THE NEW FRONT LINE IN ANTIAGEING

The epidermis is a stratified epithelium that, to maintain normal barrier function, is constantly renewed throughout life — a renewal that is mediated by stem cells in the basal layer of the epidermis. The protection or stimulation of these stem cells has become a hot topic in cosmetics and in vitro test systems using epidermal stem cells have been established to facilitate claims for epidermal stem cell actives. But what about the stem cells in the dermis? Until now, they have not been addressed by cosmetic treatments despite playing a decisive role in skin ageing. Fibroblasts, the prominent cell type in the dermis, are responsible for the continuous production of collagen and elastin; ageing skin is characterized by an increasing number of senescent fibroblasts. These cells have not only stopped producing collagen and elastin but even start to break down the existing matrix.[1] The replacement of these senescent cells by new fibroblast cells can only be triggered by dermal stem cells — treatments that reinforce the functional ability of dermal stem cells, therefore, have real antiageing potential.

THE DERMAL PAPILLA: A NICHE FOR DERMAL STEM CELLS

Compared with epidermal stem cells, research on stem cells of the dermis is relatively young, with the first reports about multipotent cells of the dermis appearing in 2001.[2] Experiments into the exact localization of these multipotent stem cells revealed that they are always located near the hair follicle, in the papilla and the perifollicular area. In late 2009, Biernaskie *et al.* showed that dermal papilla cells express the stem cell marker gene Sox2 — a transcription factor shown to be essential in maintaining the pluripotent phenotype of stem cells — and have a tendency to grow in colonies in the form of spheres.[3] The Sox2-positive cells were found to self-renew, to induce the formation of hair follicles and to migrate into the inter-follicular dermis, where they proliferated and differentiated to fibroblast cells, which are able to regenerate the extracellular matrix (Figure 1) — for the first time, the dermal papilla was identified as a niche for dermal stem cells. The door is now open to the next generation of stem cell cosmetics: the protection and vitalization of human dermal stem cells for the restoration of skin firmness and wrinkle reduction.

A NEW ASSAY

Dermal stem cells were isolated from the dermal papilla of excised human hair follicles and maintained as a monolayer culture for several passages. They then transferred into hanging drops and formed 3D spheres, thus demonstrating an important characteristic of stem cells. In addition, immunofluorescent labelling of whole mount spheres showed positive staining for Sox2, a proposed dermal stem cell marker. When cells dissociated from primary spheres were seeded back into classical cell culture dishes, numerous secondary spheres were spontaneously formed (Figure 2). To evaluate ingredients for stem cell vitalization potential, the intensity and uniformity of Sox2-

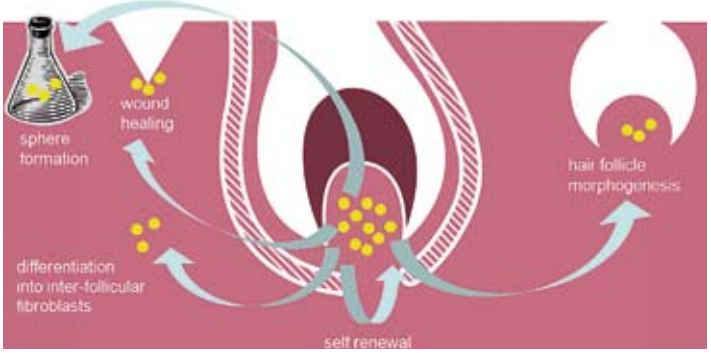

Figure 1: The dermal papilla as a niche for dermal stem cells.

BUT WHAT ABOUT THE STEM CELLS IN THE DERMIS? UNTIL NOW, THEY HAVE NOT BEEN ADDRESSED BY COSMETIC TREATMENTS DESPITE PLAYING A DECISIVE ROLE IN SKIN AGEING

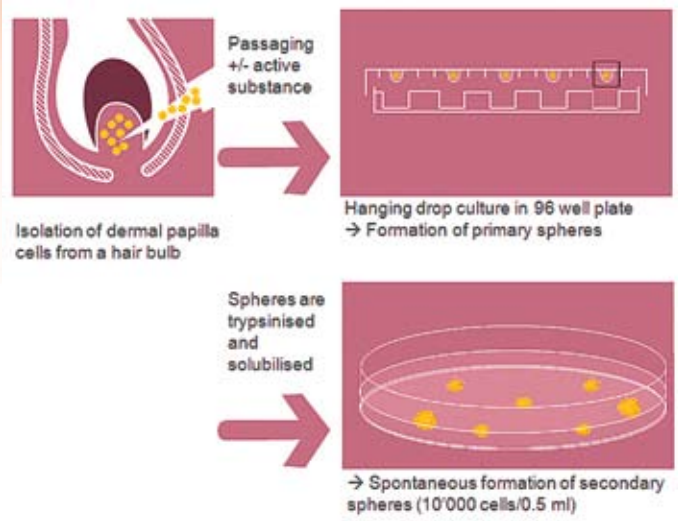

Figure 2: Formation of primary and secondary spheres as test system for dermal stem cell actives.

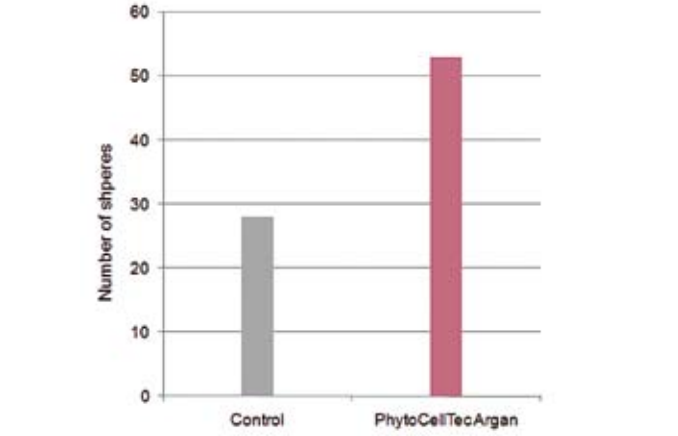

Figure 3: Number of secondary spheres.

labelling in primary spheres and the number of secondary spheres formed were used as parameters. The assay was used to screen for a dermal stem cell ingredient and an extract of plant stem cells of the Argan tree (PhytoCellTec Argan), produced by the plant tissue culture technique, was found to significantly stimulate the vitality of dermal stem cells.

VITALIZATION OF HUMAN DERMAL STEM CELLS

Dermal papilla cells, isolated from excised human hair follicles, were cultured in the presence of 0.1% PhytoCellTec Argan and the primary spheres prepared for immunohistochemical analysis of expression of the stem cell marker Sox2. Compared with control cultures, the immunofluorescence pictures clearly revealed an enhanced expression of Sox2 in spheres formed by dermal papilla cells cultured with PhytoCellTec Argan. Incubation with PhytoCellTec Argan was also found to stimulate the formation of secondary spheres (Figure 3) — compared with the control culture there was an increase of 89%. Overall, the results prove the beneficial effect of PhytoCellTec Argan on the stem cell characteristics of the dermal papilla cells. PHM

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