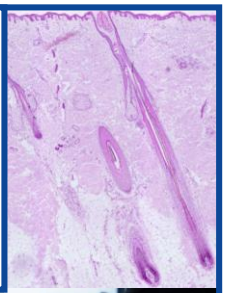
MONASTERIUM LABORATORY
A QIMA Life Sciences Company

All about skin and hair bioscience!

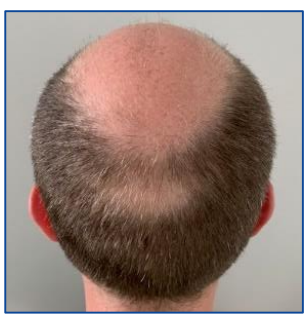
State-of-the-art technology and expertise for all your pre-clinical, mechanistic, and clinical needs in dermatology research.

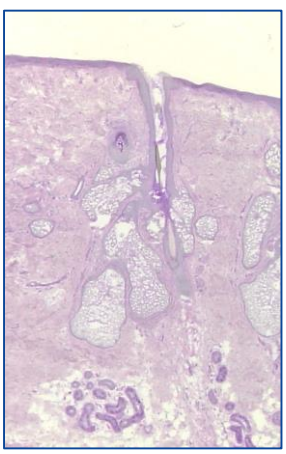


- Pre-clinical Research
- Clinical Research
- Education

Androgenetic Alopecia

male 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"

Founder & CEO:
Prof. Dr. Ralf Paus

Monasterium Laboratory
Skin & Hair Research Solutions GmbH

Mendelstr. 17, 48149 Münster, Germany
Phone: +49 (0) 251 93264-458
Fax: +49 (0) 251 93264-457

Founder & CEO: **Prof. Dr. Ralf Paus**

www.monasteriumlab.com

For enquiries, please contact:

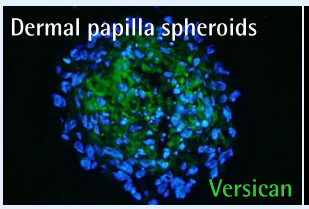
CSO & Deputy General Manager:
Dr. Marta Bertolini (PhD)

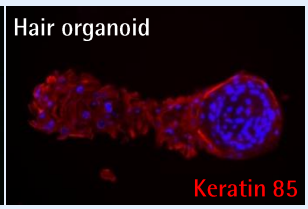
m.bertolini@monasteriumlab.com
+ 49 (0)251 93263-080

In vitro models to investigate potential beneficial effects of therapeutics on pathologic features in AGA

Studying AGA related dermal papilla dysfunction *in vitro*

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





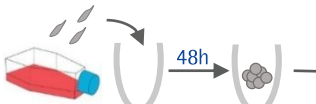
Our **methods:** 3D in vitro culture of primary dermal papilla fibroblasts spheroids (middle) or hair organoids (right)

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); production of hair follicle morphogens, ...

Study Examples

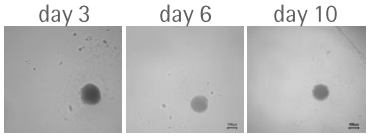
Compound X increases dermal papilla fibroblast inductivity in spheroids *in vitro*

Experimental model: Spheroid formation

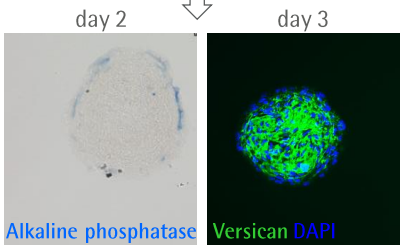


Isolation and culture of dermal papilla fibroblasts

Spheroid formation

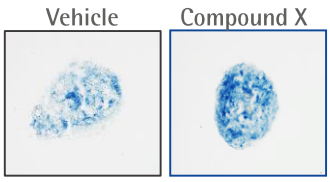


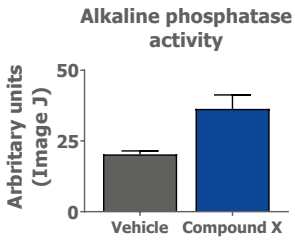
Keeping dermal papilla spheroids in culture (up to 10 days).



Spheroids show **versican expression** and **alkaline phosphatase activity**

Alkaline Phosphatase and Versican expression: Marker for dermal papilla inductivity

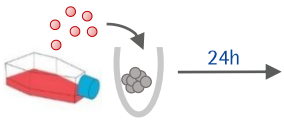




Mean±SEM, n=2-4 dermal papilla spheroids/group from 1 donor

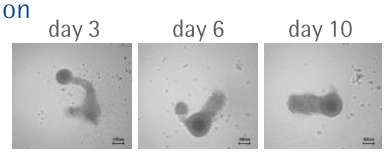
Hair organoids maintain dermal papilla characteristics *in vitro*

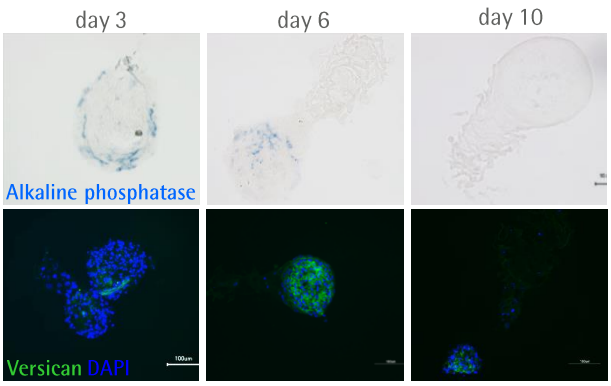
Experimental model: Organoid formation



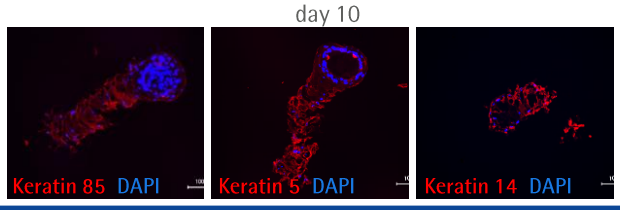
Addition of (epidermal) keratinocytes to DP spheroids

Organoid formation





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



Organoids express a variety of keratins after 10 days *in vitro*

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

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

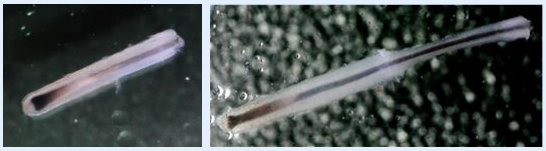
Selection of **our publications:**

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 AGA

Studying AGA related hair follicle dysfunction *ex vivo*

1) premature catagen development
2) dermal papilla fibroblast emigration
3) reduced dermal papilla fibroblast inductivity
4) reduced stem cell activity and progeny

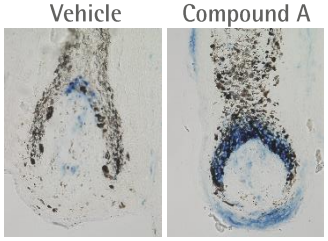


Our **methods:** Isolation and culture of healthy hair follicles *ex vivo*. Amputated microdissected hair follicle at day 0, after isolation (left). Amputated microdissected hair follicle at day 6 of organ culture with newly formed hair shaft and outer root sheath (right)

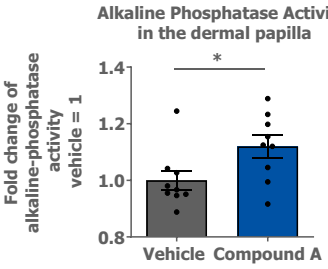
Read-Out Parameters: Hair follicle growth, hair shaft elongation, anagen (growth phase) maintenance, catagen (regression phase) induction, proliferation and apoptosis of hair matrix keratinocytes, number of stem cells, stem cell proliferation and apoptosis, stemness associated keratins, ...

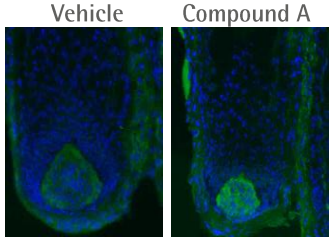
Study Examples

Application of Compound A results in increased dermal papilla inductivity

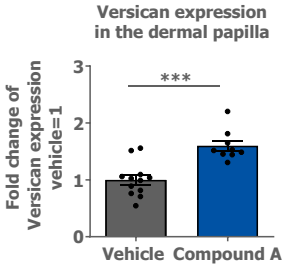


Alkaline Phosphatase



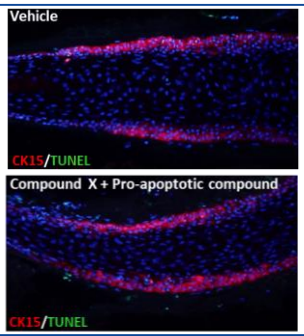


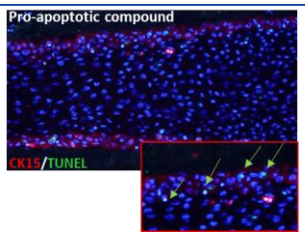
Versican DAPI



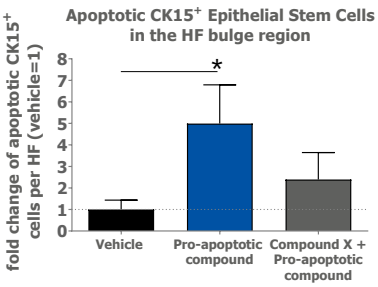
Mean±SEM n=9-12 HFs analysed/group from 3 donors. *p<0.05.; ***p<0.001

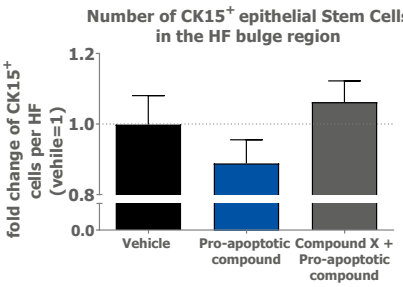
Compound X protects hair follicle stem cells from experimentally induced cell death and preserves the stem cell pool in the hair follicle





CK15/TUNEL immunofluorescence shows the apoptotic stem cells in the hair follicle bulge (stem cell niche)



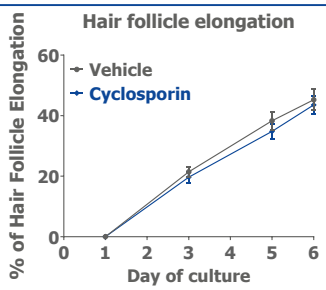


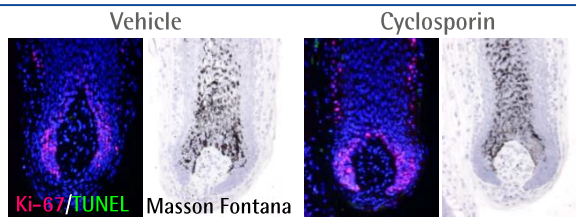
Mean±SEM n=4-9 HFs analysed/group. *p<0.05

Cyclosporin induces hair matrix keratinocyte production and maintains hair follicles longer in anagen *ex vivo*

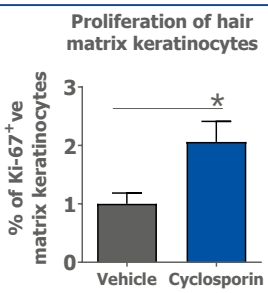
Cyclosporin: immunosuppressant drug inducing unwanted hair growth as side effect

Mean±SEM, n=21-22 HFs analysed/group from 3 donors

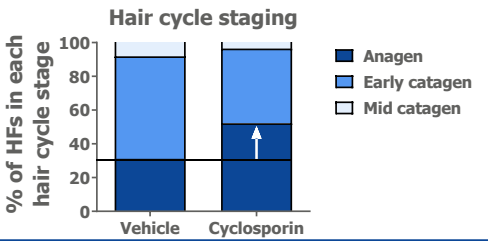


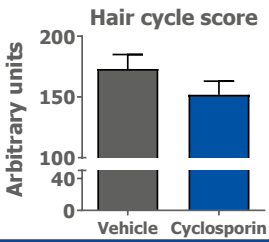


Ki-67: marker for proliferation. TUNEL: marker for apoptosis.
Masson Fontana: histochemical staining revealing melanin content



Mean±SEM n=26-28 HFs analysed/group from 3 donors. *p<0.05.





Mean±SEM n=26-28 HFs analysed/group from 3 different donors.

Selection of our publications:

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

Ex vivo models to investigate potential beneficial effects of therapeutics on pathologic features in AGA

Studying AGA related hair follicle dysfunction in human scalp skin *ex vivo*

1) premature catagen development
2) dermal papilla fibroblast emigration
3) reduced dermal papilla fibroblast inductivity
4) reduced stem cell activity and progeny

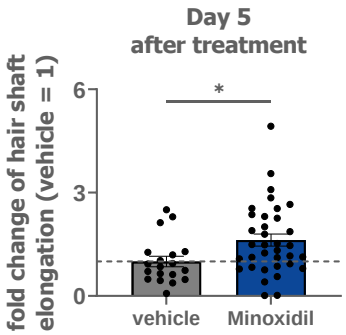
Our **methods:** human scalp skin e*x vivo* culture (left); different drug delivering modes are possible, including **topical** (middle), **systemic** (right) or **intradermal** (not shown) application.

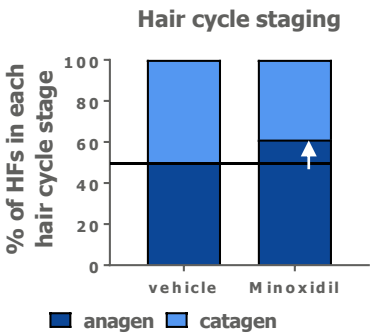
Read-Out Parameters: Hair follicle growth, hair shaft elongation, anagen (growth phase) maintenance, catagen (regression phase) induction, proliferation and apoptosis of hair matrix keratinocytes, dermal papilla fibroblast emigration, activation of signaling pathways involved in hair growth (e.g. Wnt/beta-catenin-,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

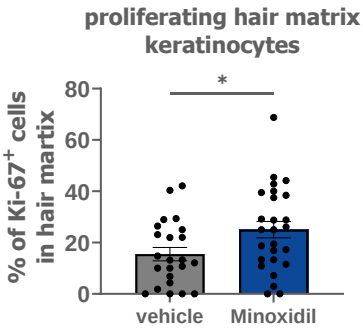
Study Examples

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

Minoxidil: FDA approved drug



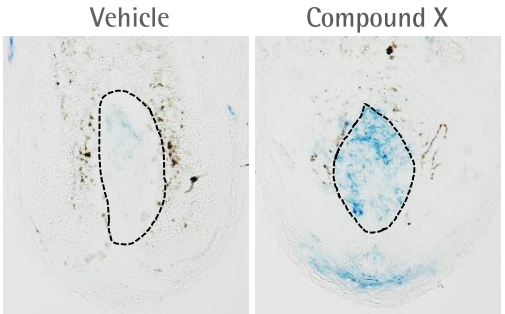




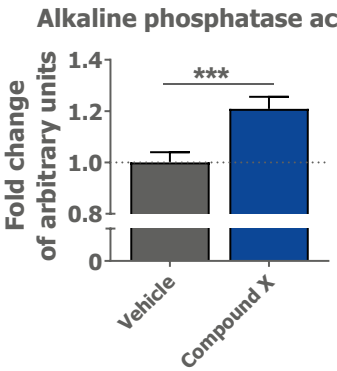
Mean±SEM, n=19-25 hair follicles/group from 2 donors, Mann Whitney test, *p<0.05.

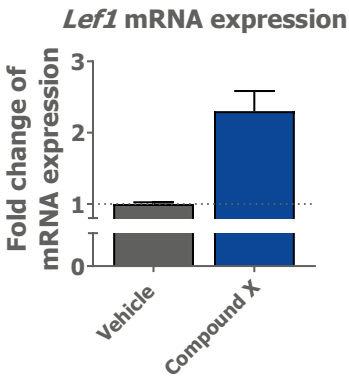
Mean±SEM, n=24-26 hair follicles/group from 2 donors, Mann Whitney test, *p<0.05.

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

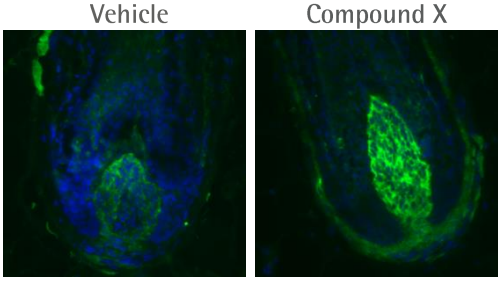


Alkaline phosphatase

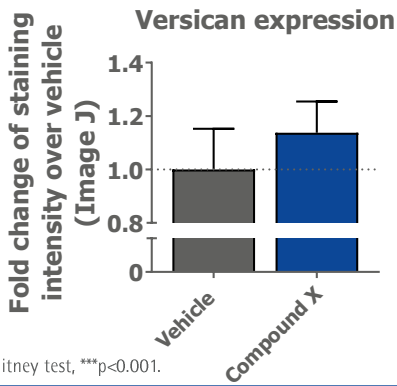




Mean±SEM, n= 3-12 HFs/group from 3 donors.



Versican DAPI



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

Selection of **our publications:**

Hawkshaw et al., PloS Biol 2018; Ahmed et al., J Cell Biol. 2014; Samuelov et al., J Invest Dermatol 2012

Investigating and characterizing affected and non-affected hair follicles from AGA patients

Studying hair follicle dysfunction in telogen hair follicles from healthy donors *ex vivo* or in hair follicles from AGA patients *in situ*

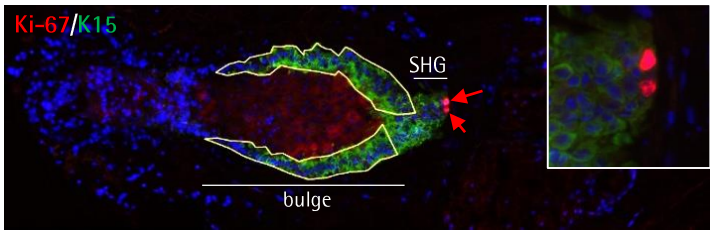
1) premature catagen development
2) hair follicle miniaturization
3) dermal papilla fibroblast emigration
4) reduced dermal papilla fibroblast inductivity
5) reduced stem cell activity and progeny

Our **methods:** isolation of telogen hair follicles from healthy donors (methylene blue staining; left); or isolation of follicular unit from balding area of AGA patients, containing terminal anagen, intermediate anagen, and telogen hair follicles (right).

Read-Out Parameters: Number of stem cells, stem cell proliferation and apoptosis; stemness associated keratins, stem cell senescence and aging, activation of signaling pathways involved in telogen-to-anagen conversion, transcriptome and proteome analyses, cytokine release, ...

Study Examples

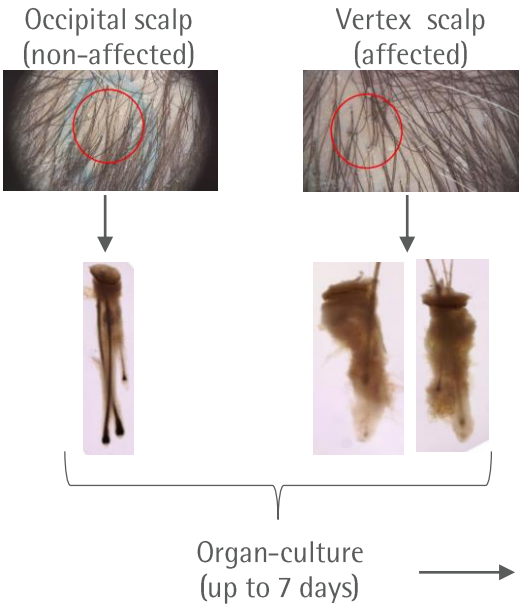
Isolation of telogen hair follicles from healthy donors



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

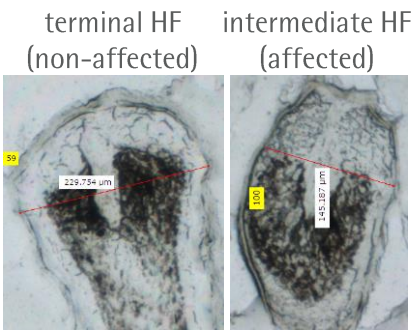
Selected publications:
Hawkshaw et al., Br J Dermatol 2019; Alam et al., Br J Dermatol. 2018; Hernandez et al., J Am Acad Dermatol. 2018

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



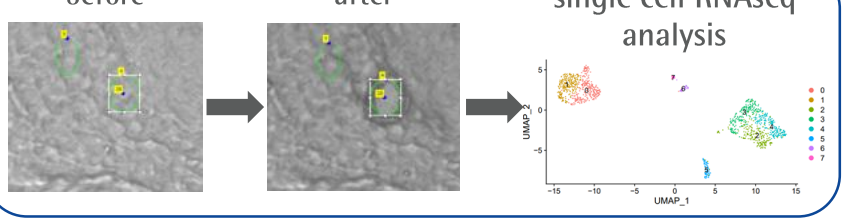
green: vertex scalp → affected scalp

pink: occipital scalp → non-affected scalp



Characterization of hair follicle miniaturization

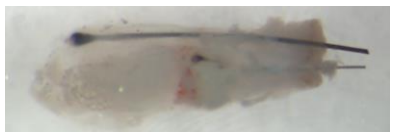
Laser Capture Microdissection (LCM) to select hair follicle compartments or single cells



Investigating the effects of therapeutics in affected and non-affected human hair follicles from AGA patients using *ex vivo* organ culture

Studying hair follicle dysfunction in hair follicles from AGA patients *ex vivo*

1) premature catagen development
2) hair follicle miniaturization
3) dermal papilla fibroblast emigration
4) reduced dermal papilla fibroblast inductivity
5) reduced stem cell activity and progeny

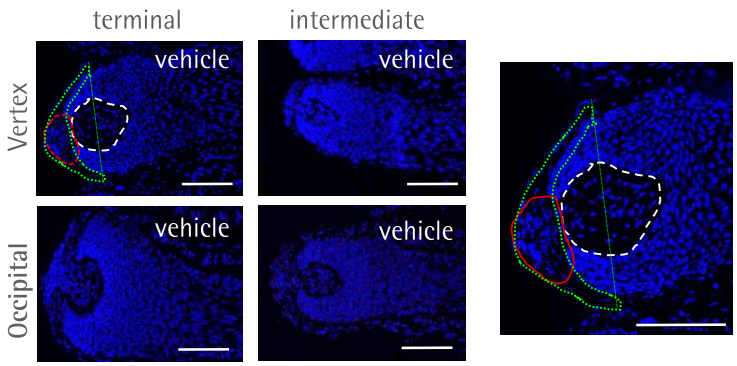


Our **methods:** isolation of hair follicular units from healthy donors (left) or isolation of follicular unit from balding area of AGA patients (right)
→ induction of hair follicle dysfunction (+/- testing compound)

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, ...

Study Examples

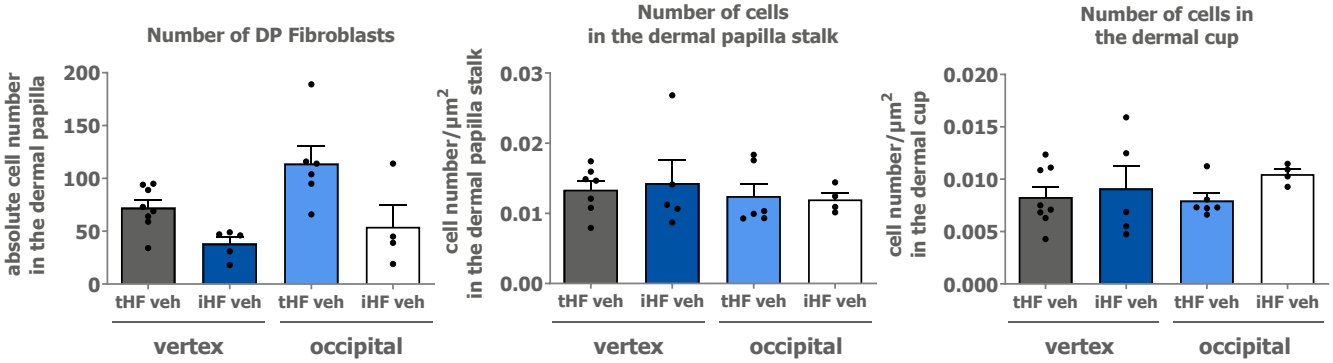
Ex vivo organ culture of hair follicles to examine emigration of dermal papilla fibroblasts



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

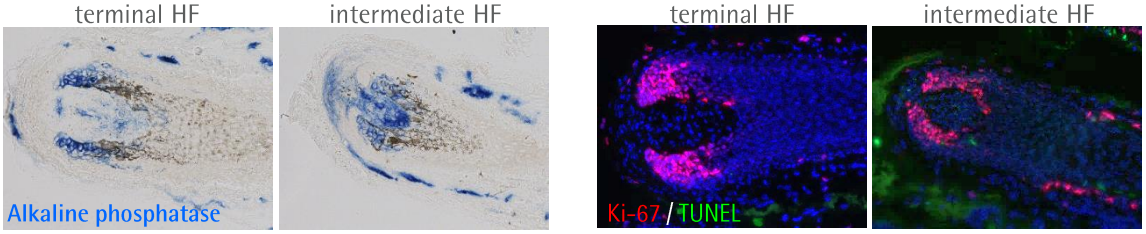
Investigation and **quantification** of hair follicle miniaturization ....

... allows for **comprehensive testing of your compound**



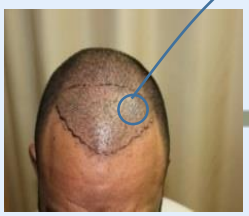
Mean±SEM n=4-8 HFs analysed/group.

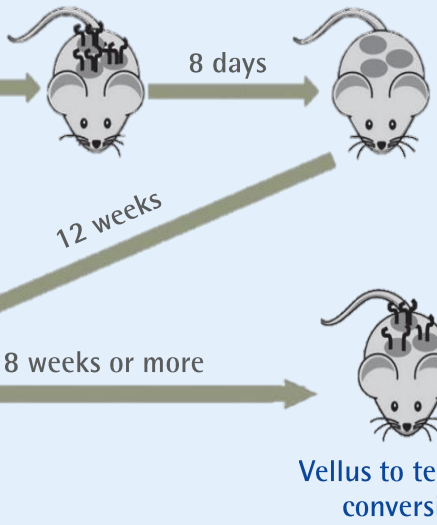
Effect of testosterone treatment on terminal vs. intermediate HFs



→ 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)

Pre-clinical Research: Humanized mouse model for Androgenetic Alopecia





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

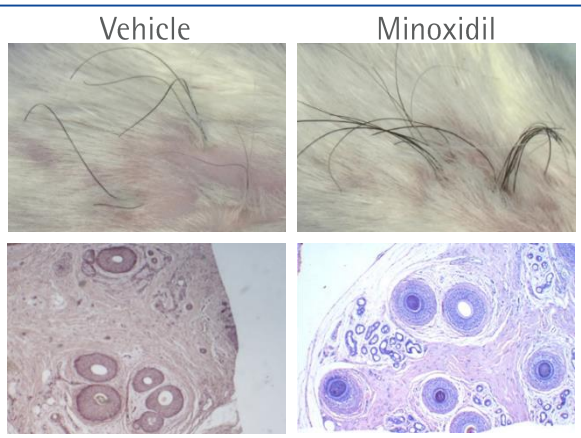
2) Vellus to terminal conversion

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 for Androgenetic Alopecia using Minoxidil to induce human hair growth

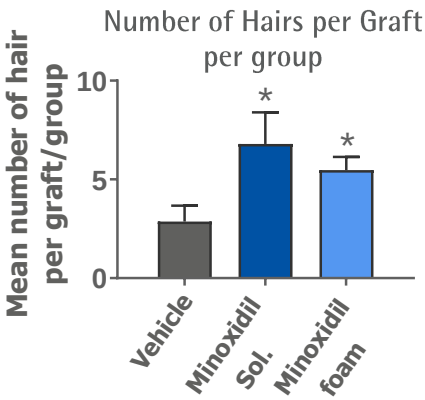


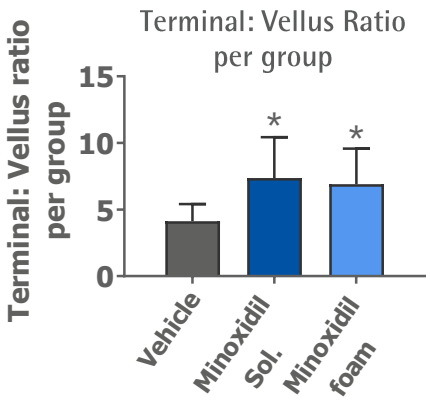
highly clinically relevant

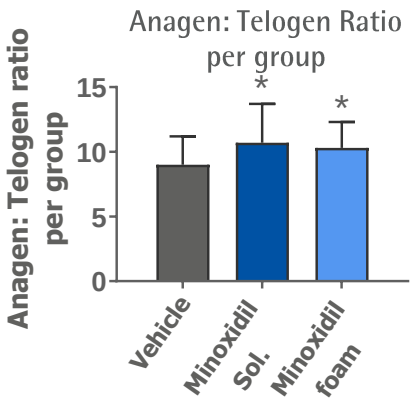
quantifiable read-out parameters

Selection of our publications:

Laufer Britva et al., Br J Dermatol 2021;
Gilhar et al., Exp. Dermatol 2022







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

WHY US?

MONASTERIUM LABORATORY
A QIMA Life Sciences Company

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:

Alfredo Rossi, Amos Gilhar, Désmond J. Tobin, Erwin Tschachler, Falk G. Bechara, Francisco Jimenez, Kristian Reich, Mauro Picardo, Thomas Luger, Tiago R. Matos, Vinzenz Oji, Athanasios Tsianakas and many more!

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