

Phenion – The Henkel brand for reconstructed human tissues

COVER STORY



A conversation with Dr. Dirk Petersohn,
Director of the Center of Excellence
Sustainability & Phenion, Henkel Beauty Care Technologies

Since 10/1998

Henkel AG & Co. KGaA

Diverse managerial functions in:

- Corporate Central Research
- Product development Beauty Care
- Biological & Clinical Research
- Currently:

Director of the Center of Excellence “Sustainability & Phenion”

01/1997 – 09/1998

Clinic and Policlinic for Dermatology

(Medical Department University of Cologne)

Post-Doc in the research team “Wound healing” of Prof. Dr. Thomas Krieg

1993 – 1996

University of Cologne, Institute of Genetics

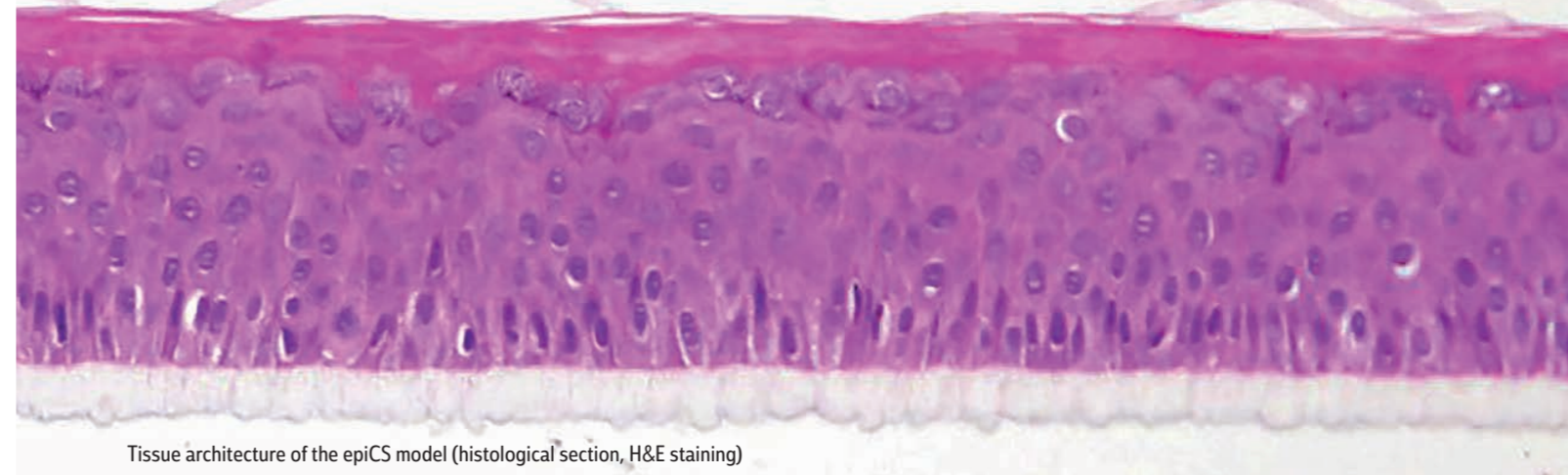
PhD-Studies on tissue specific gene regulation in the human central nervous system.

Member of the research team of Prof. Dr. G. Thiel

1988 – 1993

University of Cologne

Studies of Biology, Diploma



Tissue architecture of the epiCS model (histological section, H&E staining)

EURO COSMETICS: *Henkel is broadly known as a company that operates worldwide with leading innovations, brands, and technologies in three business areas: Adhesive Technologies, Beauty Care, and Laundry & Home Care. How does the Brand Phenion fit in here?*

Dr. Dirk Petersohn: Recognizing, that our in-house skin models are superior in predicting chemical effects, Henkel has decided in 2017 to grant unlimited access to its innovative technologies using the brand name Phenion. With this decision Henkel took the next level of responsibility to avoid animal testing and to support the development of new *in vitro* methodologies and their application. Initially, scientists at Henkel have developed skin models intended to be used for internal projects only. At that time *in vitro* grown human skin was employed in data generation, for e.g. safety assessments or product developments in all three business areas. As the skin models from Henkel are very similar to human skin in many anatomical and physiological characteristics, they are ideal tools for assessing effects on human skin. Thus, with the decision to grant access to the skin model technology Henkel supports third parties, like test laboratories or

research institutes, to reduce animal testing by using reconstructed tissues for their own research and services or also to develop additional, new alternative testing methods.

Based on the global Henkel strategies the Phenion team developed the vision of a just cause:

“Phenion facilitates the use of reconstructed human tissues to ultimately omit animal testing around the globe. To achieve this goal, we see the customers in the center of our strategy while we actively share our achievements!”

EURO COSMETICS: *I can see the visionary character of “... ultimately omitting animal testing around the globe ...”. Can you please exemplify on how Phenion strategically develops towards achieving this goal?*

Dr. Dirk Petersohn: Key for the strategic developments at Phenion is the customer. We listen very closely to their needs and aim for understanding their pain-points or challenges, to provide support and develop solutions. Thus, it becomes obvious that in our eyes, the customer is more than only the basis of a business relation – customers are our partners! Like in a good partnership we trust in, and care for each other. In

a nutshell: This is the reason why we developed additionally to the standard full thickness skin model, skin models in culture inserts, a LARGE version of outstanding size, the LONG-LIFE or the AGED versions.

We can see that today animal testing still needs to be conducted to address certain questions, particularly where alternatives are not yet in place. But frankly speaking, we at Phenion are convinced, that every single step can help to come closer to our vision and we want to provide our share of it.

EURO COSMETICS: *At the beginning of November 2020, Henkel completed the acquisition of the epiCS Technology from the SkinInVitro GmbH, which is headquartered in Troisdorf, Germany. What considerations led to this?*

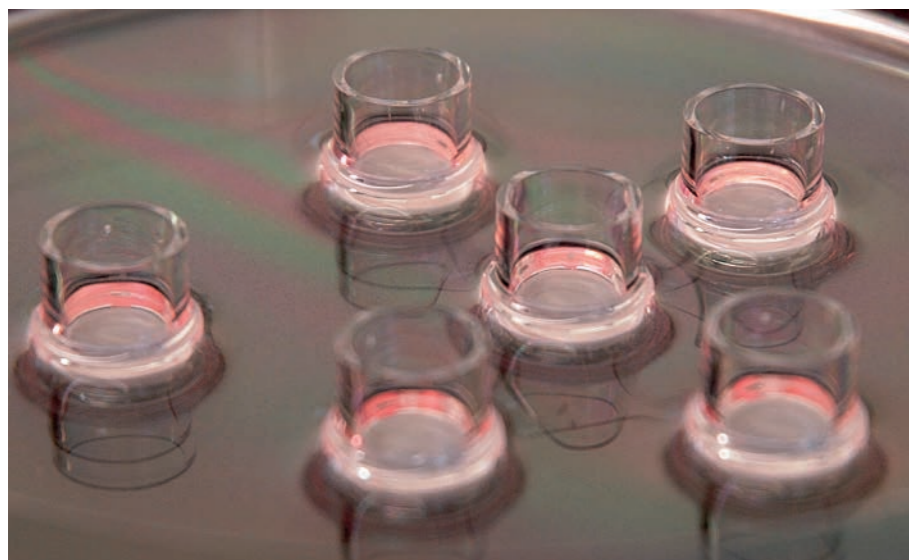
Dr. Dirk Petersohn: Our ambition for Phenion is to expedite the development, dissemination and use of alternative test methods. The partnership with our customers teaches us about the constant need for the generation of regulatory accepted data on skin irritation and skin corrosion. This is possible with test systems referenced in OECD Test Guidelines (OECD TG) like the epiCS Technology. This technology is listed in the OECD TGs for skin irritation (TG 439) and skin corrosion (TG 431).

In alignment with our vision and strategy to broaden the Phenion portfolio in a targeted way and to secure a sustainable access to the epiCS Technology we found an agreement with the SkinInVitro GmbH to continue the technology under the Phenion roof.

EURO COSMETICS: *Can you share with us the efforts that have been made to secure a sustainable access to epiCS tissues?*



Phenion FT Skin Models in the standard (left) and INSERT version (right)



epiCS models in air-liquid interface culture

Dr. Dirk Petersohn: It is to highlight that a comprehensive technology transfer was conducted to secure a seamless high-quality production of epiCS tissues under the roof of Phenion. In detail, we conducted a tiered approach, for which, in a first step, a Phenion expert was introduced into the tissue production processes at SkinInVitro. Secondly, experts from SkinInVitro and Phenion jointly produced qualified epiCS tissues. In a third step the Phenion expert produced qualified epiCS tissues on its own in the SkinInVitro laboratory. With this intensive training the Phenion expert was perfectly prepared to produce in parallel to CellSystems several qualified epiCS tissue batches in the Phenion laboratories. These tissues were subsequently used for successful skin irritation testing with identical sets of chemicals. Finally, the success of the technology transfer was proven by producing more than 20 consecutive qualified tissue batches at Phenion. In accordance with our vision to share our achievements, the data generated during the technology transfer will be published in due time.

In addition, we had the pleasure to welcome the experts of the SkinInVitro production team in Phenion. Consequently, our customers can be assured that the epiCS products are provided from Phenion at unchanged quality.

EURO COSMETICS: *And what benefits will arise from the acquisition for you and your customers?*

Dr. Dirk Petersohn: We are guided in our

decisions by our vision of a just cause, as mentioned above. May it be small, in e.g. publishing protocols or may it be bigger, in integrating e.g. the epiCS technology. With the epiCS technology on board of Phenion, our customers can now profit from a broader tissue portfolio that can fulfill different needs, e.g. to support basic research topics or to address toxicological endpoints like skin corrosion, skin irritation or gene toxicity, etc.

As we are aware of the different needs for testing of dermally applied chemicals and medical devices, we constantly expand the Phenion product portfolio to support tailor-made solutions in basic research for academic clients and across industry sectors.

EURO COSMETICS: *What can you tell us about the science of the epiCS skin model technology?*

Dr. Dirk Petersohn: With the epiCS technology, we provide human skin models that exclusively represent the epidermis, the upper part of human skin. These models consist of all relevant epidermal layers including the *stratum corneum*, which contributes to a large extent to the skin barrier. To a certain extent, epidermal models have what is needed to assess responses to external stimuli. Detrimental effects resulting in skin corrosion or skin irritation are manifested at this site of first contact, the epidermis. Thus, the respective testing of chemicals can be perfectly conducted by using reconstructed human epidermis, like the epiCS tissues.

EURO COSMETICS: *How does the epiCS skin technology fit in with your biotechnologically created skin models existing under the Phenion brand?*

Dr. Dirk Petersohn: The epiCS technology perfectly complements our existing skin model portfolio. To investigate certain physiological topics or specific toxicological endpoints, not only the epidermis but also the underlying dermis is required. The intense and physiological interaction of both skin layers can be of utmost importance. For example, the well-described effects of retinoic acid and its derivatives is highly depending on the metabolism and signaling of both skin layers. Moreover, investigation of toxicological endpoints, such as e.g. gene toxicity depends on the intrinsic capacity of skin models to reflect the natural occurring transformation of chemicals into metabolites, a characteristic which differs between epidermis and dermis.

Finally, one needs to appreciate that physiological effects upon any kind of stimuli can occur in the epidermis as well as in the dermis and consequently a comprehensive assessment can only be generated by analyzing both, the epidermis and the dermis. Being aware of these benefits, the Phenion Full Thickness Skin Models have been jointly used with diverse partners to develop the 3D Skin Comet Assay. This development was funded lately by Cosmetics Europe, the European trade association for the cosmetics and personal care industry. With its excellent predictivity, the 3D-Skin Comet Assay is on the OECD working plan for developing the respective OECD TG.

Having these examples in mind, it becomes obvious, that the choice of the test system is determined by the question to be addressed. Customers are now able to find the most relevant skin models at Phenion in one place. Additionally, we provide skin cells, namely keratinocytes, which build the epidermis, and fibroblast, which populate the dermis. Both cell types may be used for screening experiments with a higher throughput compared to complex approaches with skin tissues like the OECD approved epiCS tissues and the Phenion FT Skin Models.

EURO COSMETICS: *Human reconstructed skin has become increasingly important in various areas in recent years. How do you*

regard this development?

Dr. Dirk Petersohn: I can only echo what you have said! The development of 3D human tissue models, and in particular of 3D human skin models, has gained great momentum in the recent years. While in the past mono-layer cultures of skin cells like fibroblast and keratinocytes where the research tool of choice, 3D models of the epidermis entered the scene and are meanwhile broadly exploited. These types of tissue models were already a great achievement. The following milestone was to lift reconstructed skin models to the next level, that more comprehensively mimic the complex architecture and physiology of full thickness human skin. One great challenge for such full thickness skin models was to develop an environment for the fibroblasts that provide natural conditions for the cells. Such environment shall contain collagen as a major component of the extracellular matrix in skin. Scientists in this field have often used collagen gels, which then have been enriched with dermal fibroblasts. Despite very specific applications, this approach has a serious downside: With their integrin receptors, fibroblasts bind to the collagen fibers and reorganize the collagen gel by applying mechanical forces. Ultimately, the gel including the fibroblast shrinks to a very dense and compact structure, that is not able to provide a natural environment for the cells anymore. Knowing these undesirable effects, the Phenion scientists developed a stabilized collagen matrix which avoids the shrinking of tissues seen with

collagen gels. This sponge-like scaffold is populated by the fibroblasts, which in turn find sufficient space and build their own extracellular matrix. This *de novo* produced matrix is composed of different natural proteins including elastin, which is to our knowledge a unique and relevant physiological property of the Phenion Full Thickness Skin Models.

EURO COSMETICS: *You already mentioned, by partnering with your customers and by listening to their research needs, that you have developed very specific variants of the human skin models. Thus, you can look back across a long history. What, from your point of view, has been your biggest success?*

Dr. Dirk Petersohn: The successful development of the stabilized collagen matrix was a first milestone and represents the basis for new variants of the full thickness skin model. Meanwhile we have developed in accordance with customer needs a family of full thickness skin models, including the LONG-LIFE, AGED, LARGE and INSERT skin model variants. I would not dare to nominate “the biggest success”, as each model addresses a specific research need and represents a step toward our vision of omitting animal testing around the globe. Consequently, each tissue model is equally important on our journey. We are aware, that there is still a long way ahead of us and new challenges will cross our way. Nevertheless, I believe that with new developments and technologies, including tissue engineering, in silico-tools, artificial



Cell culture work

intelligence, 3D bio-printing, etc. animal tests will ultimately vanish and will be replaced. As Henkel has committed to that vision, it fills me with pride to contribute to this field.

EURO COSMETICS: *We have learned about your long-term goals, that are well described in your vision. What can you tell us about your medium objectives in research?*

Dr. Dirk Petersohn: Skin represents the site of first contact for a plethora of chemicals. For assessing the chemicals' safety, also the skin sensitization potential is of great interest. The current knowledge of the skin sensitization mechanism is well described by the so-called adverse outcome pathway (AOP). Currently, several methods have been developed that cover certain steps of the AOP. Wouldn't it be great to develop one method that covers several steps of skin sensitization? Jointly with academic partners we aim for a standardized immune competent skin model that provide (I) a functional skin barrier, (II) a representative skin metabolism, (III) typical skin proteins for haptenization reactions, (IV) and in addition to keratinocytes immune-competent cells for their respective activation. We consider that such a test system would be beneficial to complement the existing test methods in a tiered approach.

EURO COSMETICS: *Thank you very much for the interview.*



Phenion FT LARGE model