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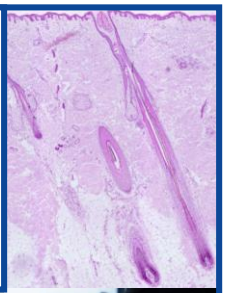
A QIMA Life Sciences Company

All about skin and hair bioscience!

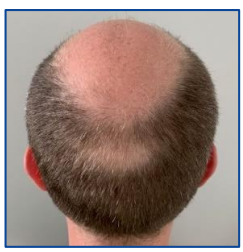
State-of-the-art technology and expertise for all your pre-clinical, mechanistic, and clinical needs in dermatology research.

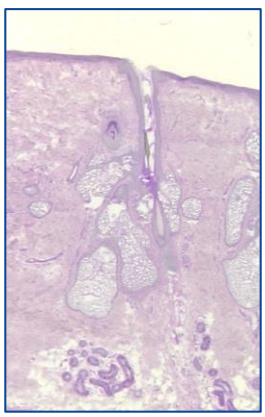


- Pre-clinical Research
- Clinical Research
- Education

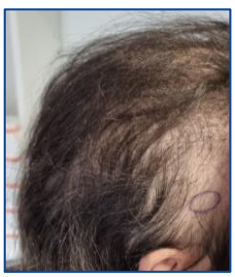
Male and Female Pattern Hair Loss

male pattern hair loss





female pattern hair loss



"We combine our unique expertise, our project design creativity, and our passion to advance our clients' success in delivering novel and game-changing skin and hair research solutions"

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Dr. Marta Bertolini

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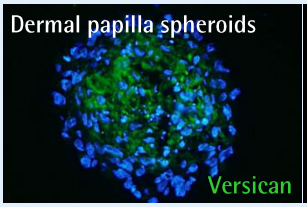
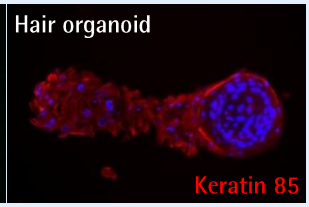
In vitro models to investigate potential beneficial effects of therapeutics on pathologic features in male and female pattern hair loss

Analysis of dermal papilla function *in vitro*

1) reduced dermal papilla inductivity
2) decreased secretion of morphogens by dermal papilla fibroblasts





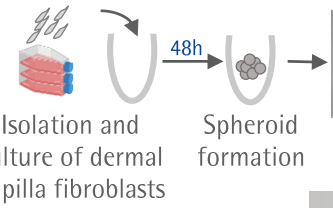
Our **methods:** 3D in vitro culture of primary dermal papilla fibroblasts spheroids (middle) or hair organoids (right)

Read-Out Parameters: Alkaline phosphatase activity (*in situ* enzymatic activity); Versican-, Noggin-, HGF expression; activation of signaling pathways involved in hair growth (e.g. Wnt/beta-catenin-, BMP-, Shh signaling); ....

Study Examples

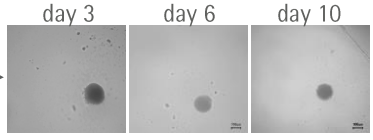
Compound X increases dermal papilla fibroblast inductivity in spheroids *in vitro*

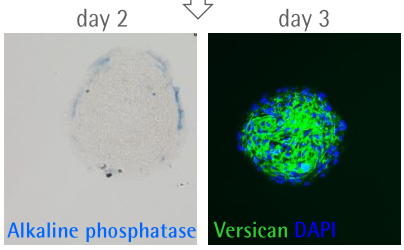
Experimental model: Spheroid formation



Isolation and culture of dermal papilla fibroblasts

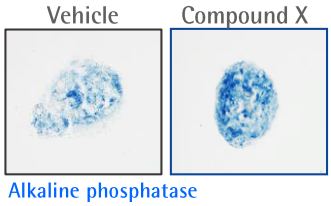
Spheroid formation



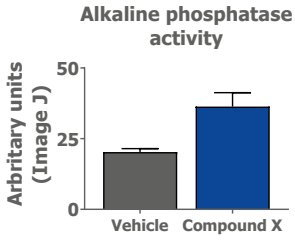


Spheroids show versican expression and alkaline phosphatase activity

Keeping dermal papilla spheroids in culture (up to 10 days).

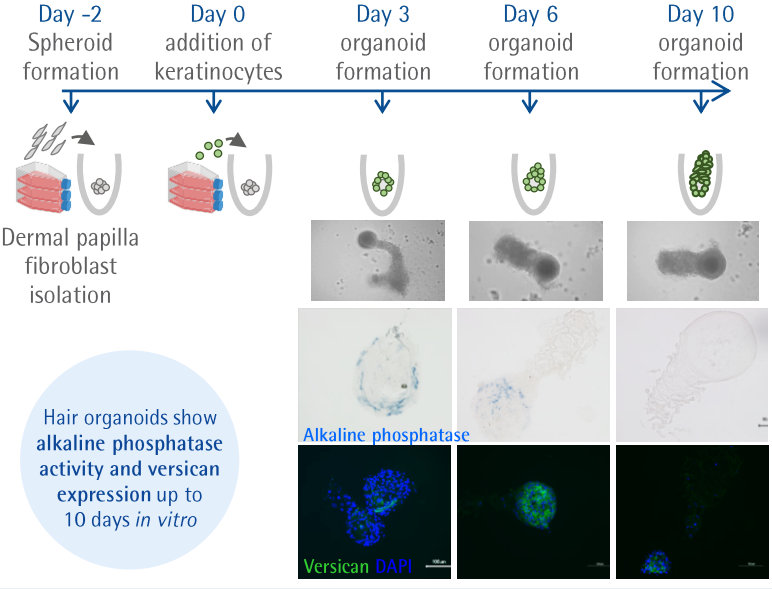


Alkaline Phosphatase and Versican expression: Marker for dermal papilla inductivity

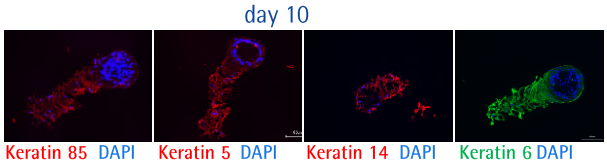


Mean±SEM, n=2-4 dermal papilla spheroids/group from 1 donor

Hair organoids maintain dermal papilla characteristics *in vitro*



Hair organoids show **alkaline phosphatase activity and versican expression** up to 10 days *in vitro*



Spheroids and organoids allow for comprehensive compound testing *in vitro* ...

... and provide a valid model to investigate complex 3D cell-cell interactions

Organoids express keratins after 10 days *in vitro*

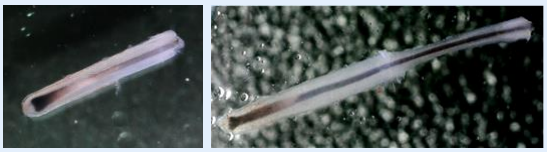
Bertolini et al. *Stem Cell Biol and Reg Med* (2022); Piccini et al. *J. Invest. Dermatol.* Suppl. (2019); Hawkshaw et al., *PloS Biol* (2018); Ahmed et al., *J Cell Biol.* (2014); Samuelov et al., *J Invest Dermatol* (2012)

Ex vivo models to investigate potential beneficial effects of therapeutics on pathologic features in male and female pattern hair loss

Analysis of healthy human hair follicle functions *ex vivo*

1) Hair shaft production
2) Hair cycle analysis
3) Dermal papilla fibroblast emigration
4) Reduced dermal papilla fibroblast inductivity
5) Reduced stem cell activity and progeny

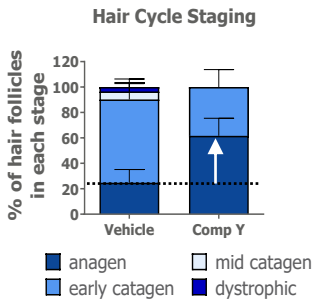
Piccini et al., *Nutrients* (2022); Campiche et al., *Int J Cosmet Sci.* (2022); Mardaryev et al., *J Invest Dermatol* (2021); Bertolini et al., *Br J Dermatol* (2021); Lisztes et al., *J Invest Dermatol* (2020); Alam et al., *Br J Dermatol* (2020); Chéret et al., *Nat Commun* (2018)

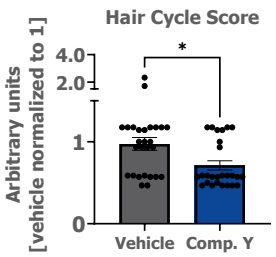


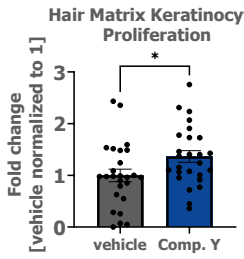
Our **methods**: Isolation and culture of healthy hair follicles *ex vivo*. Amputated microdissected hair follicle at day 0, after isolation (left). Amputated microdissected hair follicle at day 6 of organ culture with newly formed hair shaft and outer root sheath (right)

Study Examples

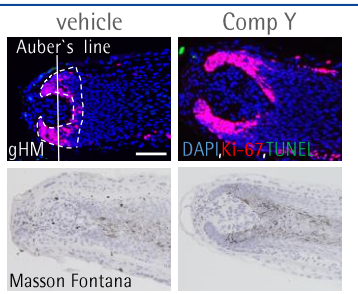
Compound Y prolongs anagen phase by enhancing DP inductivity, reducing DP fibroblast emigration and increasing HF stem cell progeny in female hair follicles *ex vivo*



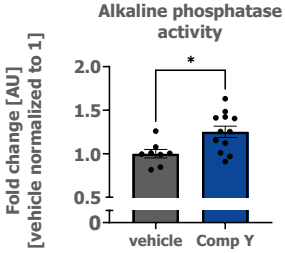




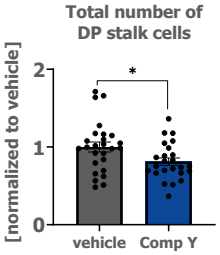
Mean±SEM n=23-29HFs/group from 4 donors



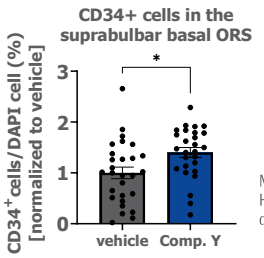
Ki-67/TUNEL immunostainig (proliferation/apoptosis) and Masson Fontana histochemistry (melanin content)



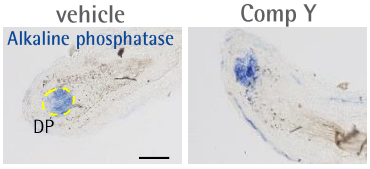
Mean±SEM n=8-11 HFs/group from 4 donors, *p < 0.05



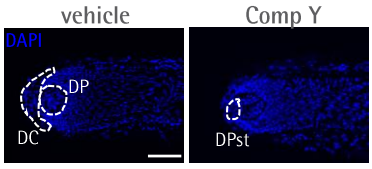
Mean±SEM n=21-29 HFs/group from 4 donors, *p < 0.05



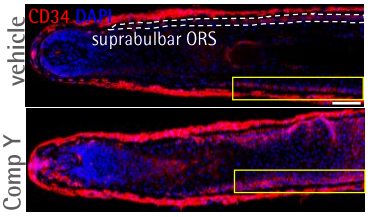
Mean±SEM n=21-29 HFs/group from 4 donors, *p < 0.05



Alkaline phosphatase activity in situ showing dermal papilla (DP) inductivity

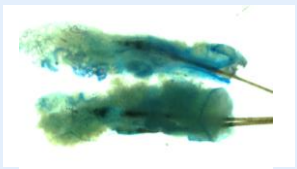


DAPI staining cell nuclei present in the dermal cup (DC), dermal papilla (DP) and DP stalk (DPst)

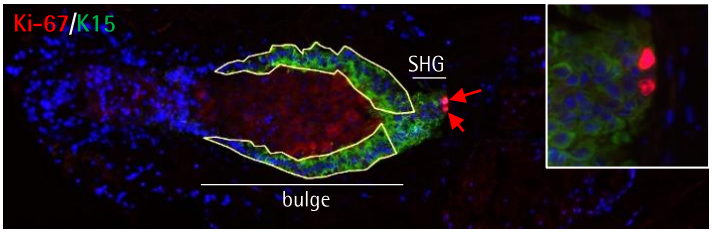


CD34 staining of the HF stem cell progeny in the suprabulbar outer root sheath

Isolation of telogen hair follicles from healthy donors



Our **methods**: isolation of telogen hair follicles from healthy donors (methylene blue staining).



Bulge area of telogen hair follicle. Ki-67: proliferation marker K15: stem cell markerSHG: secondary hair germ

1) Hair follicle stem cell proliferation
2) Expression of Wnt ligands
3) Analysis of signlling pathways associated with anagen induction

Hernandez et al., *J Am Acad Dermatol.* (2018)

Ex vivo models to investigate potential beneficial effects of therapeutics on pathologic features in in male and female pattern hair loss

Analysis of healthy human scalp skin functions *ex vivo*

1) Hair cycle analysis
2) Hair follicle miniaturization
3) Dermal papilla fibroblast emigration
4) Reduced dermal papilla fibroblast inductivity
5) Reduced stem cell activity and progeny

Our **methods:** human scalp skin e*x vivo* culture (left); different drug delivering modes are possible, including **topical** (middle), **systemic** (right) or **intradermal** (not shown) application.

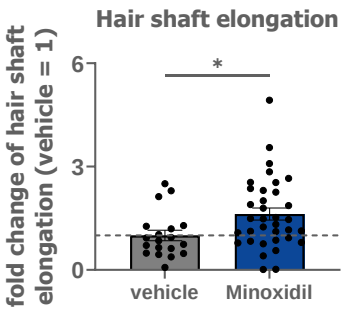
Read-Out Parameters: Hair follicle growth, hair shaft elongation, anagen (growth phase) maintenance, catagen (regression phase) induction, proliferation and apoptosis of hair matrix keratinocytes, dermal papilla fibroblast emigration, activation of signaling pathways involved in hair growth; production of hair follicle morphogens, ...

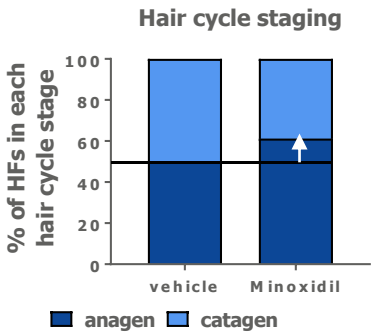
Edelkamp et al., *Skin Pharmacol Physiol* (2023); Alam et al., *Br J Dermatol.* (2020) Hawkshaw et al., *PloS Biol* (2018); Ahmed et al., *J Cell Biol.* (2014); Samuelov et al., *J Invest Dermatol* (2012)

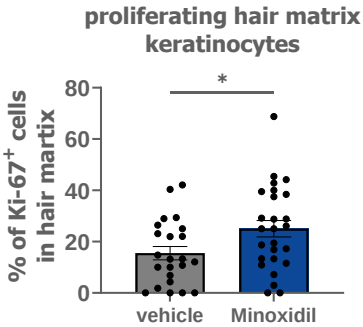
Study Examples

Topical application of Minoxidil promotes hair shaft elongation, prolongs anagen phase and induces hair matrix keratinocyte proliferation *ex vivo*

Minoxidil: FDA approved drug



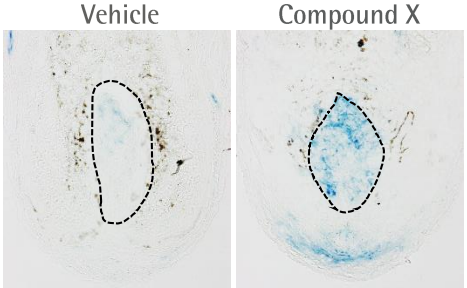




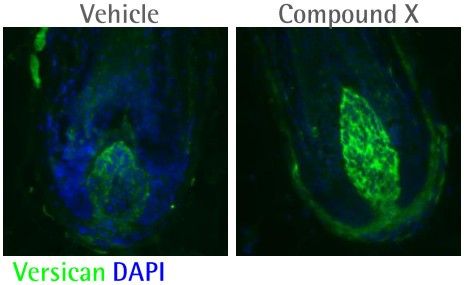
Mean±SEM, n=19-25 hair follicles/group from 2 donors, Mann Whitney test, *p<0.05.

Mean±SEM, n=24-26 hair follicles/group from 2 donors, Mann Whitney test, *p<0.05.

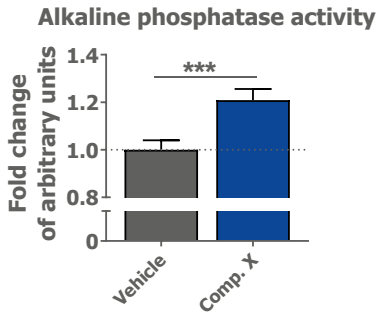
Compound X increases dermal papilla fibroblasts inductivity *ex vivo* and stimulates Wnt signaling

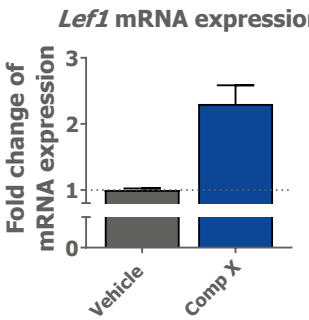


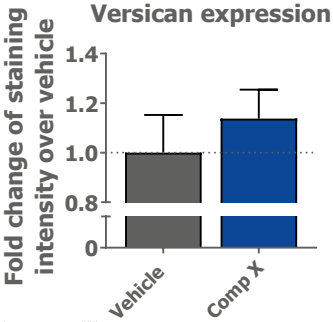
Alkaline phosphatase



Versican DAPI







Mean±SEM, n= 3-12 HFs/group from 3 donors.

Mean±SEM, n=16-22 hair follicles/group from 1 or 3 donors, Mann Whitney test, ***p<0.001.

Investigating and characterizing affected and non-affected hair follicles from male pattern hair loss patients

Analysis of lesional scalp skin samples or follicular units from AGA patients *in situ*

Our **methods:** isolation of hair follicular units from healthy donors (left) or isolation of follicular unit from balding area of AGA patients (right)
→ induction of hair follicle dysfunction
(+/- testing compound)

Read-Out Parameters:
Hair follicle miniaturization characterized by the number of fibroblasts in the dermal papilla, the dermal cup and dermal stalk; size of the dermal papilla; size of the hair bulb; activation of signaling pathways involved in telogen-to-anagen conversion, transcriptome and proteome analysis, cytokine release, ...

green: vertex scalp
→ affected scalp

pink: occipital scalp
→ non-affected scalp

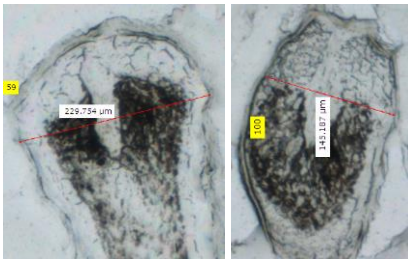
Characterization of hair follicle miniaturization

Occipital scalp (non-affected)

Vertex scalp (affected)

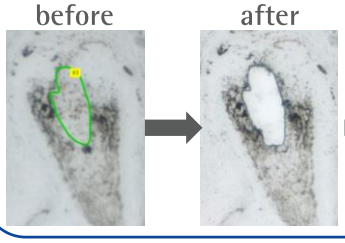
Organ-culture (up to 7 days)

terminal HF (non-affected) | intermediate HF (affected)

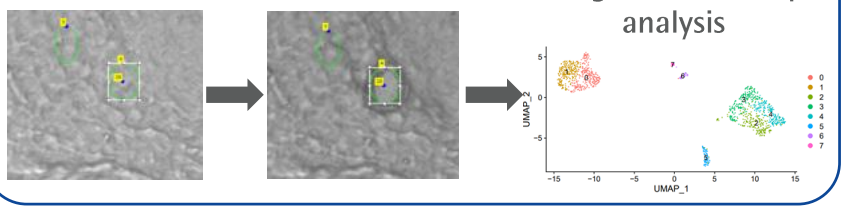


Laser Capture Microdissection (LCM) to select hair follicle compartments or single cells

before | after → bulk RNAseq analysis

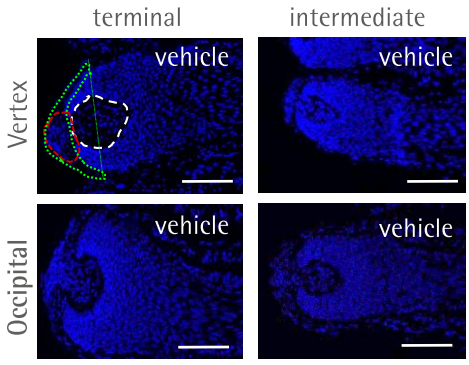


before | after → single cell RNAseq analysis

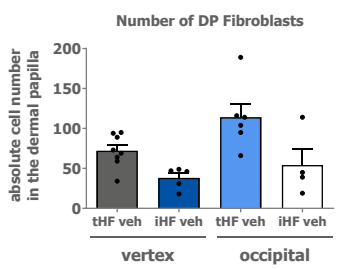


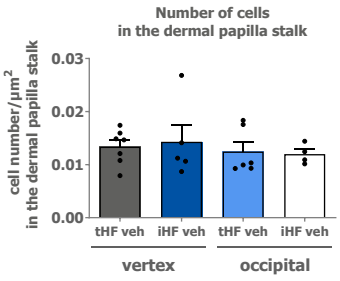
Study Example

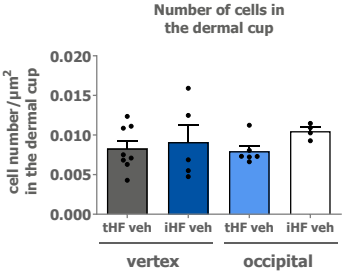
Ex vivo organ culture of affected hair follicles to examine emigration of dermal papilla fibroblasts



White dotted line: dermal papilla
Red line: dermal papilla stalk
Green dotted line: dermal papilla cup







Mean±SEM n=4–8 HFs analysed/group.

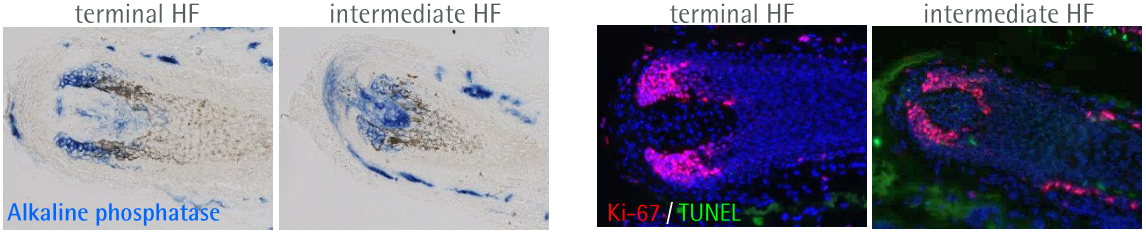
Investigation and quantification of hair follicle miniaturization allows for comprehensive testing of your compound

Investigating the effects of therapeutics in affected and non-affected hair follicles from male pattern hair loss patients

Study Example

Effect of testosterone treatment on affected terminal vs. intermediate hair follicles

terminal HF | intermediate HF | terminal HF | intermediate HF



→ Investigate the effect of testosterone on affected HFs by analysis of dermal papilla and dermal cup cell number, changes in the hair cycle, effect on dermal papilla inductivity, changes in gene expression (bulk RNAseq, *in situ* hybridization), and changes in secretory profiles (ELISA)

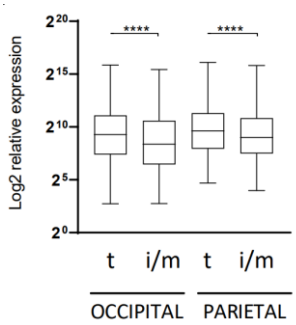
Investigating and characterizing the metabolomic phenotype of affected and non-affected hair follicles from female pattern hair loss patients

Study Example

Intermediate Hair Follicles from Patients with Female Pattern Hair Loss Are Associated with Nutrient Insufficiency and a Quiescent Metabolic Phenotype

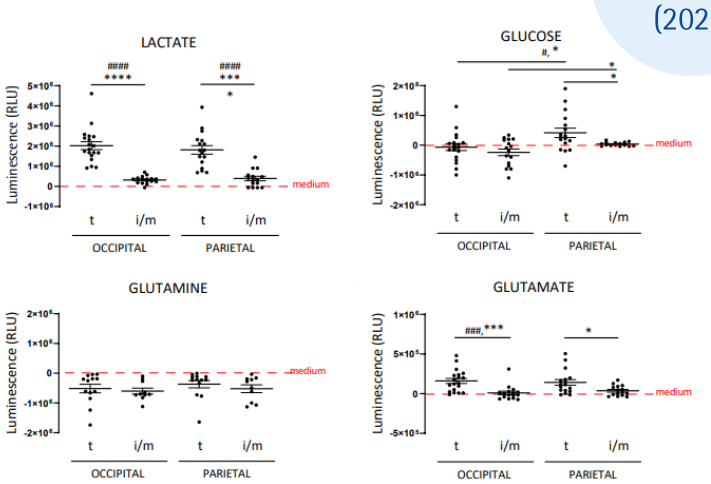
Piccini et al. *Nutrients* (2022)

1) Intermediate HFs have a significantly lower abundance of metabolites, analyzed by UPLC–MS



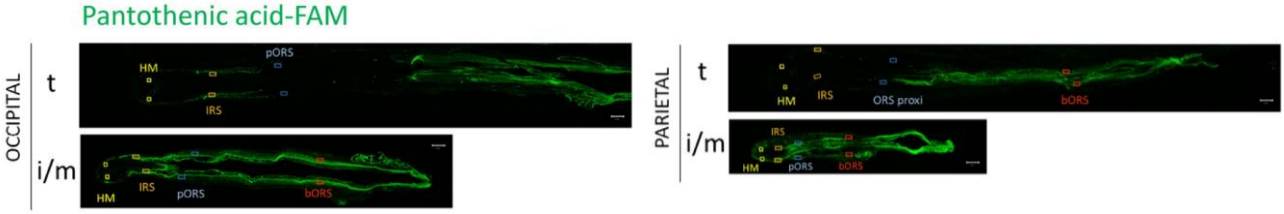
Log2 average relative expression of n=141 identified metabolites in at least 2 patients in terminal (t) and intermediate/miniaturized (i/m) hair follicles from occipital and parietal scalp skin samples from n=3 FPHL donors.

2) Intermediate FPHL HFs have a lower metabolic activity ex vivo



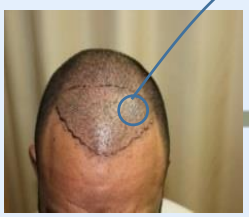
Metabolite concentrations were measured in the culture medium after 24h *ex vivo*. Mean+SEM n=9–19 HFs/ group from n=3–4 FPHL donors. Red dotted lines indicate amount in the blank, non-conditioned, WCM culture medium.

3) Intermediate FPHL HFs are able to absorb fluorescent labeled metabolites ex vivo



Terminal hair follicles (t) from FPHL occipital and parietal scalp skin and of intermediate/ miniaturized hair follicles (i/m) from FPHL parietal scalp skin absorb Pantothenic acid-FAM (green).

Pre-clinical Research: Humanized mouse model for male and female pattern hair loss



Initiation of the treatment

8 days

12 weeks

8 weeks or more

Hair regrowth

Vellus to terminal conversion

Our **methods:** Xenotransplantation of balding human scalp skin on immune-deficient SCID mice. After 12 weeks, hair regrowth occurs and 8 weeks later, vellus to terminal hair conversion can be observed under treatment.

long-term *in vivo* observations allow for ...

... unique investigation of

1) Hair regrowth

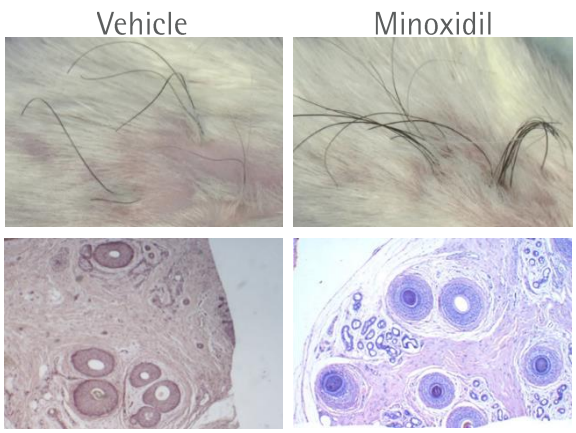
2) Vellus to terminal conversion

Analysis of preventive or therapeutic effects of test agents on hair physiology and pathology *in vivo*

Read-Out Parameters: Number of hairs per xenograft, terminal to vallus ratio, anagen to telogen ratio...

Study Example

Validation of the humanized mouse model formale pattern hair loss using Minoxidil to induce hair growth

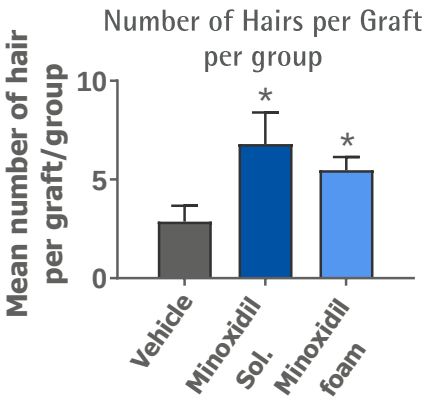


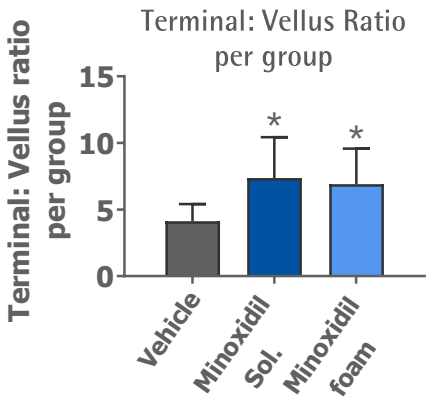
highly clinically relevant

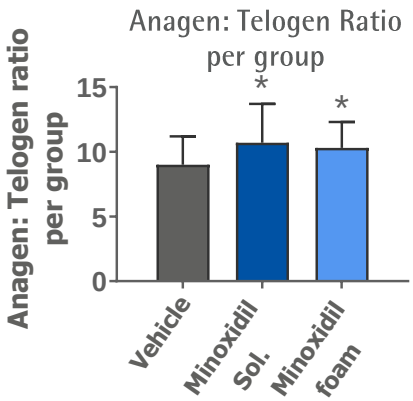
quantifiable read-out parameters

Selection of our publications:

Gilhar et al., *Acta Derm. Venerol* (2023);
Gilhar et al., *Exp. Dermatol* (2022);
Laufer Britva et al., *Br J Dermatol* (2021)







In collaboration with **Prof. Amos Gilhar,** Skin Research Laboratory, Rappaport Faculty of Medicine, Technion -Israel Institute of Technology, Haifa, Israel.

WHY US?

Our **vision** is to provide our clients and partners with the highest quality research in investigative dermatology and trichology – from basic science to translational applied and contract research of high relevance for clinical applications.

Great network of dermatologists and plastic surgeons collecting samples from healthy and diseased skin

World-class scientific leadership & international team

Clinically-relevant *ex vivo* and *in vivo* models

Strong academic background & publication record

What we can do for our clients:

- **Conceptualize & build proof-of-concept studies**
- **Carry out full service portfolio for pre-clinical skin & hair research** (*in vitro*/*ex vivo* assays, and humanized mouse models)
- **Investigate side effects in the skin or hair follicle**
- **Establish novel cutting edge methodologies and techniques**
- **Design tailor-made & customized assays for all needs**
- **Identify, characterize, or validate novel targets and therapeutics for skin & hair disorders**
- **Discover mechanistic action stories, biomarkers & predictors of response**
- **Conduct investigator initiated skin & hair clinical trials**
- **Provide access to human healthy & diseased skin and hair specimen**
- **Prepare comprehensive project reports & manuscript drafts**

Our ambition is to establish and refine research techniques: Advanced Methodology Program

Global client list & testimonials

Investigative dermatology: Acne Vulgaris, Atopic Dermatitis, Psoriasis, Alopecia Areata, Androgenic Alopecia, Hidradenitis Suppurativa, Vitiligo, Chronic Itch, Prurigo Nodularis, etc.

Biobank: Full access to skin & hair samples (patients & healthy subjects)

Exceptional state-of-the-art research technology

We are supported by **world-wide recognized experts** in dermatology

Monasterium Laboratory Skin & Hair Research Solutions GmbH was founded in 2015 by **Prof. Ralf Paus**, MD, FRSB.