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Dr Fred Zülli, Mibelle Biochemistry

"10 YEARS: PLANT STEM CELLS"

VIP of the Month

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Interview with:
Dr Fred Zülli, Managing Director, Mibelle Biochemistry
Buchs, Switzerland
www.mibellebiochemistry.com

10 YEARS OF PLANT STEM CELLS

Interview | On the occasion of the 10th anniversary of plant stem cells, Dr Fred Zülli from Mibelle Biochemistry looks atthe advantages and sustainability of plant stem cells and the potential of biotechnology for cosmetics.

photos: Mibelle Biochemistry

COSSMA: What gave rise to the creation of plant stem cells for cosmetics?

Dr Fred Zülli, Managing Director, Mibelle Biochemistry: At **In-Cosmetics 2008** in Amsterdam, we launched the product **PhytoCell-Tec Malus Domestica** as a new active onto the market, and in doing so we pioneered the trend of **stem cell cosmetics**. More than ten years after the Amsterdam launch, this trend continues to grow. Research into life science topics such as nanotechnology, neuroscience or stem cells is a very promising and successful approach for bringing innovation to the cosmetic industry.

How are plant stem cells created?

Plant stem cells can be obtained with the help of plant cell culture technology. This involves a plant material, such as a leaf or a fruit, which is then wounded and incubated on special agar plates, see fig. 1. The plant develops a wound-healing tissue called callus. This tissue is based on de-differentiated cells, which are pluripotent stem cells.

Please explain to us how these plant stem cells can be produced for cosmetic applications?

The large-scale production of plant stem cells is a major challenge. From the plate, the cells have to be transferred into liquid media containing sugar. This means that the entire process of growing the cells has to be conducted under strict sterile conditions which is difficult to realise as the plant stem cells grow very slowly in comparison to bacteria. However, we solved this problem by constructing our own disposable bag reactor called 5-wave bio-reactors. These reactors allow us to simultaneously cultivate five times 25 litres of cell cultures.

How do plant stem cells work in cosmetics?

The skin undergoes a constant cell turnover in order to maintain, renew and repair its tissue. Adult stem cells that reside in special niches in different layers of the skin are responsible for this regenerative capacity. Stem cells are defined by their ability to self-renew and differentiate into mature specialised cell types. However, stem cells are also subject to ageing which leads to reduced vitality and a decrease in the stem cell pool. The depletion of stem cell activity is a major cause of skin ageing. Therefore, cosmetic ingredients that vitalise skin stem cells provide a real anti-ageing potential, see fig. 2.

Do you have data which prove the effect of plant stem cells on skin stem cells?

Extracts of different plant stem cells were tested on human keratinocyte progenitor cells (epidermal stem cells). Skin stem cell cultures treated with plant stem cell extracts showed an increased vitality in a colony forming efficacy (CFE) assay. Further studies showed that plant stem cells can protect skin stem cells against UV irradiation. The most convincing study showed that the application of plant stem cell extract led to the formation of a 3-dimensional skin tissue out of aged skin stem cells.

RESEARCH

R&D into **nanotechnology**, **neuroscience** or **stem cells** helps to bring innovation to the cosmetics industry

Plant stem cells can be obtained with the help of plant cell culture technology

The **large-scale production** of plant stem cells is a major **challenge**

Research into exosomes is relevant for **understanding cell-to-cell communication**

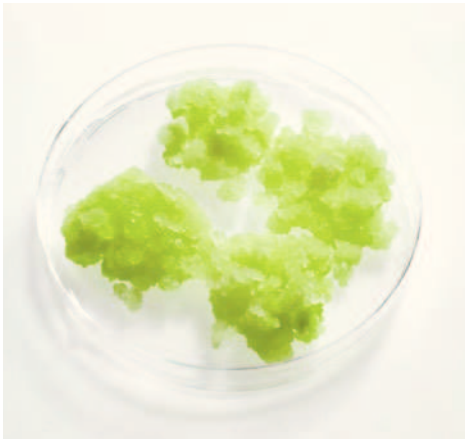

fig. 1: Callus tissue on agar plate

But how can plant stem cells work on human stem cells and how does this benefit cosmetic formulations?

The activity of plant stem cells on human stem cells is based on the fact that stem cells require special nutrients in order to be able to grow. An extract of plant stem cells contains precisely the relevant nutrients to vitalise human

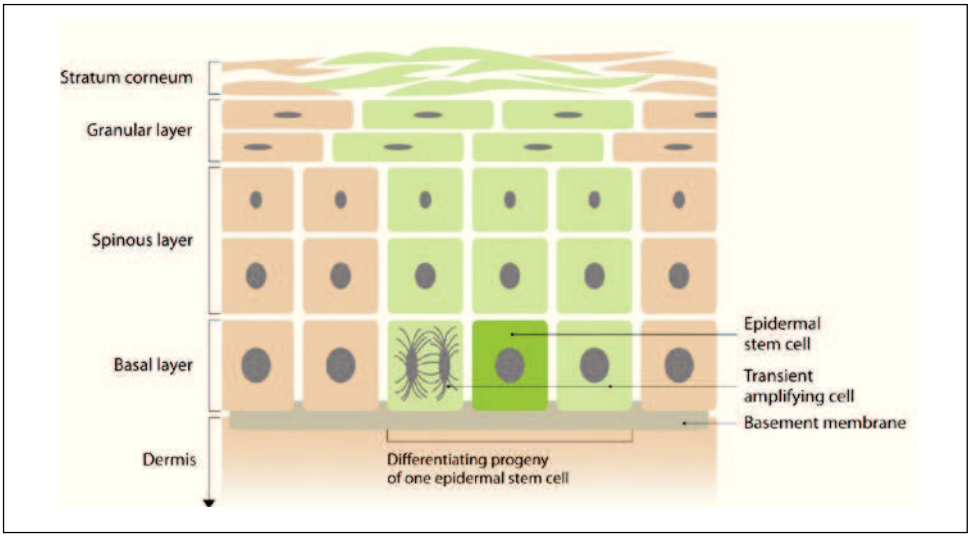

fig. 2: Skin renewal by epidermal stem cells

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"OUR AIM IS TO FIND NEW ACTIVES THAT WILL PROTECT THE SKIN AGAINST EPIGENETIC EFFECTS"

Dr Fred Zülli, Managing Director, Mibelle Biochemistry

stem cells. An extract of plant stem cells has a different composition from a normal plant extract. In clinical studies we managed to prove that different plant stem cell extracts can improve the density of the skin, reduce wrinkles and increase the skin renewal.

What were the latest findings in the field of plant stem cell technology?

In the past ten years, our company has launched seven different plant stem cell products that have come from different plants such as apple, grape, alpine rose, comfrey, argan, saponaria and goji. With the help of new cell culture techniques, we proved that different stem cells activated different biochemical mechanisms of skin stem cells and hair stem cells. In our latest research we demonstrated that our product activates mesenchymal stem cells to release more exosomes which then activate the collagen production of fibroblasts. Finding out how exosomes work is a very new field of science and relevant for understanding cell-to-cell communication.

CULTIVATION
Cultivating **stem cells** requires no further biomaterial from the wild

Once **mesenchymal stem cells** have been activated, released **exosomes** activate the **collagen** production of fibroblasts

Plant stem cells are produced with the help of biotechnology. What role does biotechnology play in Mibelle Biochemistry's research?

Biotechnology is part of our strategy to create innovative actives in a sustainable way. Our first stem cell product was based on an old apple cultivar called Uttwiler Spätlauber. In fact, today, there is only a small number of trees of this rare apple cultivar still alive. However, only very few of these apples were required in order to establish the plant cell culture of this origin. We have now been cultivating the stem cells for over 10 years without using further biomaterial from the wild.

Is this thus a contribution to the big trend of sustainability?

Yes, it is. The concept of using rare and exotic plants in cosmetics appeals to consumers and researchers alike. Unfortunately, the sustainable use of these plants is very often not possible since the plants cannot be cultivated. The production of plant stem cells from endangered plant species overcomes this problem because only small amounts of the plant are needed to start the stem cell culture in bioreactors. Therefore, the **PhytoCell-Tec** technology of **Mibelle Biochemistry** was recognised at the **United Nations Conference on Sustainable Development** in Rio de Janeiro 2012 as a breakthrough technology for the development of new natural cosmetic ingredients.

Have you developed other ingredients by biotechnology?

Yes, we have. Over the last few years, we have developed two new ingredients that are based on unique technologies. One ingredient is based on the cultivation of a red snow algae in photo-bioreactors in a cold room. In contrast to this, the other ingredient is based on the cultivation of a moss protonema tissue culture in sterile bags, see fig. 3.

After stem cell cosmetics, what do you think will be the next future key topics in the world of cosmetics?

We are convinced that the new findings in epigenetics will be integrated into novel developments of actives.
The influence of the environment, for example air pollution and psychological stress, can cause epigenetic modifications in the skin. These negative effects will be long-lasting and could even be passed on to the next generation. This is why, in our research we are focusing on finding innovative active ingredients that will help to protect the skin against epigenetic effects such as DNA methylation, histone modifications or miRNA expression. □

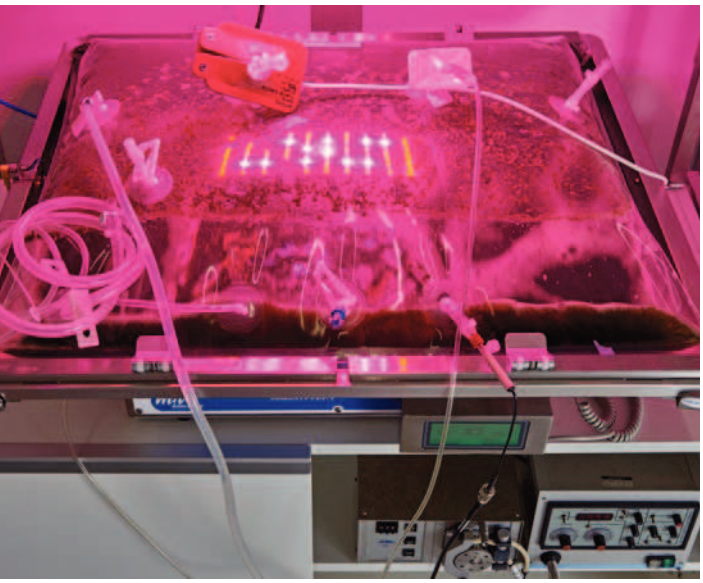

fig. 3: Snow algae and moss tissue cultivation in bioreactors

Additional information can be found on the Internet – see Internet panel

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