

Dermal Stem Cells - the next target

Skin renewal and regeneration depends on stem cells

Our body's tissue is subject to a continuous regeneration process. The ability of adult stem cells to self-renew and to generate fast proliferating progenitor cells is an absolute prerequisite for tissue regeneration. Because the skin is an exceptionally highly regenerative tissue, the skin stem cell population represents the most important target for anti-ageing treatments. But, regardless of the regenerative power of stem cells, our skin loses its elasticity and firmness and forms wrinkles as we age. The regenerative potential of the stem cells apparently does not last forever; they too age. Ingredients, specifically designed to delay the depletion of their regeneration capacity, are a most promising solution to keeping skin looking youthful longer.

We are in need of novel in vitro models to test stem cell claims

Meanwhile a lot of research is being done on the mechanism of epidermal regeneration by stem cells embedded in specific niches located at the basal layer of the epidermis. In vitro test systems using epidermal stem cells have been established which allow claims for epidermal stem cell actives. Also dermal stem cells could be targeted by cosmetic ingredients. Fibroblasts, the prominent cell type in the dermis, are responsible for the continuous production of collagen and elastin. These proteins form the so called extracellular matrix, a three dimensional structure that confer elasticity and firmness to the skin. Age-related reduction in the formation of the extracellular matrix and environmental stress factors that lead to the breakdown of the existing matrix are key elements in the skin ageing process and directly involved in wrinkle formation. Controlling the

regenerative potential of dermal stem cells would make it possible to correct loss of skin firmness and elasticity and to prevent wrinkles.

A novel cell culture assay to address dermal stem cell activity

Details of the dermal stem cell niche and marker expression remained scarce. But recently, a research group at the University of Toronto showed that the dermal papilla is a niche for dermal progenitor/stem cells. These 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, able to regenerate the extracellular matrix. Other characteristics of these cells were the expression of a specific marker gene Sox2 and the tendency to grow in colonies in the form of spheres.

Mibelle Biochemistry is now working on a human dermal papilla cell line as a new test system for the evaluation of active ingredients for stem cell vitalization potential. The established cell line was found to effectively form sphere-like colonies and the cells in those spheres were found to be uniformly Sox2-labelled, thus representing real dermal stem cells.

Working with human dermal stem cells

Progenitor cells isolated from the dermal papilla of excised human hair follicles could be maintained as a monolayer culture for at least 11 passages. At both passage 3 and passage 11 cells transferred into hanging drops formed 3D spheres, demonstrating that this important characteristic of progenitor cells was retained even after longer-term cultivation. In addition, immunofluorescent labelling of whole mount spheres showed

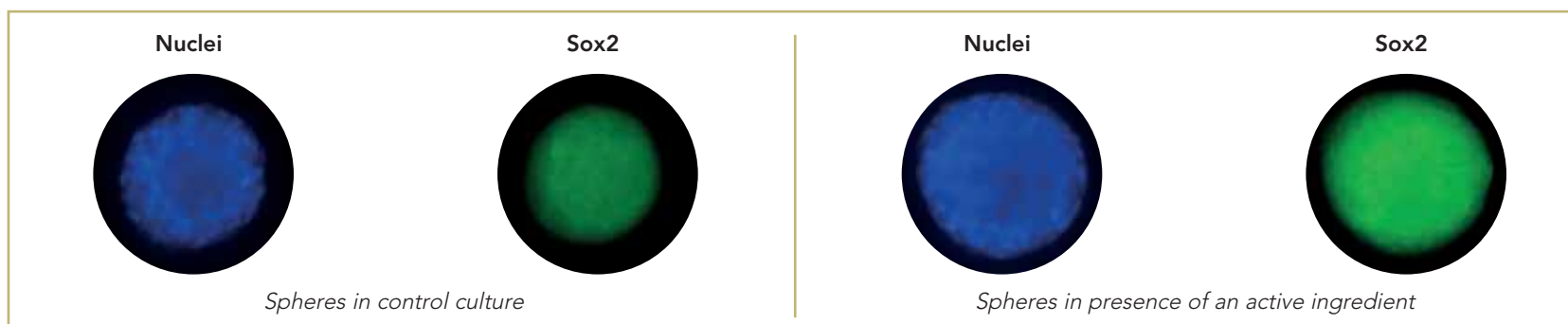
positive staining for the Sox2, a proposed dermal stem cell marker. When cells dissociated from primary spheres were seeded back into classical cell culture dishes used for routine monolayer culture, numerous secondary spheres were formed. This indicates that once cells have formed primary spheres, they seem to retain a memory of the 3D progenitor phenotype, and preferentially re-form spheres where normally monolayer cultures would be expected to form.

Conclusion

A stable culture of progenitor cells isolated from the dermal papilla could be established. Even after 11 passages, cells retained the ability to both form 3D spheres and express the stem cell marker Sox2, suggesting a stem cell phenotype. Using this culture we can now effectively evaluate the influence of cosmetic actives on dermal stem cells. A variety of evaluations may be made, including both molecular (i.e. stem cell marker expression) and phenotypic (i.e. number of spheres, proportion of complete spheres, serial passaging of 3D spheres etc). This approach will provide us with detailed insights into the behaviour and activity of dermal stem cells in the presence of cosmetic actives, thus enabling the evaluation of their ability to maintain or restore their regenerative potential in the dermis.

Protection and vitalization of human dermal stem cells is the next generation of stem cell cosmetics. Active ingredients with these properties offer a deep-seated rejuvenation of the skin, resulting in restoration of firmness and wrinkle reduction. In addition, such products could also be beneficial in wound healing and the treatment of stretch marks.

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