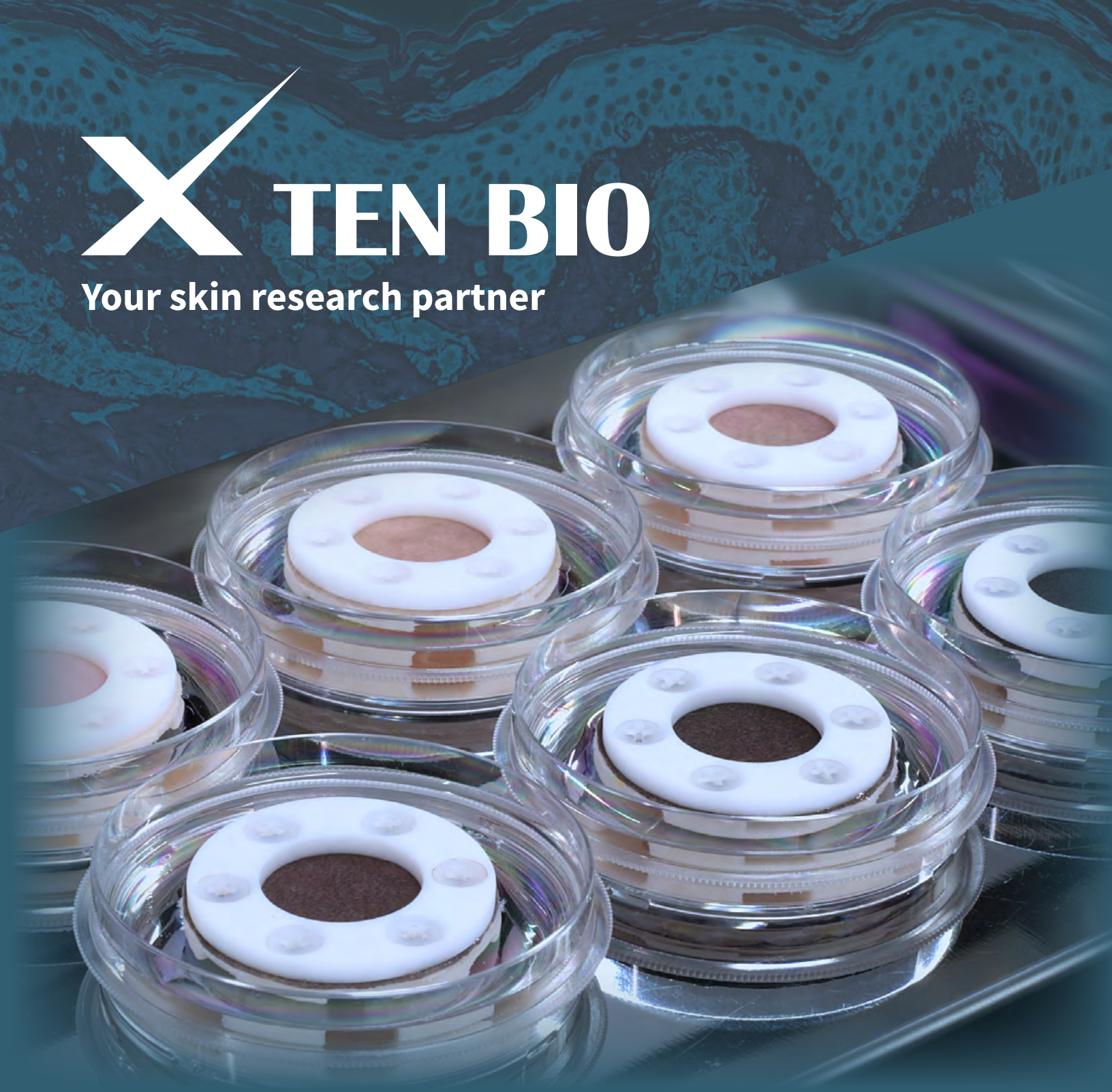
TEN BIO

Your skin research partner



Transforming skin research with our advanced *ex vivo* human skin models

www.ten-bio.com

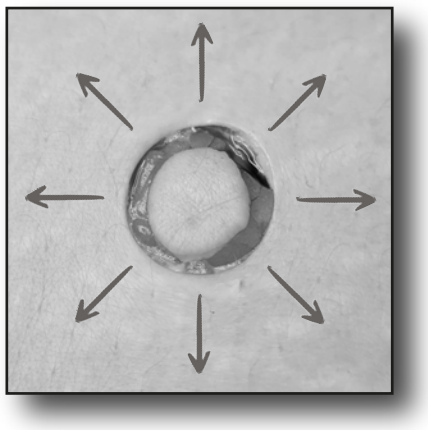
Skin tension

A critical factor in skin homeostasis

Mechanical tension is an essential factor in biological tissue morphology and function. It influences cell proliferation and differentiation, stimulates extracellular matrix (ECM) production and tissue remodeling, and allows tissues to adapt and respond to changes in mechanical loading.

Human skin is a heterogeneous layered material with complex physical and mechanical properties and provides several important roles in human health, including:

- Protection from the external environment
- Sensation - touch, temperature, pain
- Endocrine and exocrine activity
- Innate and adaptive immunity
- Regulation of temperature



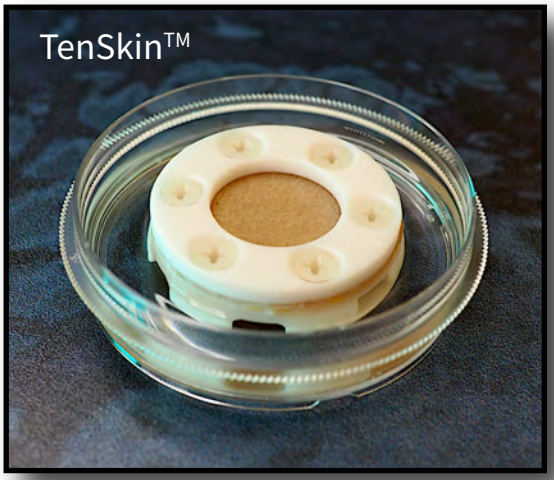
Skin on the body is under a consistent range of physiological tension. When a full thickness incision is made, this tension is released, the traction force balance between cells and the extracellular matrix is lost, and the tissue contracts, resulting in induction of several mechanoreceptor pathways, including:

- Integrin-mediated signaling
- Focal adhesion-mediated signaling
- Piezo channels
- Transient receptor potential (TRP) channels

Similarly, when skin is removed from the body for use in *ex vivo* assays, this tension is lost, reducing its viability and ability to respond to external stimuli as it would when on the body. TenSkin™ addresses this issue by restoring physiological tension.

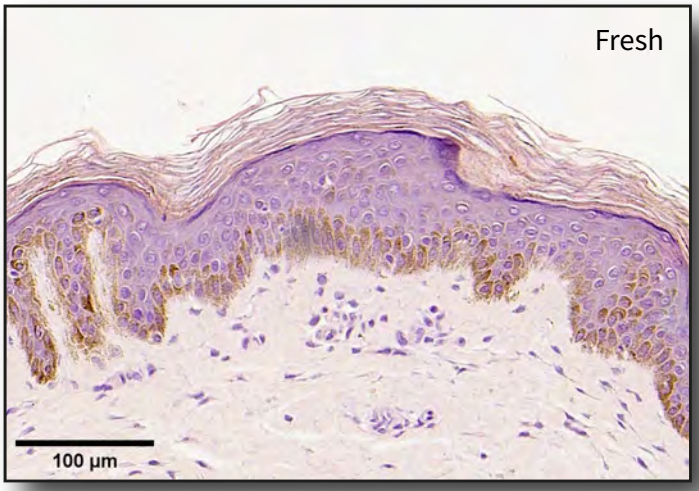
Optimal tension for optimal results

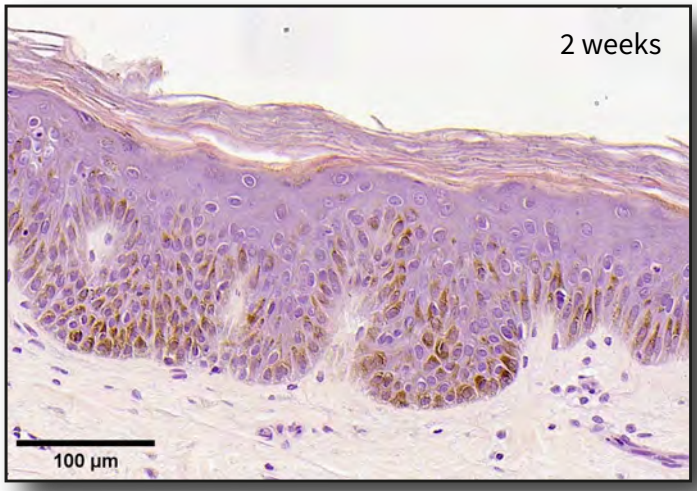
Following nearly a decade of development, Ten Bio has succeeded in creating a truly functional and realistic testing platform for skin-based research. TenSkin™ is full thickness human skin cultured at optimal tension, which enables the model to mimic skin's innate *in vivo* behavior and maintains tissue viablity for extended periods – up to 14 days.



By restoring skin's inherent mechanobiology, our unique culture system retains skin's physiological complexity, metabolic activity, and structural integrity, allowing the generation of more clinically-relevant data to help de-risk clinical trials and bringing products to market.

Using the TenSkin™ technology, Ten Bio provides expert skin research partnering services allowing our clients to make more informed decisions at every stage of R&D. Better decisions drive better results, rapid progess, and lower costs.



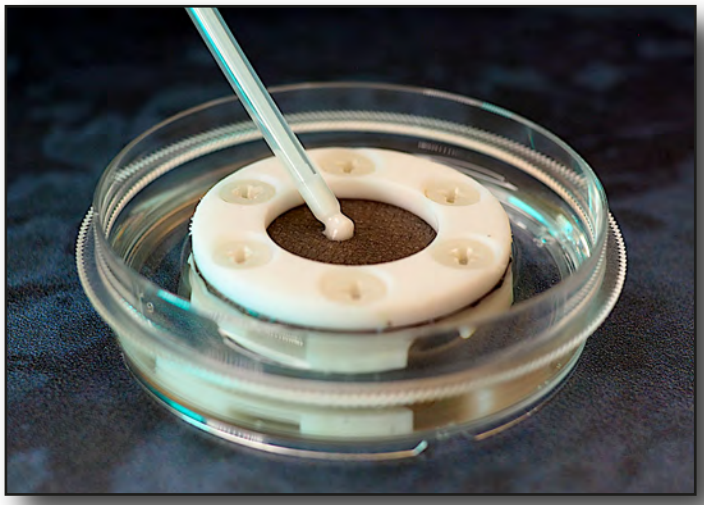


TenSkin™ maintains tissue integrity for two weeks in culture (minimal observation of cell vacuolization and necrosis; intact basement membrane, etc).

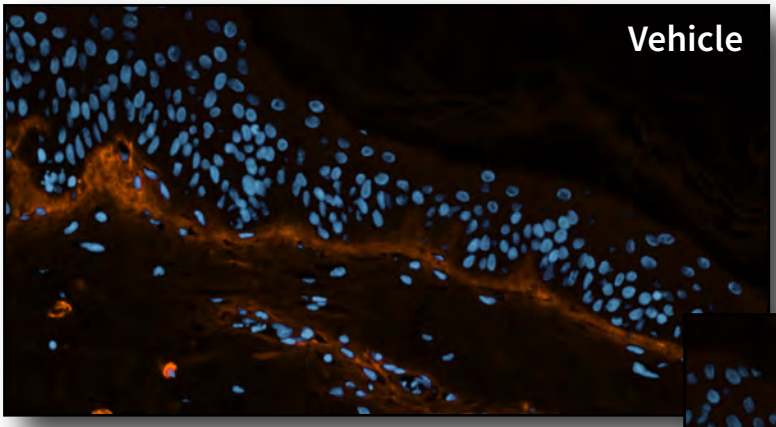
Skin rejuvenation

Extended culture periods essential to evaluate dermal remodeling

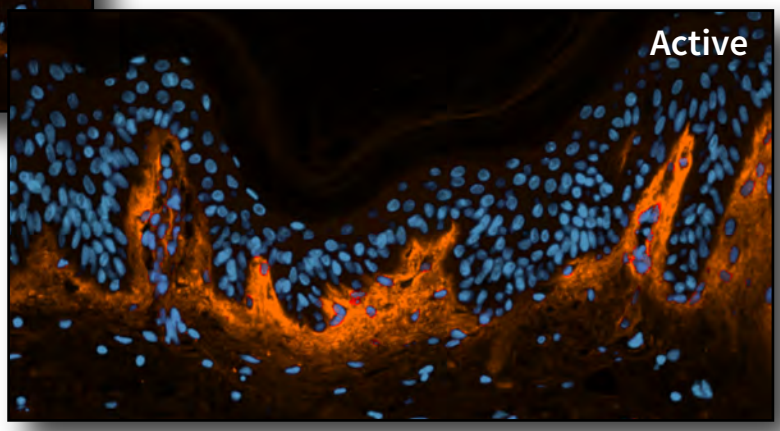
The TenSkin™ culture technology results in skin that mimics *in vivo* biology and also maintains the surface properties of skin. TenSkin™ is an ideal platform for evaluation of topical application as the tensioned skin presents identically to a patient's skin.



Ten Bio works with an established network of surgical clinics to obtain fully consented tissue from a broad range of donor age groups and all Fitzpatrick skin types, providing custom solutions to support even the most complex R&D requirements.



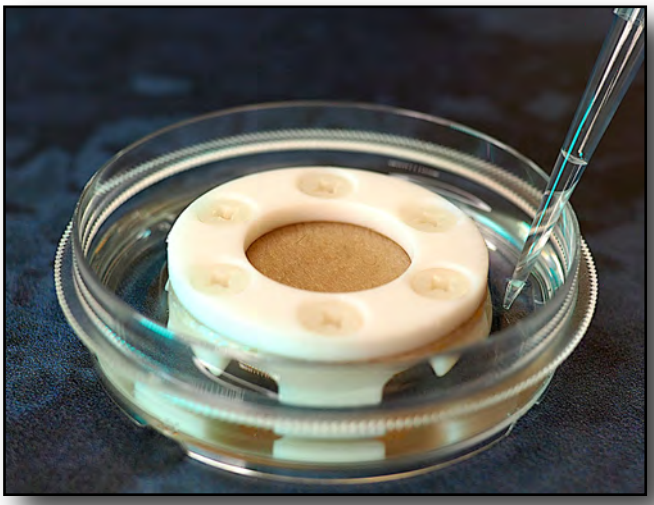
Extended culture periods make TenSkin™ ideal for evaluating dermal remodeling (e.g., inhibition of collagen breakdown and stimulation of collagen synthesis). Here, increased procollagen 1 is observed 14 days following topical treatment.

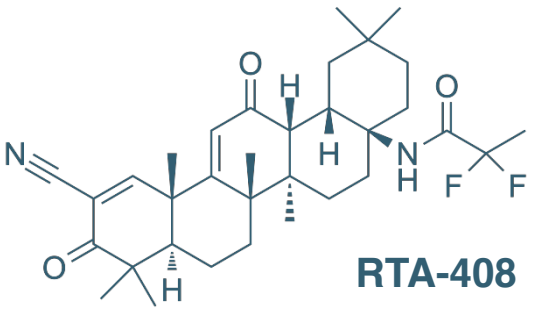


Systemic treatment

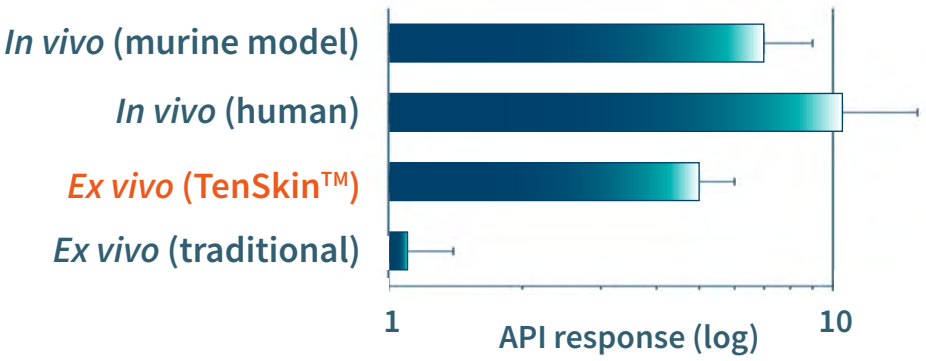
Clinically relevant biological response

Our products and research services help generate exacting and clinically relevant data to more accurately predict product performance *in vivo*. TenSkin™ treated with RTA-408 (an NRF2 activator) exhibited a biological response (i.e., upregulation of NQO1 mRNA) similar to *in vivo* data, while traditional *ex vivo* models (cultured without tension) showed little response.





RTA-408

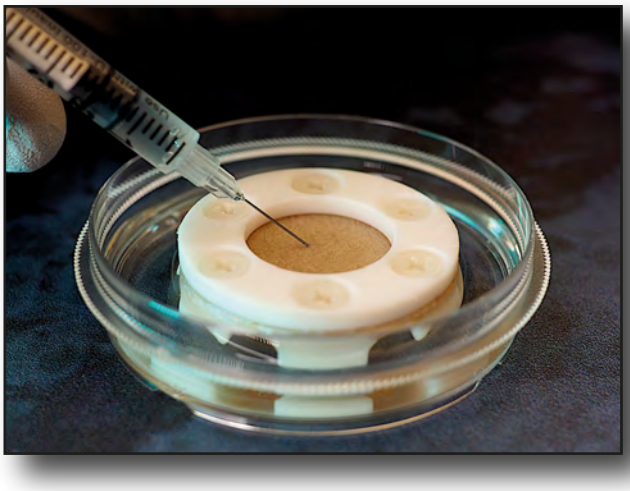


Intradermal and subcutaneous injection

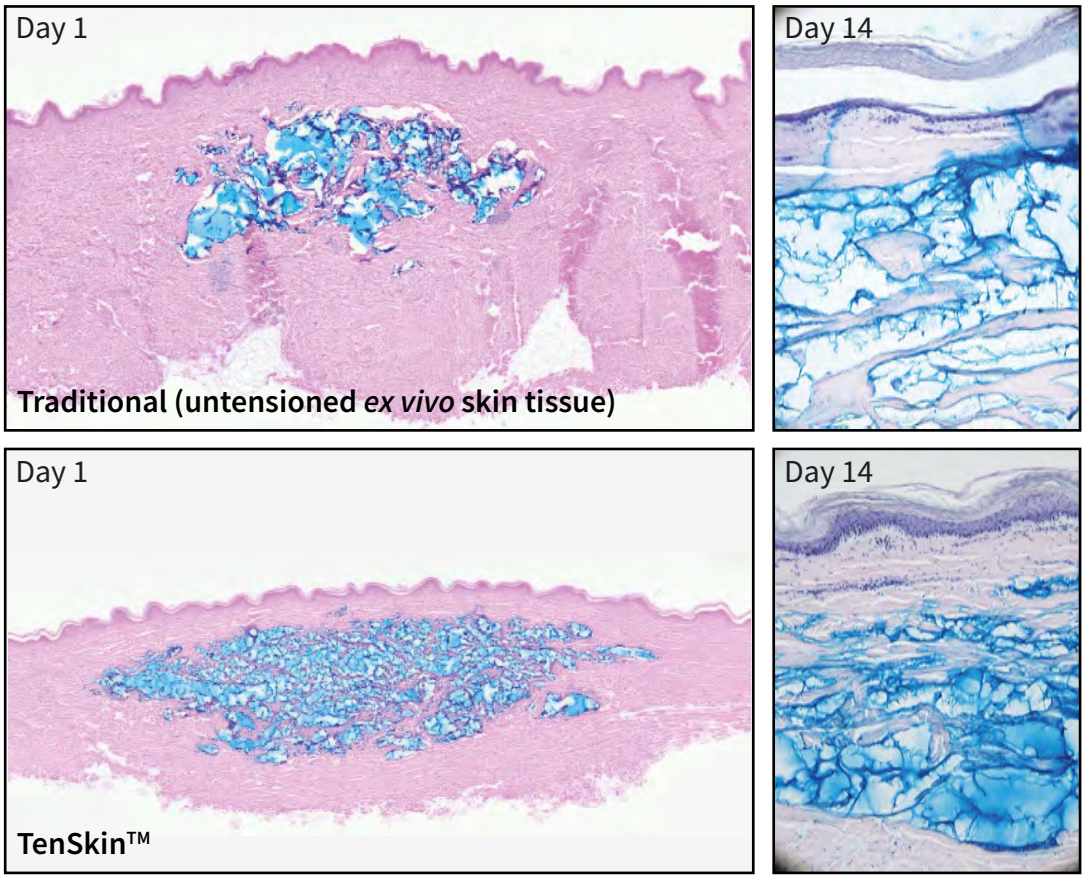
Tissue integrity is essential for reliable delivery

Intradermal or subcutaneous delivery performance depends heavily on the physical interaction of an injection bolus with the surrounding tissue. During injection, physiological tension is an important factor in both the resulting bolus shape/distribution and tissue integration.

Maintaining proper alignment of dermal fibres contributes significantly to the ability of the tissue to resist rupture and a subsequent loss in viability, therefore enabling recapitulation of *in vivo*-like biological responses.



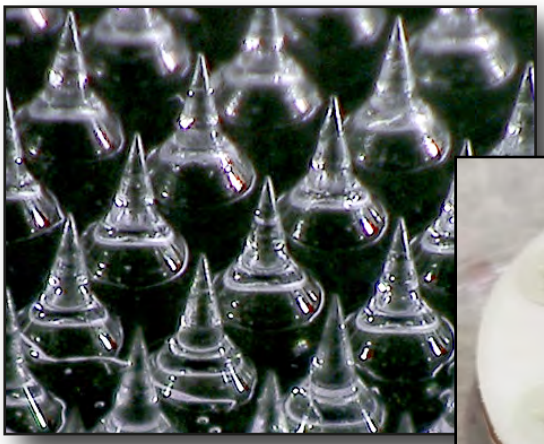
Intradermal injection of a hyaluronic acid-based dermal filler showing the benefit of tensioned skin in achieving even distribution and improved integration



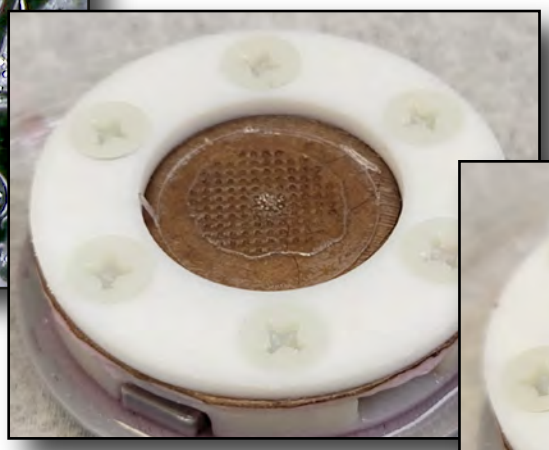
Microneedle Injection

TenSkin™ - a robust *ex vivo* platform for microneedle application

For successful evaluation of molecule delivery to skin during preclinical development, it is important to replicate the *in vivo* physiological and mechanical environment. Reproducible application of microneedle arrays depends heavily on both the tension present in skin tissue and the properties of the underlying substrate. The TenSkin™ platform restores skin's mechanobiology to allow accurate recapitulation of the *in vivo* environment enabling generation of the most relevant preclinical data.

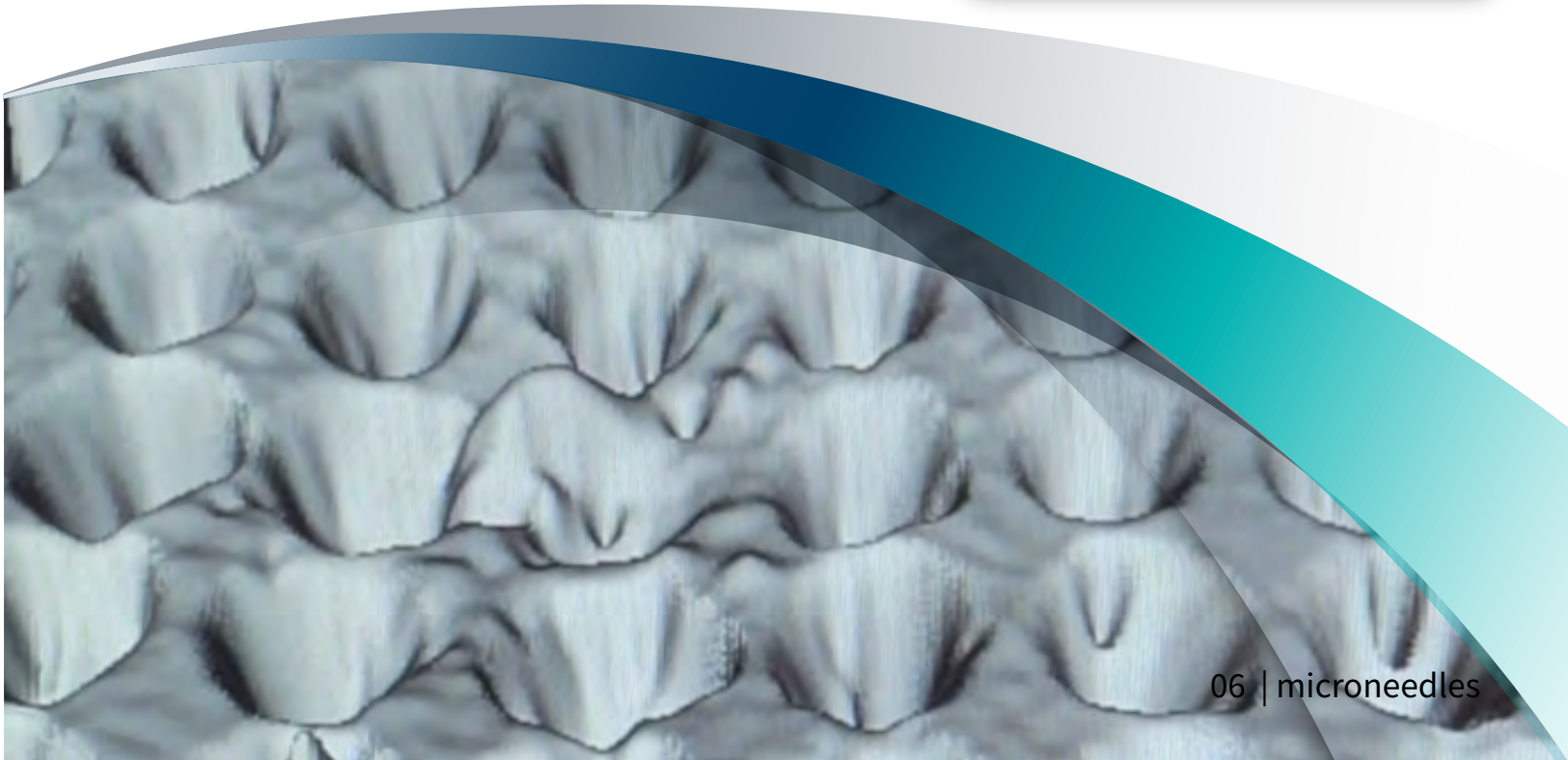


These data were generated in collaboration with the Prausnitz group at the Georgia Institute of Technology



Patch application

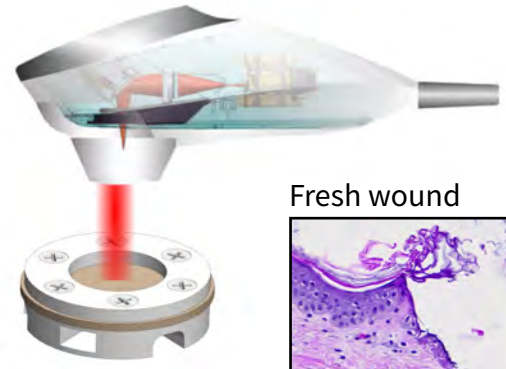
Patch removed



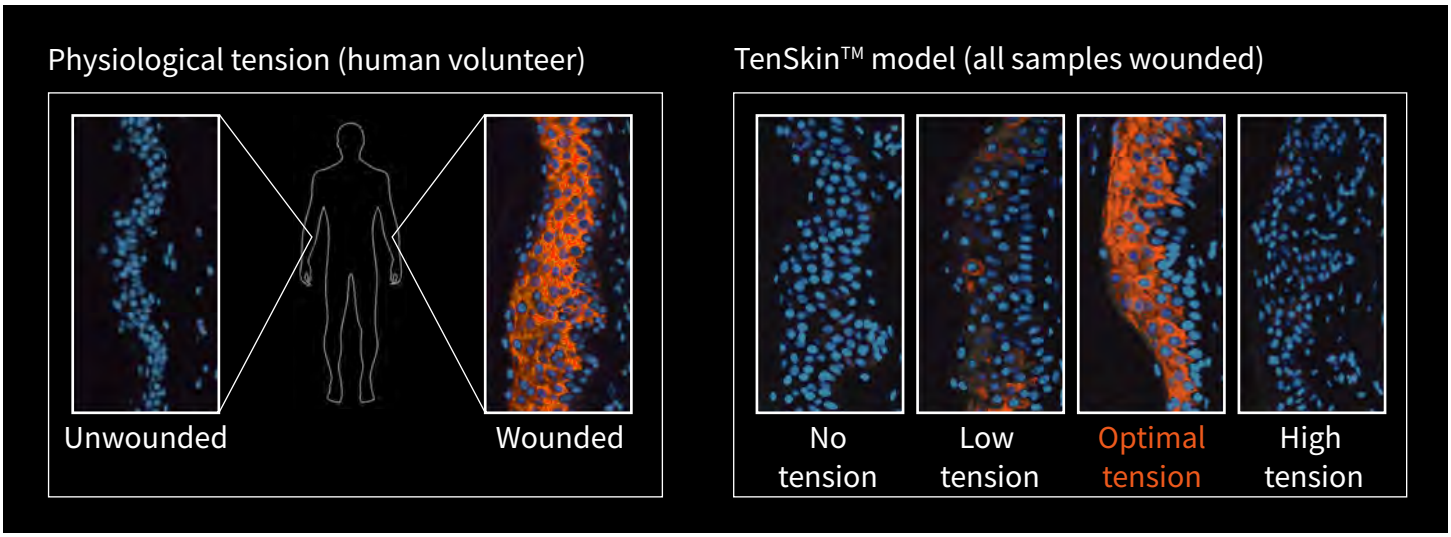
Wound healing

Optimal tension is required for wound response and healing

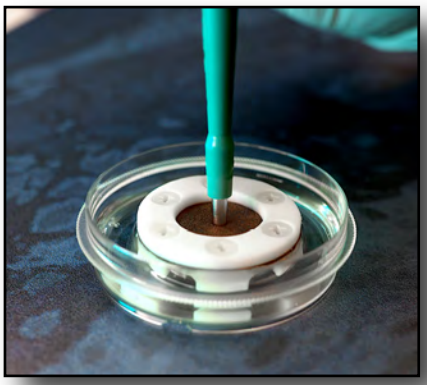
Wound healing in skin is a complex process that involves the coordinated activity of various cell types, signaling pathways, and extracellular matrix components. Reliably recapitulating an *in vivo*-like wound response in explant tissue is a challenge that requires thorough consideration of all aspects of the tissue culture process. By restoring skin's inherent mechanobiology, our unique culture system, TenSkin™, retains skin's physiological complexity, metabolic activity, and structural integrity, enabling the tissue to behave as it would on the body in response to wounding, such as fractional laser ablation or superficial biopsy.



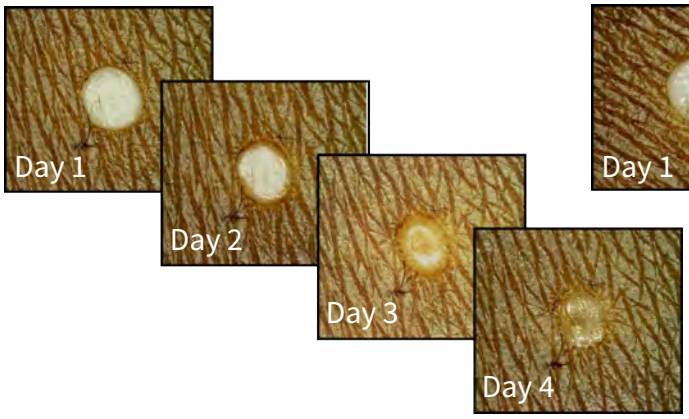
Optimal mechanical tension allows TenSkin™ to mimic complex biological processes (e.g., response to wounding). The figure below illustrates virtually identical expression levels of wound healing proteins in TenSkin™ (keratin 17 shown in orange) when directly compared to the wounded skin of a human volunteer.



The interaction of our skin with the external environment can have significant effects on wound healing. One such example is photobiomodulation from exposure to solar radiation, in particular the UV component of the spectrum. While certain doses can induce positive health benefits, e.g., vitamin D synthesis, higher doses can have detrimental effects on skin health, including its ability to heal. Addionally, consideration of the melanin content of the skin is essential to fully understand the variability of the effects of UV on a population.

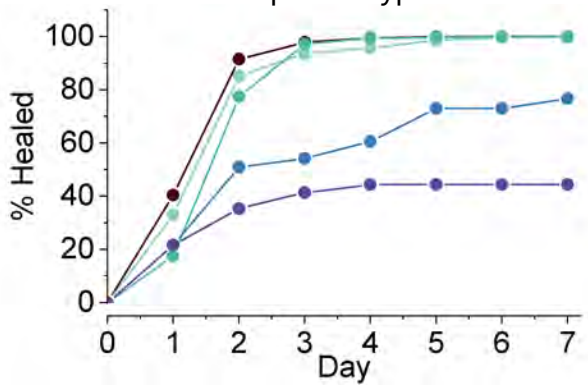


Control (no UV)

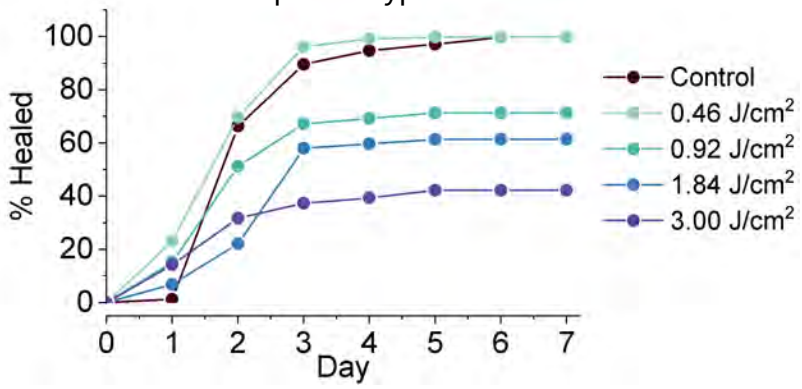


UV exposed

Fitzpatrick type IV



Fitzpatrick type II

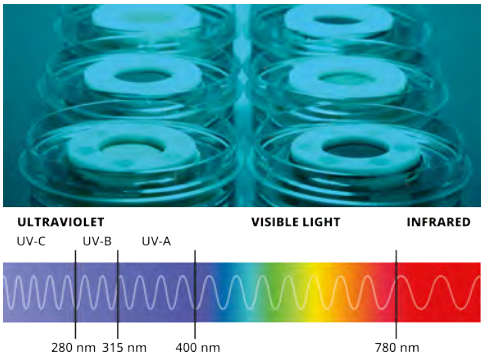


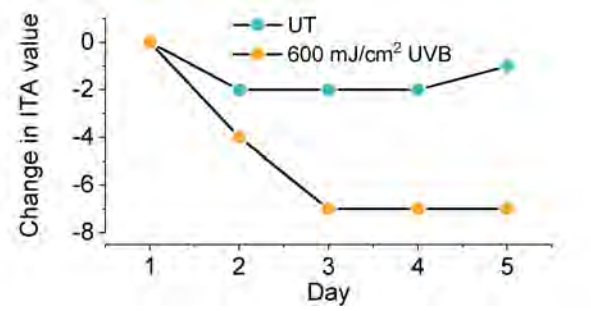
Melanin offers a protective effect in response to UV exposure in wounded skin.
Type II skin exhibits reduced healing at lower doses when compared to type IV skin.

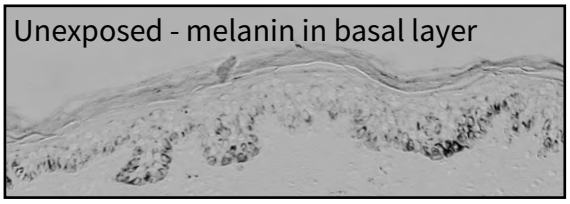
Photobiology

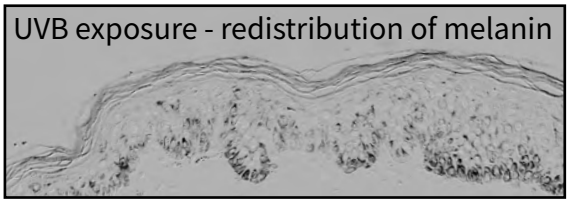
Broad spectrum of capabilities to evaluate skin's response to light

The interplay of light with our skin is unavoidable. These interactions can have both beneficial and harmful effects depending on a wide range of conditions. Excessive ultraviolet (UV) radiation from solar exposure is known to cause skin damage and contribute to the development of skin cancers. However, this UV radiation is also necessary for the natural synthesis of Vitamin D in the skin. Ten Bio has developed a wide range of photobiology capabilities to enable a deeper understanding of the interaction of light with skin.





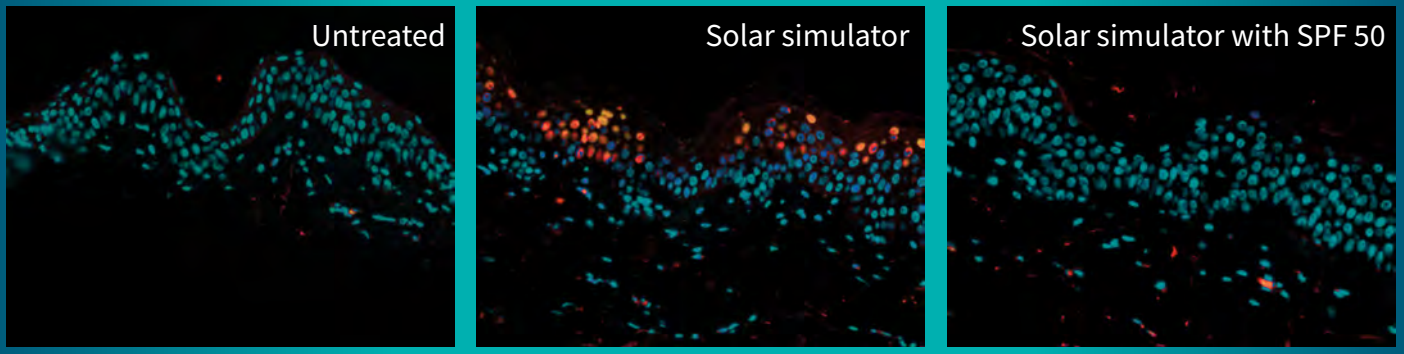




Photobiology capabilities:

- Solar simulated, visible, UVB and UVC light sources
- Fontana-Masson staining
- Quantitative skin color measurements
- Evaluate of DNA damage (CPD, 6-4 PP)
- Evaluate changes in skin pigmentation
- Access to a diverse range of skin phototypes (Fitzpatrick I-VI)
- SPF testing

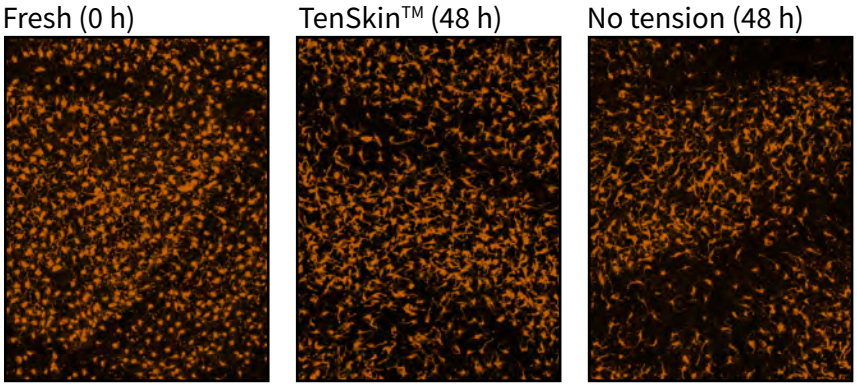
Assessment of DNA damage in Fitzpatrick skin type V

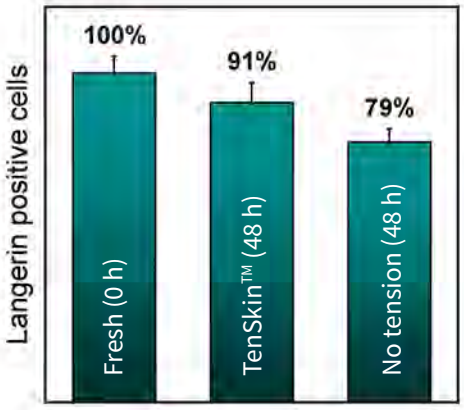


Immunocompetent model

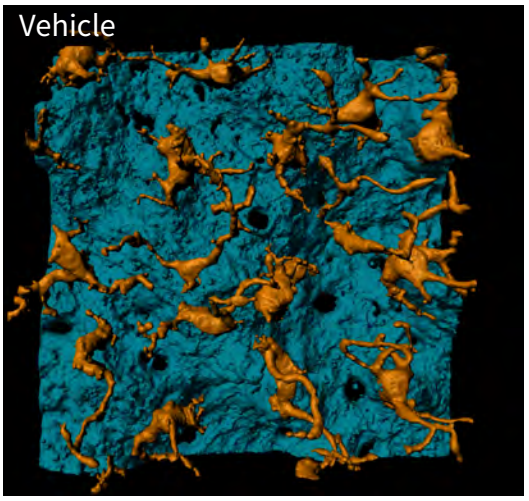
Extended immune cell retention to provide accurate preclinical testing

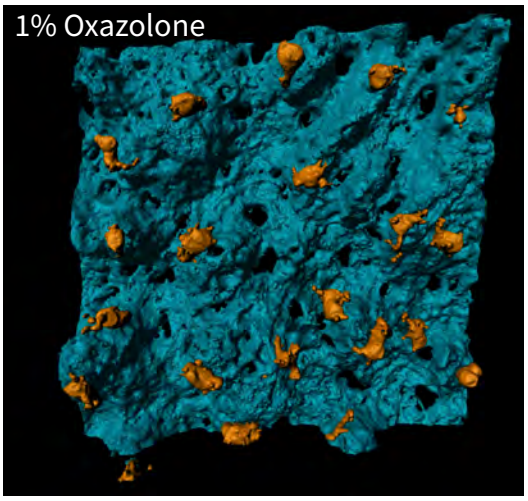
Compared to traditional *ex vivo* models, the intact mechanobiology of TenSkin™ maintains the skin's resident immune cells in a more normal state. When skin is removed from the body, an accelerated spontaneous migration of Langerhans cells (orange) occurs (10-20% of the cell population every 24 hours), limiting the practical window available for immune reaction studies. Culturing skin at physiological tension significantly reduces this rate of migration, allowing in-depth and extended assessments of immune response.

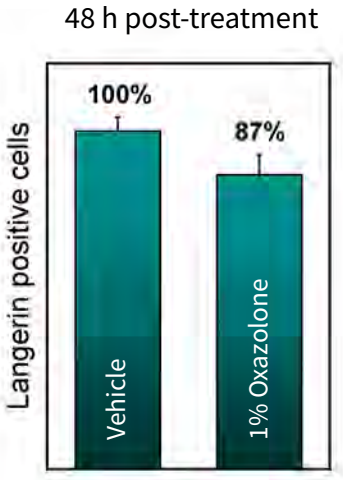




Using advanced microscopy techniques, visualization of initial immune reactions in skin is possible. Whole-mount imaging shows Langerhans cells (orange; shown against the basement membrane in blue) mature and migrate in response to a contact allergen (oxazolone) in the TenSkin™ model.





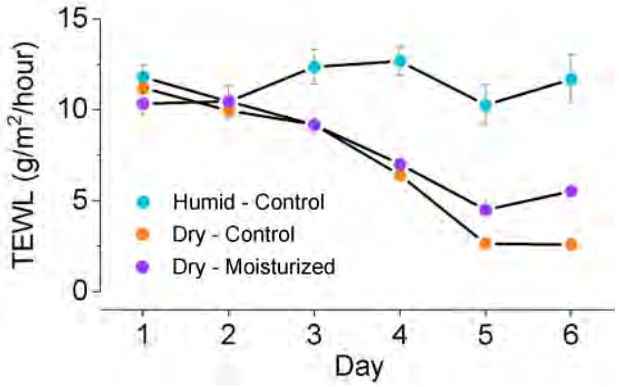


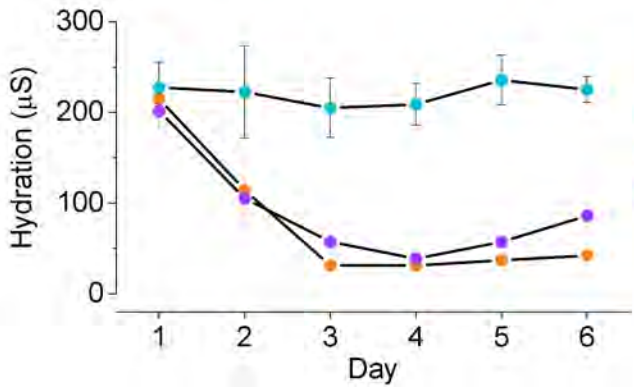
Physical measurements of skin health

Uniquely compatible with clinical tools for clinically relevant data

The barrier function of skin is essential for human health. However, various factors, both endogenous and exogenous, can influence the performance and integrity of this tissue function. Numerous non-invasive instruments and methods have been developed to evaluate these areas of skin health in clinical settings. Measurements such as trans epidermal water loss (TEWL) and skin hydration (through the quantification of skin capacitance) offer valuable insights into the interface of the skin with the ambient environment. Successful use of these probes rely on consistent contact with the skin surface and a consistent surface area within the probe apertures, which is often difficult to achieve in traditional *ex vivo* skin models lacking tension.

TenSkin™ is uniquely designed to be compatible with these probes, allowing direct comparisons to clinical data. Utilizing these measurements, advanced studies on the performance of topical treatments are possible, including protection in adverse climate condition such as humid (90% rel. humidity) and dry (20% rel. humidity) environments.



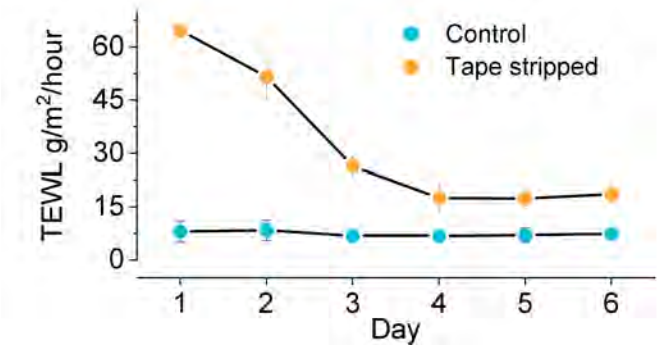


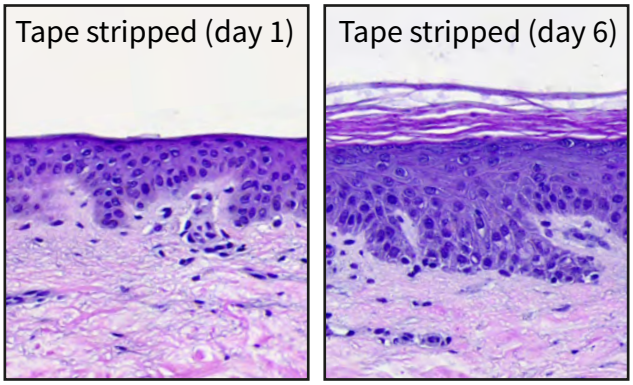
Skin barrier research

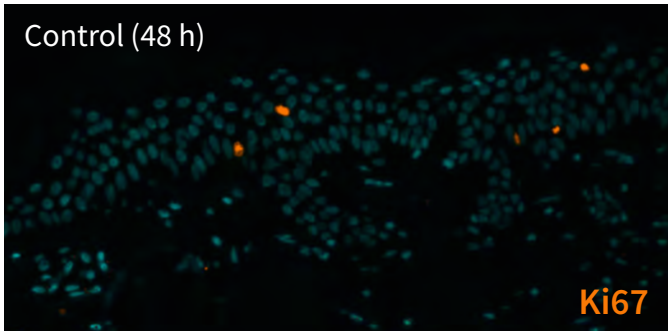
A robust model for long term skin barrier assessment

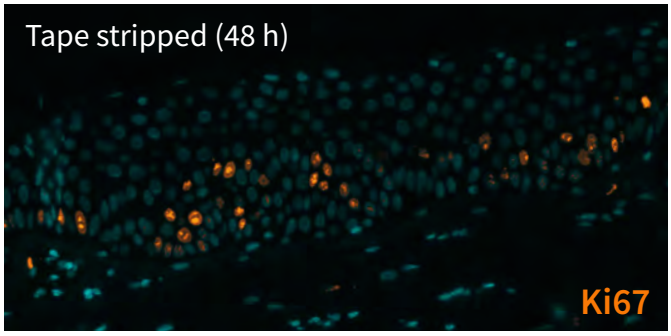
The skin is a multilayered, mechanically complex tissue where elasticities of each layer can vary by several orders of magnitude. For example, the *stratum corneum* is ~10-fold less elastic than the "live" layers of the epidermis and ~20-fold less elastic than the dermis. The TenSkin™ culture frame uniquely supports *ex vivo* skin tissue in an *in vivo*-like physical environment maintaining its mechanobiology in a similar fashion to how the underlying tissue on the body supports the skin.

TenSkin™ is an ideal *ex vivo* model for evaluation of dermal barrier properties. Here D-squame stripping discs are used to remove the *stratum corneum*, leading to an initial increase in transepidermal water loss (TEWL). The tissue then recovers to near baseline levels within 4 days due to increased cell proliferation as determined by increased Ki67 expression.









Tapestripping results in a significant increase in keratinocyte proliferation as evidenced by a 6-fold increase in Ki-67 positive cells at 48 h when compared to untreated control tissue.

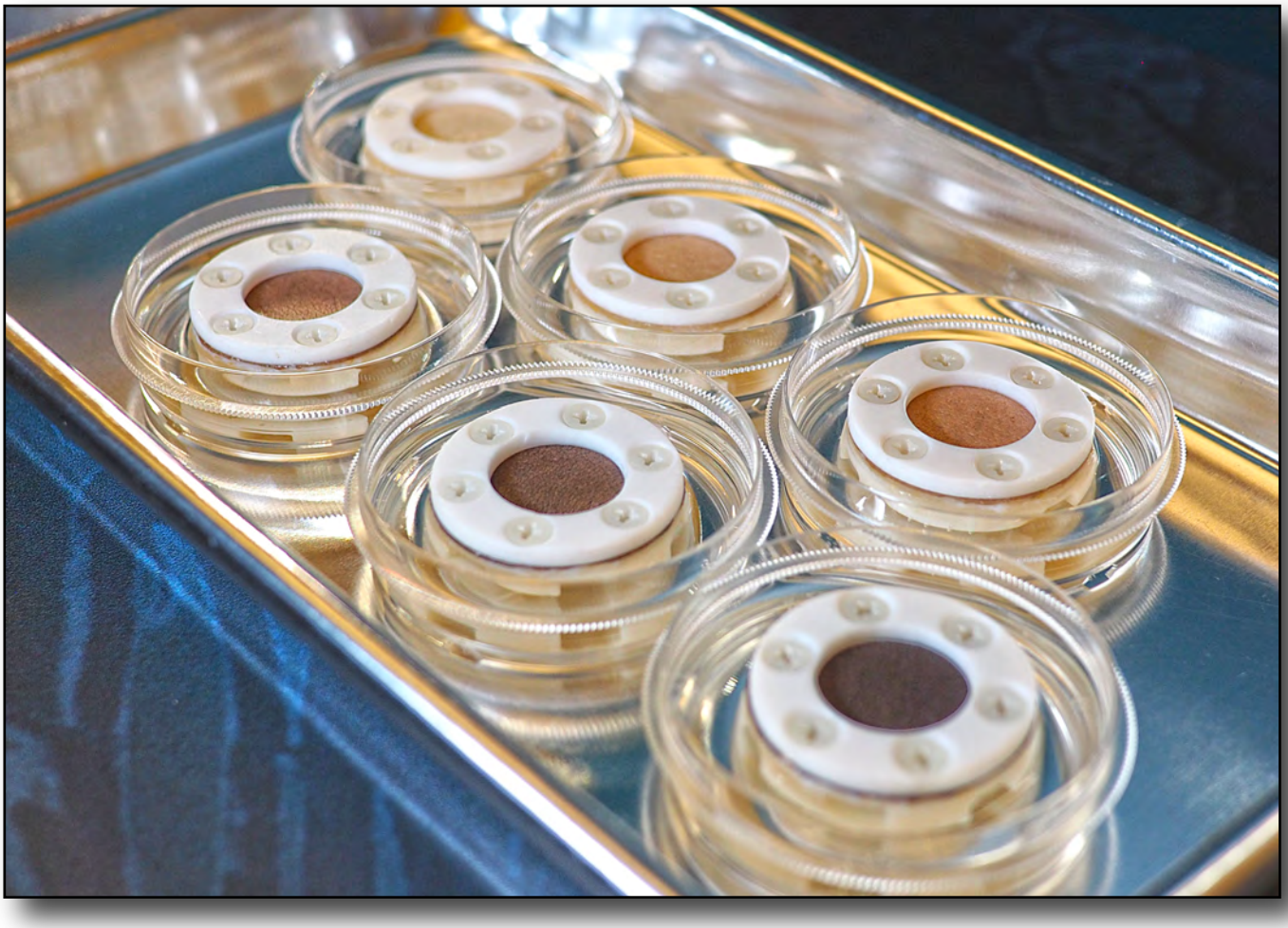
Research partnering services

Accelerate your R&D with TenSkin™

Our clients and research partners receive a wealth of support from their earliest engagement and can take advantage of our full-spectrum of expertise, including experimental design and execution along with an extensive catalog of SOPs to accelerate R&D programs. Ten Bio's multidisciplinary team of experts apply expertise in skin biology, physics, and tissue mechanics to enable rapid progression of our client's research.

We offer a comprehensive range of sample analysis techniques, including histological analysis, RT-qPCR, TEWL, hydration, and complete data analytics including bespoke interpretation packages for a wide range of application areas including but not limited to:

- Skin rejuvenation
- Wound healing
- Photobiology
- Substantiation of efficay claims
- Immune response
- Environmental stress



Better decisions drive better results, rapid progress, and lower costs

Global reach

Providing skin expertise - wherever your research is taking place

Ten Bio has established a network of clinical partners from which we source ethically and fully patient consented tissue samples with IRB approval. This consistent supply enables timely delivery of client projects - even those requiring specific donor criteria, including age range, gender, phototype, and more.

Let's connect

Our team is ready to tell you more about TenSkin™ technology and the broad testing and research services we offer.

info@ten-bio.com

TEN BIO

Research Partnering Services

Ten Bio's unique TenSkin™ platform allows real human skin to be cultured at physiological tension, which assures a normal and realistic tissue response. This enables evaluation of a broad range of responses over longer durations and more accurately than in other systems, allowing research teams to make more informed decisions at every stage of R&D.

Better decisions drive better results, rapid progress, and lower costs. Ask us about:

- State-of-the-art *ex vivo* capabilities
- Industry-leading technology with end-to-end services
- Expert team to assist with study design
- Cost effective R&D solutions