucas, and Salinas, Cell 2000*
 - *Presenilin function: connection to Alzheimers disease and signal transduction, Fraser, Yu, Nishimura, Yang, mount, Westaway, St. George-Hyslop, Biochem Soc Symp 2001*
- Cardiac
 - *Wnt-11 promotes cardiac tissue formation of early mesoderm, Eisenberg, and Eisenberg, Dev Dyn 1999*

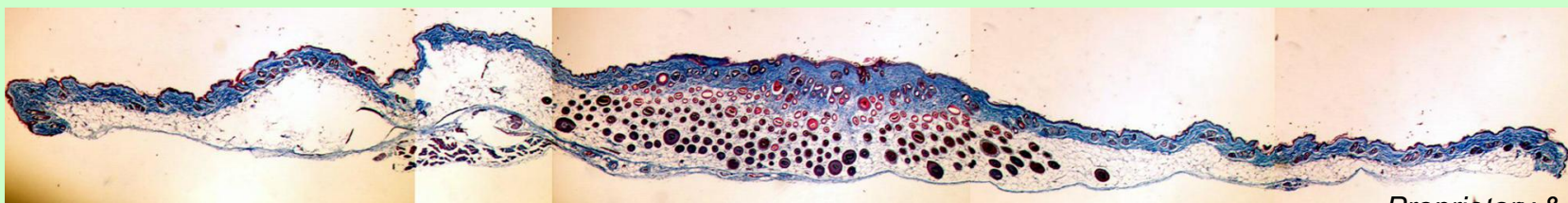
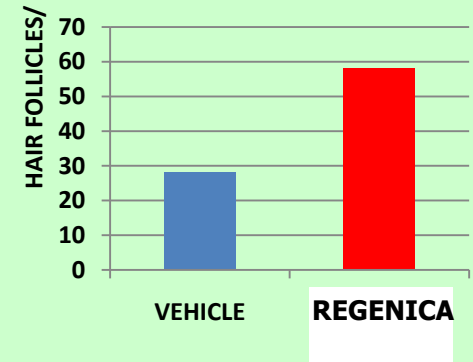
Histogen

Evaluation of ReGenica for WNT Activity In Murine Skin

- Mice were injected with a single 0.1 ml dose of ReGenica
- Hair growth induction at injection site apparent in 10 to 14 days
- Histological evidence of follicular neogenesis
- Epidermal stem cell response consistent with wnt activity



Evidence Of Hair Follicle Neogenesis



Hair Growth Trial: De novo Follicular Hair Regeneration

- **24 subjects – Male Pattern Hair Loss (MPHL) 18-45 years**
- **No prior invasive, minimally invasive topical scalp Tx, Minoxidil, Finasteride**
- **PI's Drs Craig Ziering, David Perez-Meza, CRO SymBio, Port Chester, NY**
- **Laser - Palomar Starlux 550p 1540-non-ablative, 2940 ablative**
- **Study duration-upwards to 12 months for follow-up, baseline, and 5 months (following single sc injection)**
- **3 day wash-out - can use only Cetaphil Shampoo throughout study**
- **Combination of lasing, microdermabrasion prior to injection**
- **Tx ReGenica, vehicle w/o ReGenica, and saline**

Endpoints:

- **7 point clinical grading system (3 blinded hair transplant surgeons)**
- **Clinical macrophotography (follicle counts)**
- **2mm punch biopsies**
- **Subject self assessment questionnaire**

Subject 014 Global

Baseline

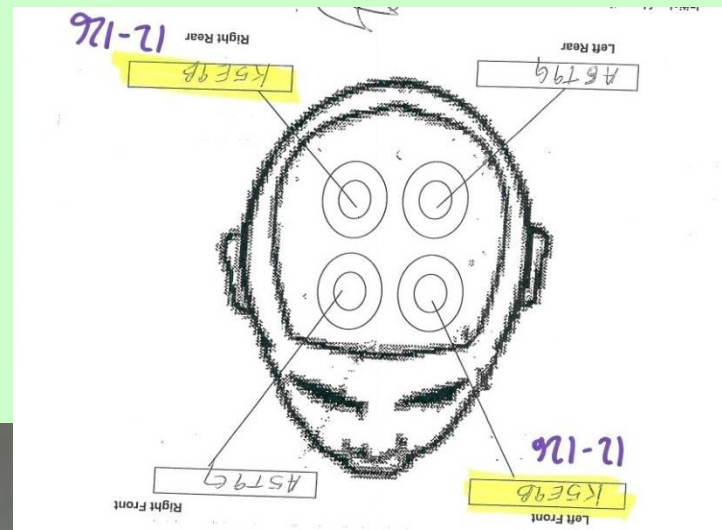


08_HIS003_HON_0811182107_FFI_119

12 week



08_HIS003_HON_0902051706_FFI_481



Subject 14 Left Anterior (Active; No Perturbation)

Baseline



08_HIS003_HON_0811182156_FFI_126

12 week



08_HIS003_HON_0902051909_FFI_494

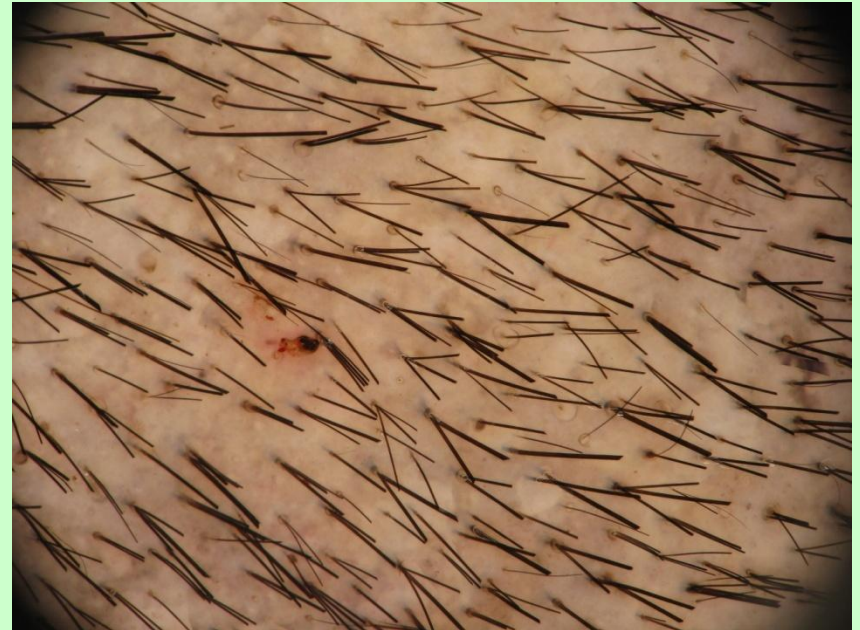
Subject 014 Right Posterior (Active; Perturbation)

Baseline



08_HIS003_HON_0811182154_FFI_125

12 week



08_HIS003_HON_0902051902_FFI_493



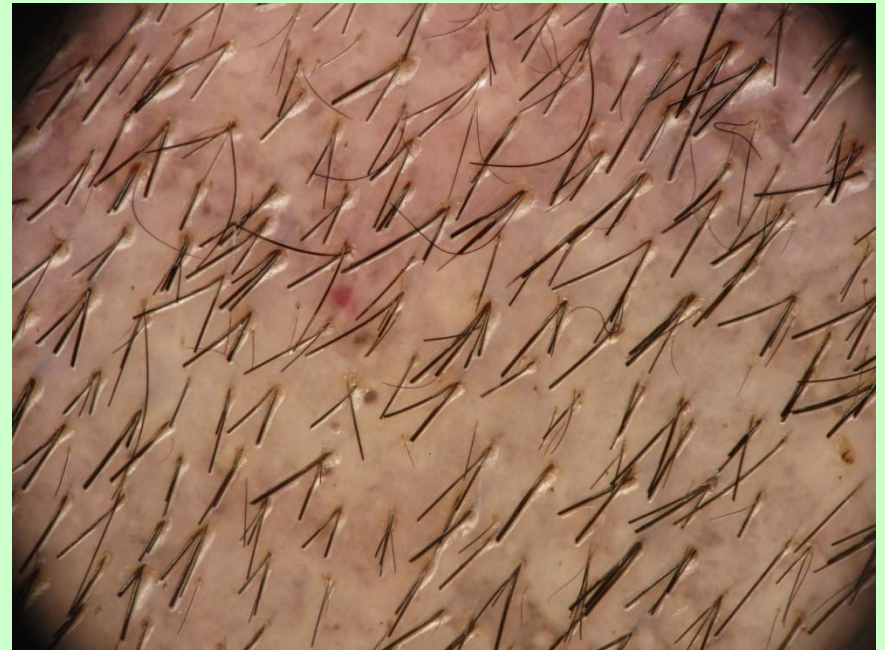
Subject 006 – Left Anterior (Active; No Perturbation)

Baseline



08_HIS003_HON_0811181351_FFI_60

12 week



08_HIS003_HON_0902051531_FFI_472



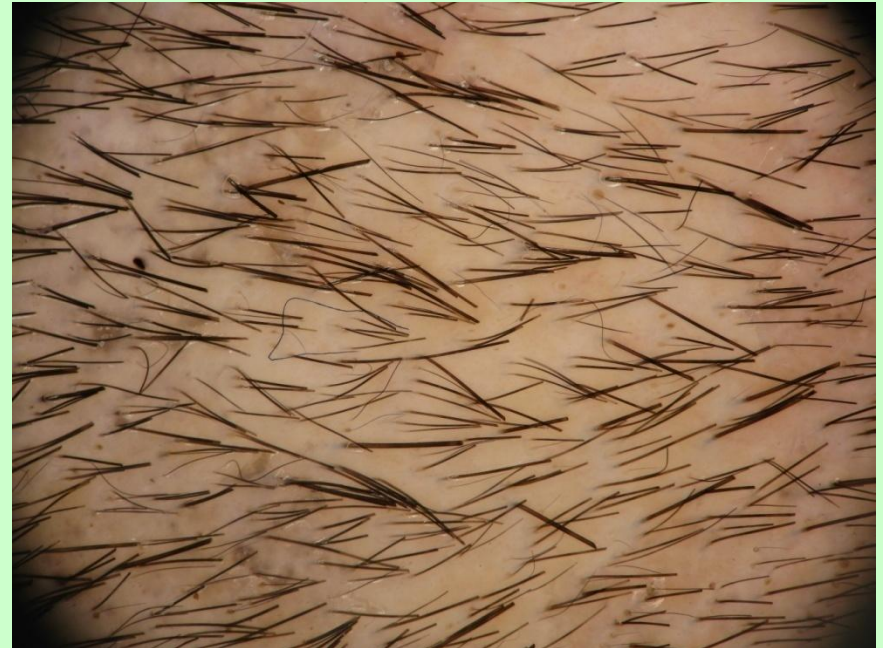
Subject 007 – Right Anterior (Active; No Perturbation)

Baseline



08_HIS003_HON_0811181414_FFI_65

12 week



08_HIS003_HON_0902050931_FFI_437

Histogen

Subject 20- Active Treatment Zone



Subject 20 at Baseline (RR)



Subject 20 at Week 12 (RR)

Treatment: Ablative Laser + Active

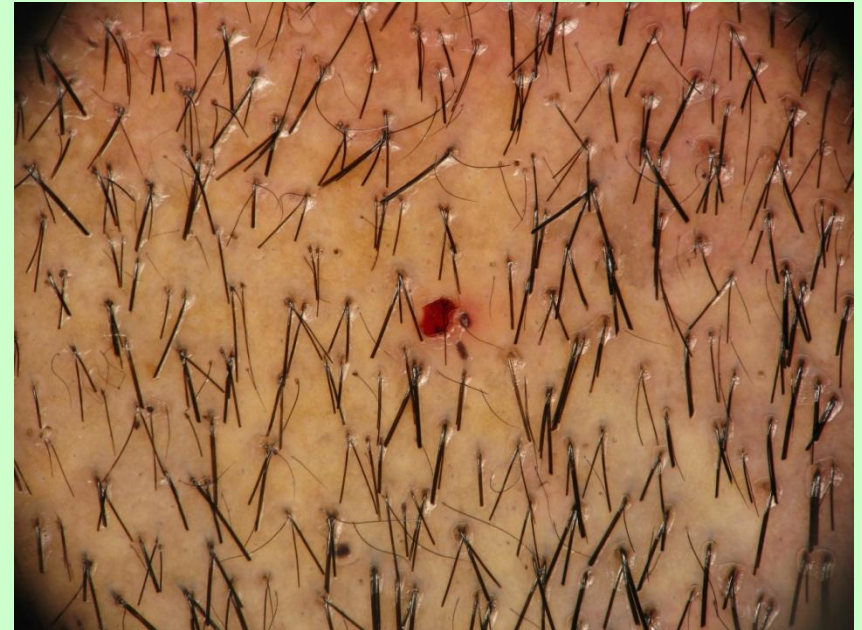
Subject 16 Left Anterior (Active; No Perturbation)

Baseline



08_HIS003_HON_0811191423_FFI_158

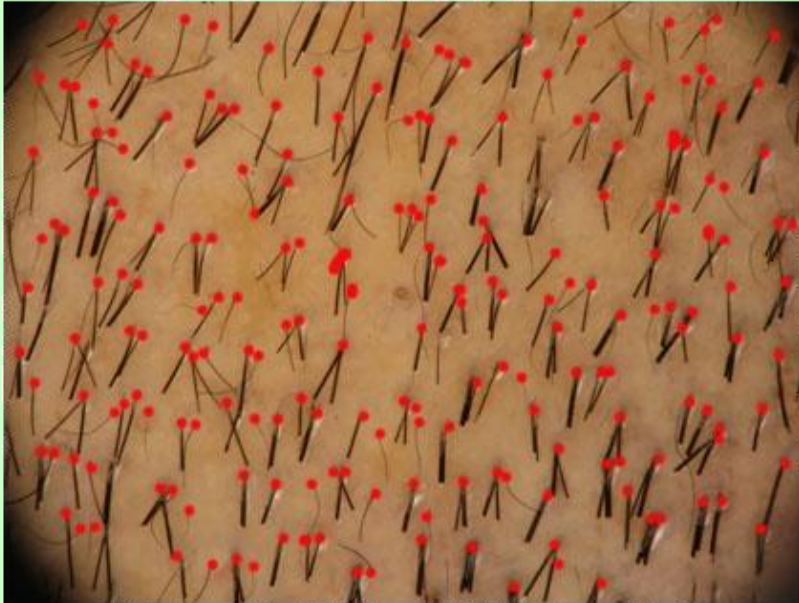
12 week



08_HIS003_HON_0902061245_FFI_514

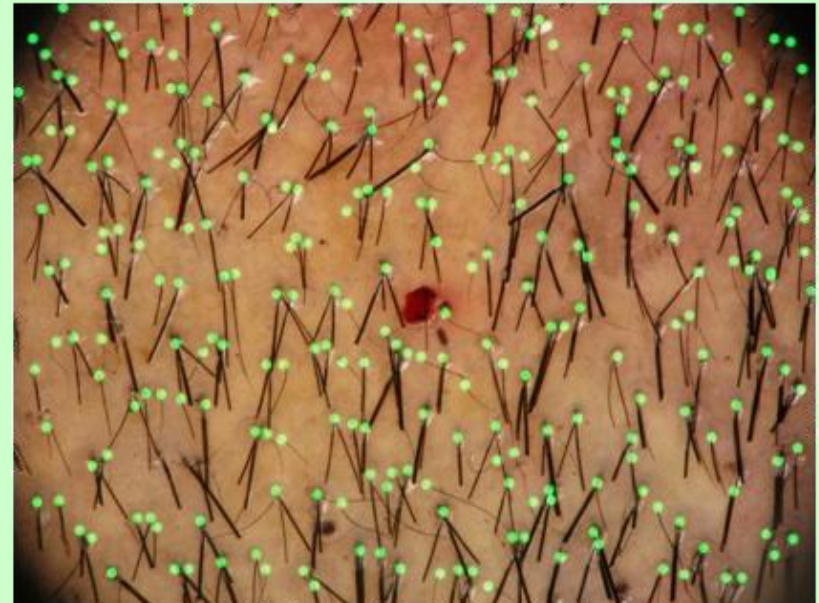
Histogen

BASELINE- 217



08_HIS003_HON_0811191423_FFI_158

12 WEEKS- 265



08_HIS003_HON_0902061245_FFI_514

Analysis:

Individual follicular units were counted, and this subject increased the number of apparent hair follicles from 217 to 265. Total hair counts showed an increase from 307 to 360 This is approximately a 20% increase overall.

Next Steps in Hair Growth

- **5 month follow up**
 - **Clinical macrophotography (follicle counts)**
 - **2mm punch biopsies**
 - **Subject self assessment questionnaire**
- **Meeting with FDA- CBER**
- **Series B financing for establishment of GMP manufacturing facility completion/validation**
- **Clinical trial for use of ReGenica for maintenance of hair follicle retention post transplantation**
- **Clinical trial for topical application of ReGenica-hair growth and thickening**
- **US Phase I/II clinical trial for hair growth stimulation**