

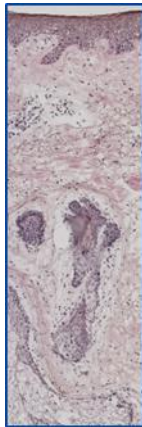
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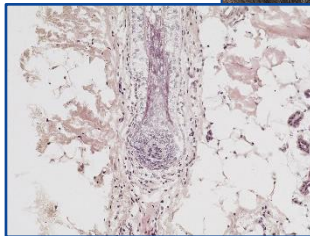


Alopecia Areata

chronic AA



acute AA



"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

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Skin & Hair Research Solutions GmbH

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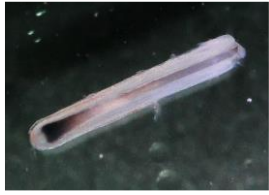
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Modeling alopecia areata-like phenotype in human HEALTHY hair follicles ex vivo

Effect of a drug on hair shaft production



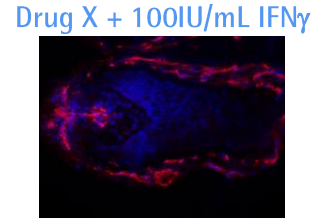
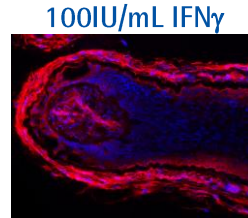
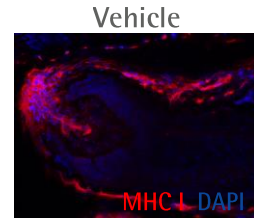
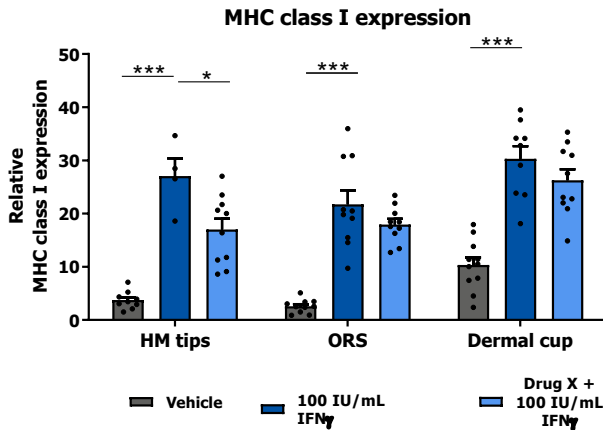
Amputated microdissected hair follicle at day 0, after isolation



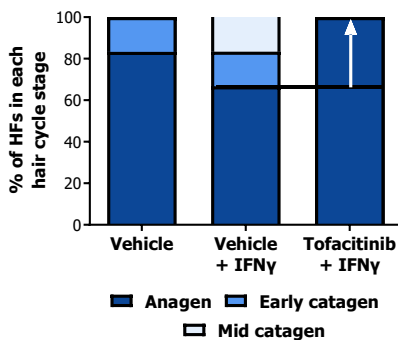
Amputated microdissected hair follicle at day 6 of organ culture: Note the newly formed hair shaft and outer root sheath

Our models can be utilized to identify the role of specific cytokines in disease pathogenesis as well as beneficial effects of new therapeutics.

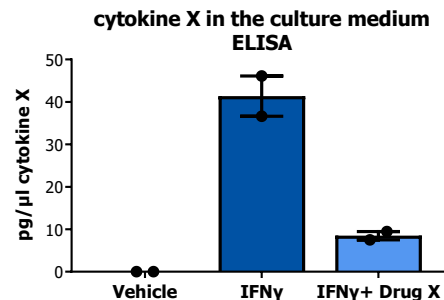
Prevention or rescue of immune privilege collapse



Prevention or rescue of catagen induction

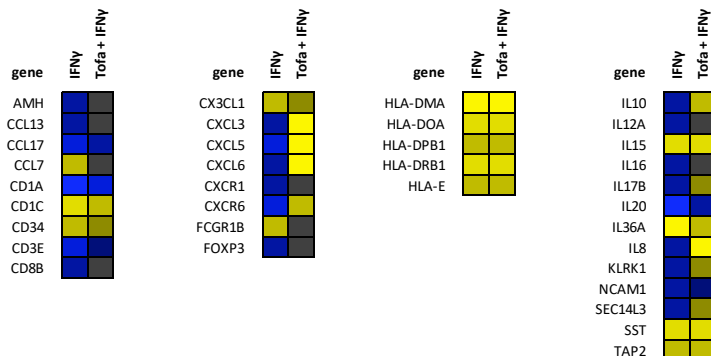


Inhibition of cytokine release

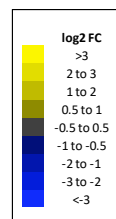


IFN γ : Key cytokine involved in alopecia areata pathogenesis inducing hair follicle immune privilege collapse, catagen promotion and activation of resident immune cells (Bertolini et al., Exp Dermatol 2020)

Short-term effect on hair follicle transcriptional changes induced by IFN γ



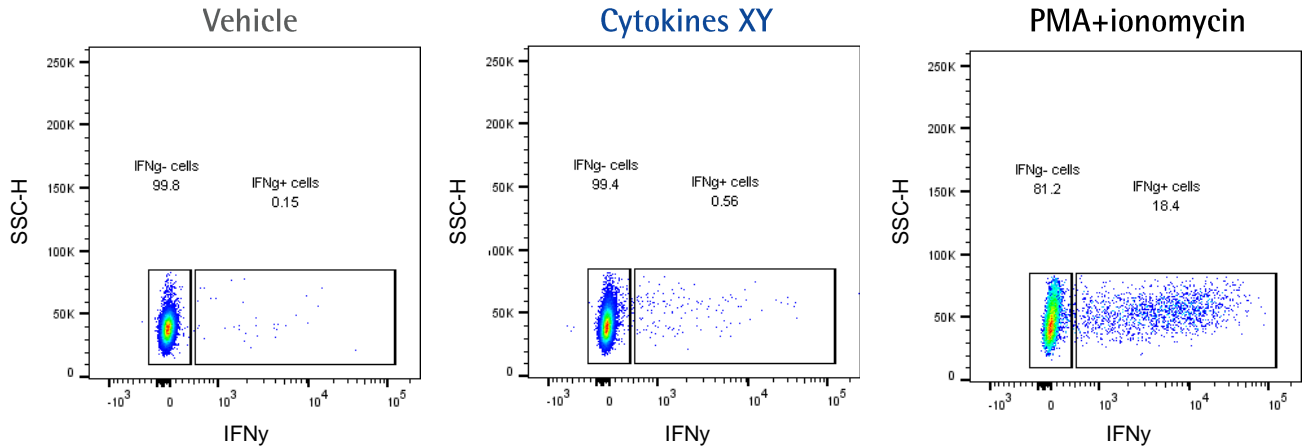
Transcriptional profiling hair follicles treated with IFN γ and IFN γ + Tofacitinib (Tofa) versus vehicle



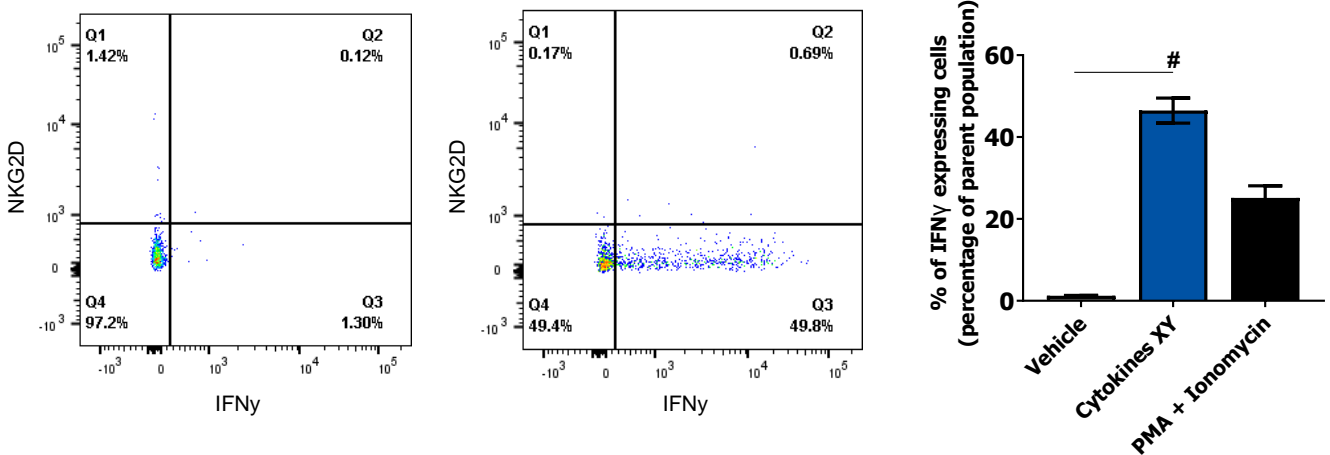
Investigating responses of circulating immune cells

Study Example: Investigating the effect of cytokines XY in inducing IFN γ production in CD45 $^{+}$ cells isolated from PBMCs:

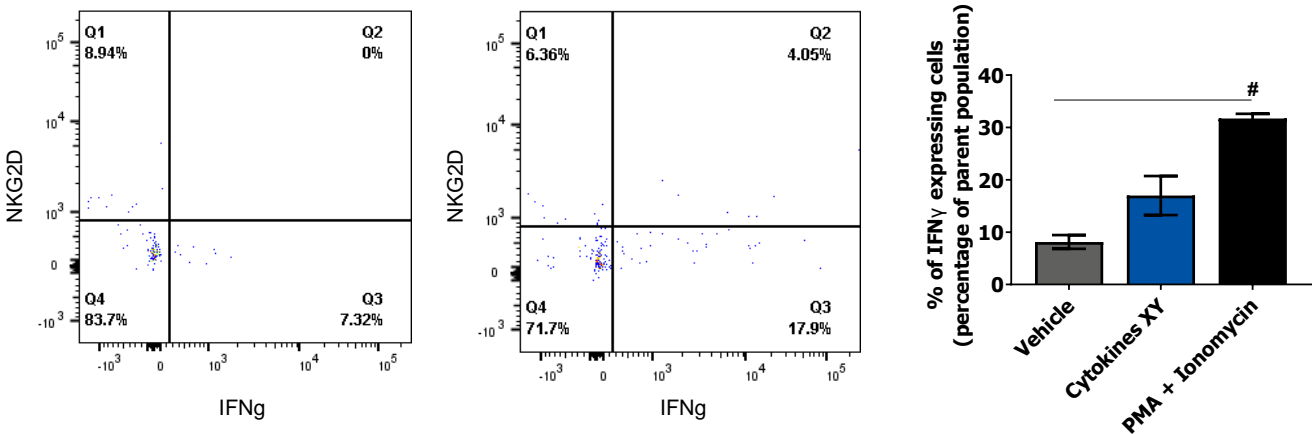
Gated on CD3 $^{+}$ cells (T cells)



Gated on CD56 $^{+}$ CD3 $^{-}$ NKG2D $^{-}$ cells (NK cells)



Gated on CD56 $^{+}$ CD3 $^{+}$ CD8 $^{-}$ gdTCR $^{-}$ NKG2D $^{-}$ cells (NKT cells)



Characterization or validation of a target in diseased tissue or blood:

Selected immune cell populations can be isolated from skin or PBMCs for phenotypic characterization in patients versus healthy subjects. Additionally, the effects of selected stimuli on cell phenotypes or the inhibition of pro-inflammatory responses by a drug can also be investigated.

Investigating the inhibitory effect of a drug on immune cell attacks against "weak/stressed" hair follicles

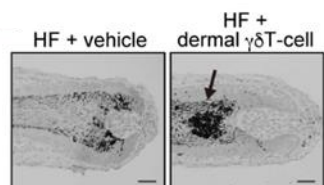
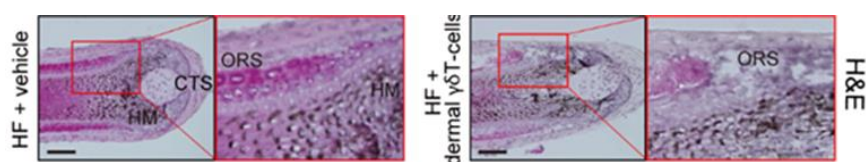
Study example: Isolated primary skin-resident $\gamma\delta$ T-cells attack human "weak/stressed" autologous hair follicles *ex vivo*



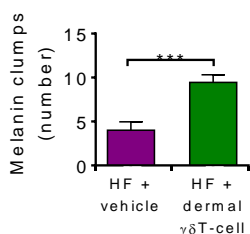
Our methods: Primary $\gamma\delta$ T-cells are isolated from human scalp skin, labelled, and co-cultured with human "weak/stressed" hair follicles microdissected from the scalp skin of the same donor

"Weak/Stressed":
Microdissected hair follicles which show weak immune privilege (protection towards immune-cell attack), and express molecules/cytokines as well as chemokines to attract immune cells

Induction of hair follicle cytotoxicity and dystrophy



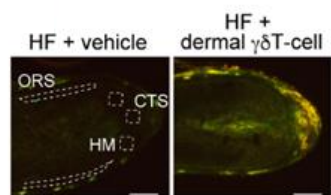
Masson-Fontana



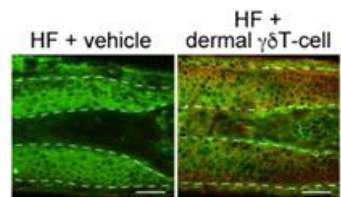
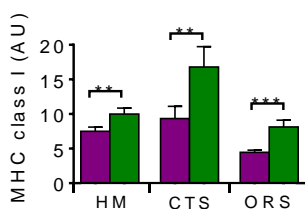
Also possible:
FACS to analyse activation status of immune cells, and customized read-out parameters *in situ*

Additional info:
Uchida et al., J Autoimmun. 2021

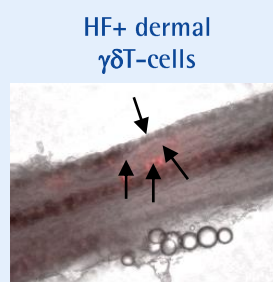
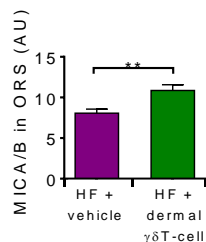
Induction of hair follicle immune privilege collapse and MICA/B overexpression



MHC class I / β 2MG



CD1d / MICA



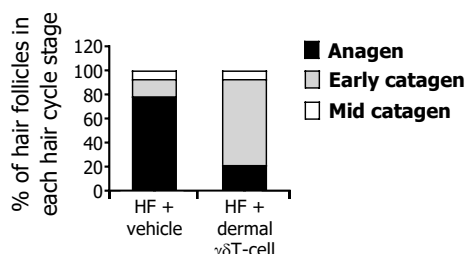
"Weak/Stressed" hair follicles co-cultured with $\gamma\delta$ T-cells in absence of Drug X \rightarrow $\gamma\delta$ T-cells infiltrate into the hair follicle (see arrows)



"Weak/Stressed" hair follicles co-cultured with $\gamma\delta$ T-cells in the presence of Drug X \rightarrow $\gamma\delta$ T-cells DO NOT infiltrate into the hair follicle

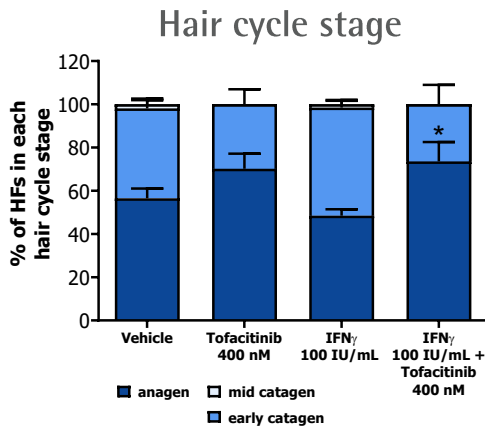
Drug X prevents infiltration of $\gamma\delta$ T-cells in "weak/stressed" hair follicles *ex vivo*

Premature catagen induction

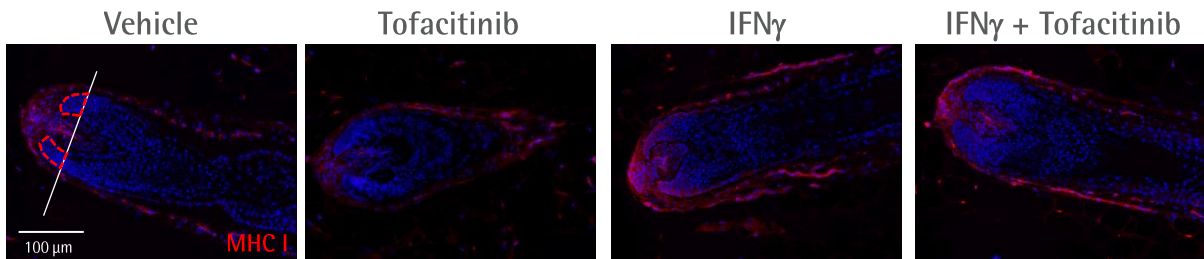
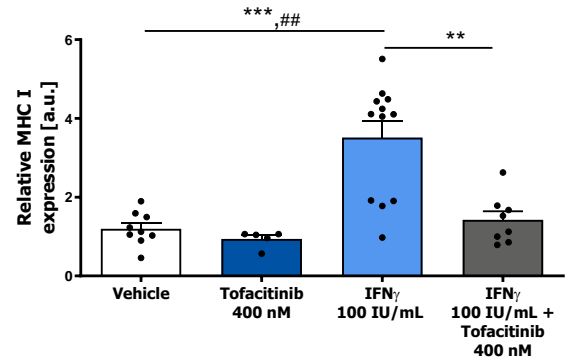


Modeling alopecia areata-like phenotype in human HEALTHY scalp skin *ex vivo*

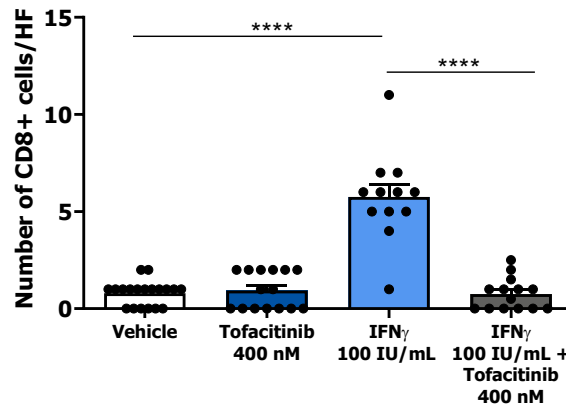
Study Example: Tofacitinib inhibits IFN γ -induced premature catagen induction, immune privilege collapse and expansion of perifollicular CD8+ T-cells



**Immune privilege collapse:
MHC class I expression in the hair matrix**

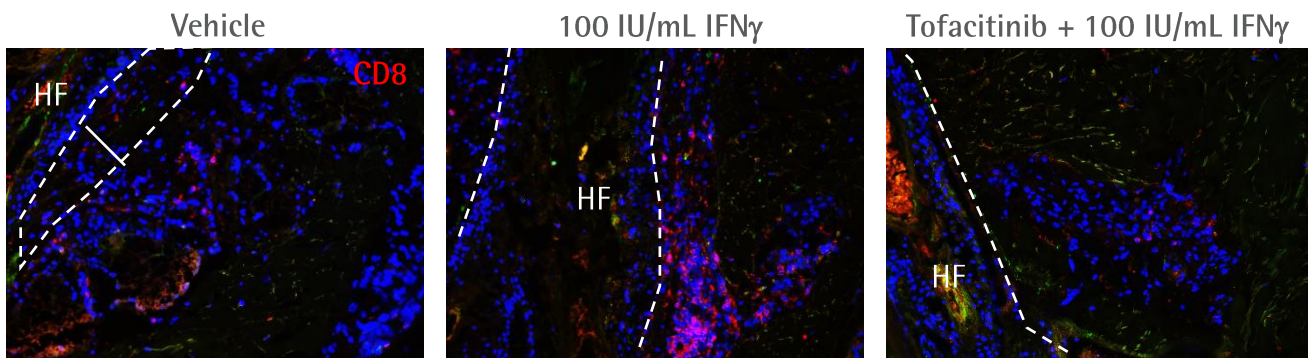


**Immune cell infiltrate
(perifollicular CD8+ cells)**



Resident skin
immune cells still
present and
responding to
IFN γ

Additional
standardized read-
out parameters
associated with
alopecia areata
pathogenesis
available!



HF: Hair follicle

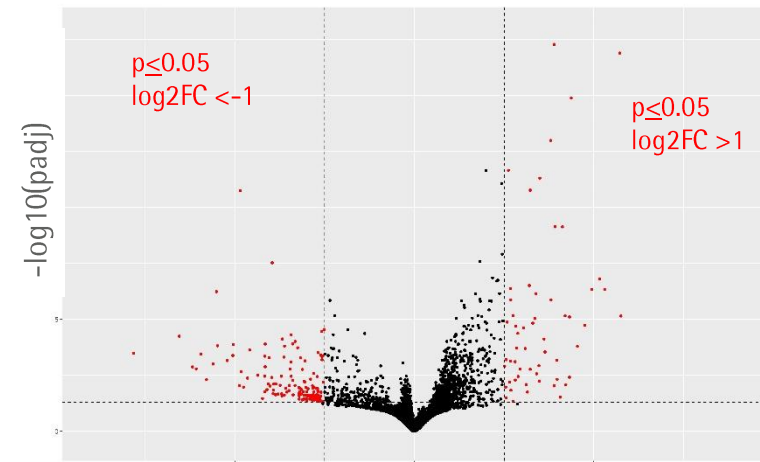
Customized markers:

We customize multiplex immunostainings, FACS panels, ELISA and cytokine arrays according to your target or cell type of interest.

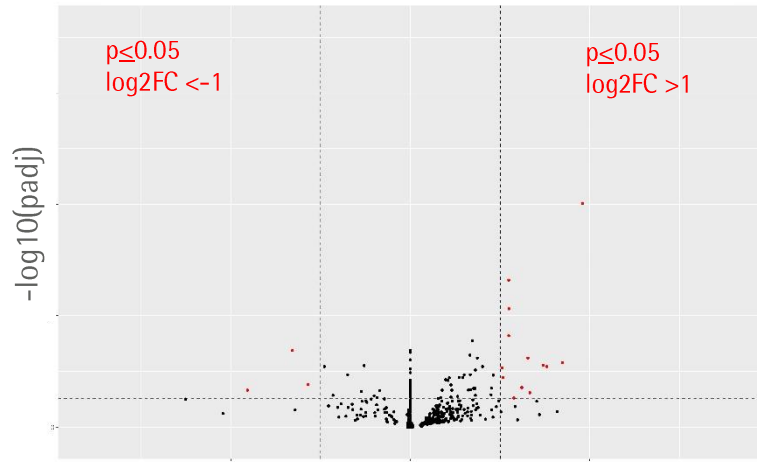
Investigating the effect of a drug in scalp skin from patients ex vivo: lesional and non-lesional alopecia areata skin organ culture

Transcriptional profiling showing deregulated genes
lesional or drug X treated vs. non-lesional scalp skin from alopecia areata patients

AA Lesional vs Non Lesional skin

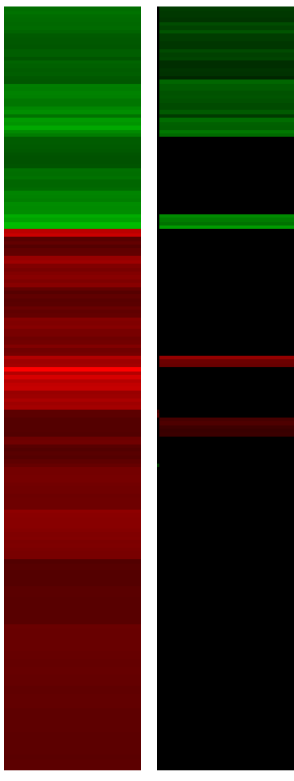


Drug X AA Lesional vs Non Lesional skin



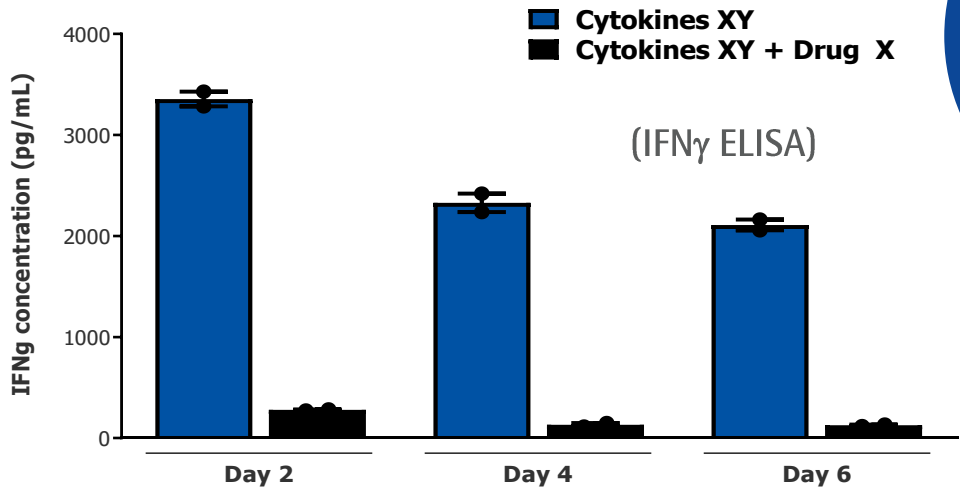
Log2 Fold Change

AA Lesional VEH AA Lesional Drug X



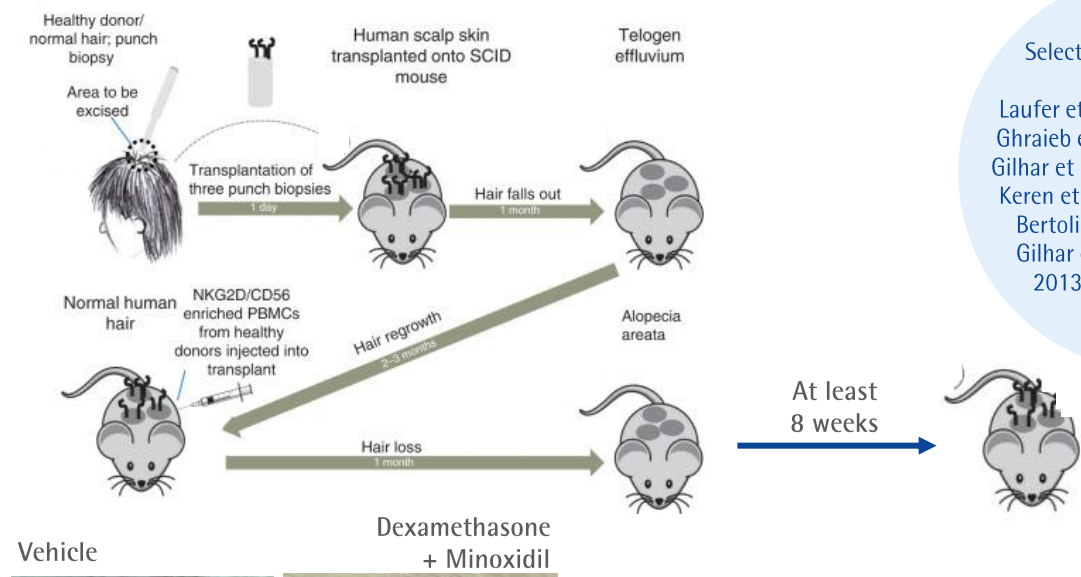
Vs AA Non Lesional

Treatment with cytokine XY induces IFN γ release into the medium in affected scalp skin from alopecia areata patient ex vivo



Customized analysis of your target of interest by: multiplex immunostaining, FACS analyses, transcriptome or proteome analyses

Investigating the effect of a drug on inhibiting alopecia areata-like phenotype *in vivo*: Humanized mouse model



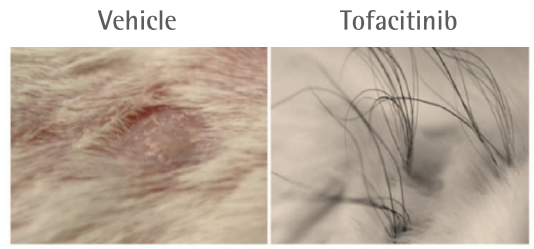
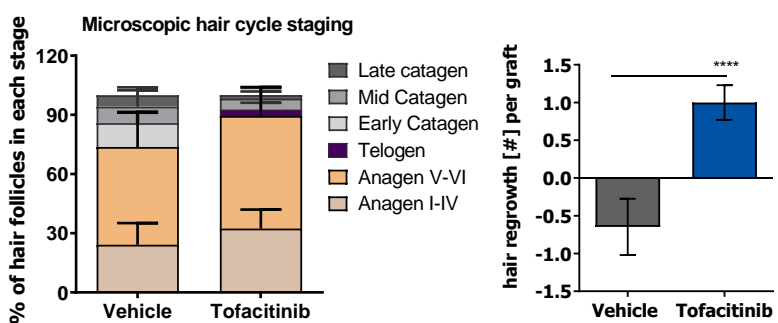
Selected publications on the model:

Laufer et al., Br J Dermatol. 2019;
Ghraieb et al., J Autoimmun 2018;
Gilhar et al., Autoimmun Rev 2016;
Keren et al., J Dermatol Sci. 2015;
Bertolini et al. PloS One 2014;
Gilhar et al., J Invest Dermatol 2013;
Gilhar et al., J Invest Dermatol 2013



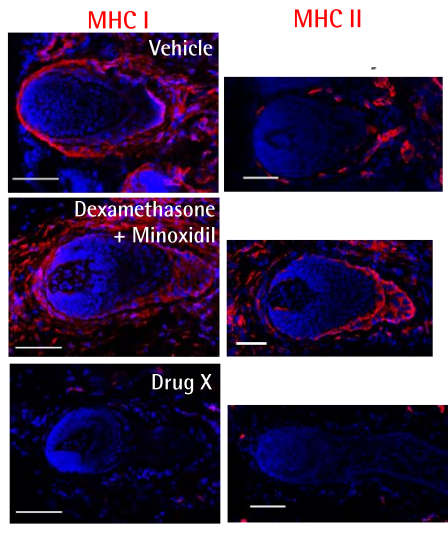
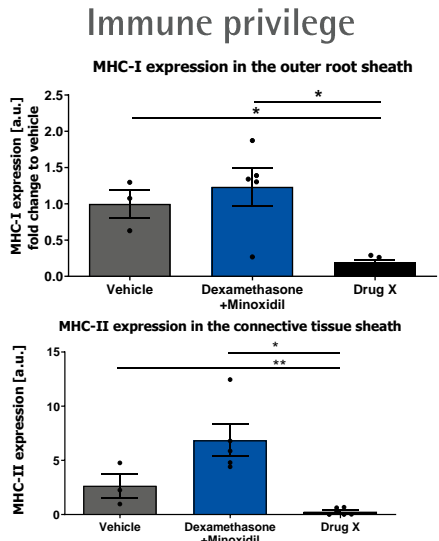
Hair regrowth promoted by dexamethasone+ Minoxidil (Macroscopic analysis)

Hair regrowth promoted by Tofacitinib (Macroscopic and microscopic analysis)

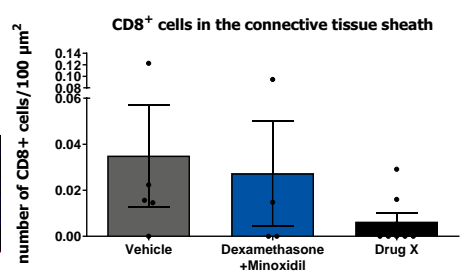


Study example: Drug X also inhibits immune privilege collapse and the number of perifollicular CD8+ T-cells

Additional standardized read-out parameters associated with alopecia areata pathogenesis available!



Immune cell infiltration



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:
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!