Do Stem Cells Hold the Key To Younger-Looking Skin?

Stem cells, though controversial, often play a key role in drug research. Now these materials are finding new applications in skin care, and stem cells are the latest buzzword in the anti-aging category. Yet scientific opinion remains divided on their origin. One opinion is that stem cells arise when sperm fertilizes an egg, while the other is that they originate in the inner cell mass of the blastocyst. Stem cells have the ability to go through numerous cycles and cell divisions while maintaining their undifferentiated state. They also have the capacity to differentiate into other cell types such as muscle, blood and nerve tissue.

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Adult stem cells reorganize, heal and repopulate the skin with new cells. They arise from the basal layer of the epidermis and at the hair follicle base. Adult stem cells, as opposed to embryonic stem cells, repair and regenerate damaged tissues. Theoretically they possess the ability to create new skin cells and regenerate the skin for a lifetime, but age and environmental factors cause them to function less efficiently, resulting in older-looking, aged skin. Stem cell-based creams reportedly stave-off this process by either stimulating or protecting stem cells deep in the basal layer of the epidermis.

Stem cells are readily available in hair follicles and sweat glands.

Stem cells divide relatively infrequently. With age, stem cells lose their proliferative capacity and perhaps their ability to respond to signals to produce more epithelial cells, according to R. Ghadially, a dermatologist and skin stem cell specialist at the University of California at San Francisco's Institute for Regenerative Medicine. Increasing proliferation is the ultimate complexion rejuvenator.

Stem Cells in Skin

Epithelial skin stem cells are found in the basal layer of the epidermis, while hair bulge stem cells are found in hair follicles. Furthermore, hair follicular stem cells, tooth stem cells and skin stem cells all show therapeutic promise and may one day restore hair to bald men, teeth to those in need and skin to scarred patients, according to Dr. Denis English, editor of *Journal of Stem Cells* and director of cell biology at the University of South Florida.

Changes in the skin are caused by aging, disease or injuries. Although drugs can relieve consequences of the disease, they will not suppress the cause. Therefore, the most attractive strategy is to replace disabled cells, and to this end, to take advantage of stem cells.[1] According to Gregory Brown, creator of ReVive, accessibility also makes skin stem cells appealing to cosmetic chemists. Stem cells are readily available in hair follicles and sweat glands. The ratio of stem cells to regular cells in skin is still hotly debated. It was once thought to be 1 in 10, but is now suspected to be more like 1 in 10,000.

Stem Cells and Aging

Stem cells have a limited life expectancy because UV, smoking and ozone all hasten skin cell depletion, resulting in DNA damage, telomere shortening and oxidative stress. Cell depletion does not activate stem cells to change into new cells. Aging stem cells lead to a decreased capacity for repair, an increased incidence of degenerative diseases and an increased incidence of cancer in tissues that contain stem cells. Skin rejuvenation comes to a halt when stem cells remain inactive. Under the right stimulus, stem cell activity could be jump-started to initiate skin rejuvenation.

Stem cells have unique secondary structures of DNA and RNA. Stem cells have special components in the cytosol-epigenetic factors. Stem cells are sensitive to environmental stress factors and hence protection and maintenance of stem cells is of great importance. Epigenetic profiles regulate the gene expression in stem cells, which enable cells to stabilize and maintain different characteristics despite containing the same genomic material. This is achieved by chromatin remodeling by DNA methylation (gene silencing), post-translational modification of histone proteins (e.g., acetylation for transcriptional competence) or mRNA inactivation through micro RNAs or small interfering RNA (siRNA).

Voss' Amatokin

High-Priced Products

Marketers are presenting stem cell creams as the future of skin care. This article will review major stem cell-based anti-aging consumer products and the science surrounding stem cell technology.

Amatokin is available from Voss Laboratories in collaboration with Beilis Development Company. It has a hefty price tag of 190 euros or $258 per 30ml. Less expensive is Christian Dior's Capture R 60/80 XP cream, which still costs more than $100 for 30ml. StimulCell from N.V.Perricone retails for $155 for 1.7fl.oz. Another product based on cellular tune-up action that is similar to stem cell is Estée Lauder's Re-Nutriv, which costs approximately $130. But the costliest product is ReVive's Peau Magnifique Youth Recruit. It comes in a lucite cube that houses four small silver tubes. A one-month supply of this super serum costs $1,500...can you believe it? The company insists that the high cost is because of a telomerase which is a bio-engineered enzyme costing about $4 million per gram.

Estee Lauder's Re-Nutriv creme does not contain stem cells, but its formula provides many of the same benefits.

Actives and Claims

Although all of these products make similar claims, their backgrounds are quite different. For example, Amatokin got its start in 1988 when Russian scientist Taras Nikolaev from the Biotechnical Institute in Moscow and St. Petersburg studied peptide research to accelerate wound healing and skin repair. His team created a polypeptide with the ability to stimulate dormant stem cells in the skin, rejuvenate the skin and speed healing—truly a bold, astonishing claim. Amatokin is the first topical polypeptide that lights up stem cell markers (the means by which cell activity is measured). The polypeptide acts as a catalyst when it comes into contact with the upper keratinocyte cells of the epidermis, initiating a molecular signaling cascade that produces the increase in activity which was measured by the stem cell markers.[2]

In the case of StimulCell, young, undamaged cells were created by applying chemically reproducible oxidative stress to stem cells, which forces them to pump out 145 different proteins, carbohydrates and lipids. These materials are protect cells and relay regenerating messages, according to Dr. Perricone.

For Dior Capture R 60/80 XP crème, the active is a vitamin E derivative called alpha-tocopheryl phosphate, which creates a protective shield. ReVive Peau Magnifique Youth Recruit has an enzyme active called telomerase, which was first discovered in 1984, according to Bays Brown, the brand's founder. Finally, Re-Nutriv contains a stabilized version of reservatrol, an antioxidant produced by some plants to ward-off fungi and bacteria.

Amatokin initiates the release of very powerful growth factors responsible for cell proliferation, according to Louie Rinaldi of Voss Laboratories.

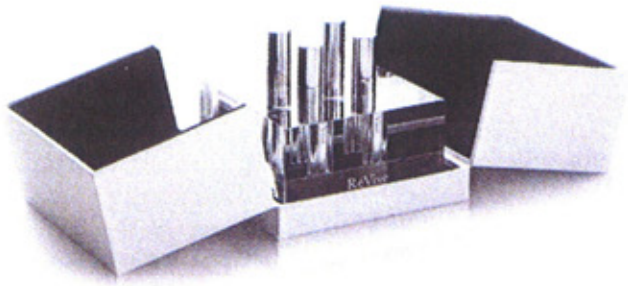
According to R. Ghadially a dermatologist and skin stem cell specialist at the University of California at San Francisco's Institute for Regeneration Medicine, this product increased the expression of certain stem cell markers. We only know what those markers indicate in embryonic cells. It has not been proven that they have the same correlation in adult cells. It is very promising, but more work needs to be done. His lab is conducting independent research on whether the markers in question do in fact indicate the presence of adult stem cells.[3]

How it Works

Amatokin highlights the expression of stem cell markers in the skin to reduce the appearance of serious wrinkles. It focuses on using polypeptides and enzymes to "awaken" the body's own reservoir of stem cells. We only know what those markers indicate in embryonic cells. There is no proof that the same holds true in adult cells. While very

promising, more work needs to be done.

StimulCell contains cell-protecting and regenerating messengers. When the product is applied topically, these messengers reportedly attach to skin cells, signaling them to begin the reparative process. In one study, Dr. Perricone's product reduced acne, skin damage and wrinkles using the cell's own messengers.



ReVive Peau Magnifique Youth Recruit's efficacy is due to the telomerase enzyme.

A cell is carefully guided toward rejuvenation.

In an in-vitro study by Dior, the alpha-tocopheryl phosphate in Capture R60/80 XP reduced the number of stem cells lost in the epidermis after sun exposure. The company recruited 30 women scheduled for facelifts and asked them to use the cream on one cheek for two months before surgery. The treated skin showed 19% more epidermal cells. Rather than purporting to stimulate stem cells, this product makes rather modest claims that it protects and prolongs the functioning of the stem cells. The company asserts that the product's effectiveness is due to Stemsome, a sophisticated delivery system that transports ingredients into the skin. The system envelops each active ingredient in multi-stacked layers, which progressively melt as they are absorbed by the skin, releasing the active ingredient. According to Edouard Mauvais-Jarvis, director of scientific communications, each time a layer melts, the next one opens, enabling the ingredients to reach their target deep within the skin. This technology doesn't enhance the cells in any way, it merely creates a more beneficial environment to allow the stem cells to play their optimum role in regulating the skin.

ReVive Peau Magnifique Youth Recruit's efficacy is due to telomerase, an enzyme that aids DNA replication to prevent chromosomal strands from losing bits of information when they split, thus warding off genetic mutations. When applied topically, it can also send a signal to stem cells, rallying them to respond as they would to an injury. Epidermal Growth Factor (EGF), a protein found naturally in the human body that is released from the cells after injury to increase cell turnover, does accomplish regeneration of aging skin. The product does not alter the body's natural functions nor changes skin in any abnormal way. It does not add or inject stem cells into the skin. It merely stimulates and accelerates a natural process. It purports to convert resting adult stem cells to newly minted skin cells.

The active in Re-Nutriv, reservatrol, extends the life of cells, actually slowing down turnover rather than speeding it up—possibly the best way to ward-off cell breakdown.

Too much cell division has the potential to cause mutations.

Discussion

Some observers complain that Amatokin, and any other ingredient that causes cells to multiply, could cause cancer due to cell division.

"You don't want a signal that just says: 'turn on' to stem cell activity. That's like a car that just has a gas pedal—it could be dangerous, resulting in overproduction, potentially even cancer," agreed Dr. Perricone. "You want cells that turn on, cells that moderate, cells that suppress activity, cells that steer."

However such fears are dismissed[2] because you are stimulating adult stem cells which start as pristine, unformed cells. Given the proper environment, they undergo a maturation process to become a new cell and then migrate, through cellular communication, to the area of damage, telling the fibroblast cells, "it is time for you to die, I am here to take your place."

So, you get a brand new cell replacing an old, aging cell that is removed naturally from the body.

Stem cells' low rate of division is actually a protective measure, according to Dr. Geraldine Guasch, a researcher at Rockefeller University, New York, NY. The more cells divide, the greater their chance of DNA mutation. Cancer is basically the result of haywire cell production. Mutated stem cells may cause cancers to grow back even after chemotherapy, which could make skin stem cells' inherent accessibility more of a bane than a benefit. Susceptibility to UV damage could mean they are prey to even more mutations than internal cells. In skin, it has not been demonstrated yet that a stem cell can be the start of cancer. If a

company claims to increase stem-cell activity, Dr. Guasch wants proof that the chromosomes of these new cells do not accumulate mutations. Besides, as Dennis Gross, a New York City dermatologist, points out, anything that alters cellular activity, constitutes a drug claim and require FDA approval. Dr. Perricone is considering equipping his Madison Avenue flagship boutique with a machine that would enable him to harvest and store clients' individual stem cells—other innovators are focusing on preserving the cells we already have.[1]

Dior was the first luxury brand to tap into stem cells.

Some experts question whether the enzyme found in ReVive Peau Magnifique Youth Recruit truly ignites stem cell differentiation. Telomerase plays a role in some, but probably not all, stem cells, says Amy Wagers, a principal faculty member of the Harvard Stem Cell Institute in Cambridge, MA. Dr. Wagers is not familiar with any data suggesting it directs their differentiation or wakes them up. Regarding before and after photos that show a dramatic improvement in skin tone and texture with fewer fine lines, Dr. Gross noted that many active ingredients work on skin cells to stimulate them to make byproducts like collagen. This is very different from stem cell technology in which the cells themselves form tissue.

Meanwhile, with the debut of Capture R60/80 XP, Christian Dior became the first global luxury brand to tap into stem cell technology.

Storage Banks

Recently two teams of researchers transformed ordinary skin cells into batches of cells that look and act like embryonic stem cells—those master cells that give rise to every cell and tissue in the body. Moreover, they accomplished that without cloning technology or embryos.

Dr. Shinya Yamanaka of Kyoto University, Japan, recently said that creating a bank to store a new type of stem cell produced from donor's ordinary skin cells could reduce time and money for treating patients. This research makes it possible to reset an aging cell to become an entirely new being, and may give rise to powerful anti-aging actives in the future. Several companies, including Bio Eden, C'elle, Neostem and Store A Tooth, provide stem cell extraction and storage services, though viable therapies may be years away

Apple Stem Cells

Mibelle Biochemistry launched an anti-aging active based on an extremely rare form of apple stem cells. It promises to protect skin stem cells and slow the senescence of hair follicles. In vivo and in vitro tests proved that the ingredient, PhytoCell TecMalus Domestica, boosted the production of human stem cells, protected them from stress and decreased facial wrinkle depth. It also delayed the aging of the hair follicles, suggesting a possible use in anti-aging hair preparations.

An apple a day...keeps wrinkles away?

Not every one is convinced that stem cell creams are the future of anti-aging. There are not enough published scientific data available to support its safety and efficacy in skin care products at this time. Stem cells are very popular, but many dermatologists remain skeptical. Alan Matarasso, a cosmetic plastic surgeon in New York City, noted that the theory of stem cells sounds good but the question is, whether or not a topically-applied cream can send signals to activate these stem cells. Until there are double-blind clinical studies, their efficacy is unproven. Ultimately it is up to the consumer to decide if the results live up to all the hype.

According to David Colbert, a New York City dermatologist, it may be premature to choose a stem cell cream over one with, say, time-proven retinols or hydroxyl acids. Stem cell research is still very young. There is much more information to unravel.

Nanotechnology, DNA and now stem cell technology have all recently entered the skin care category. My concern is that these highly scientific technologies are marketed to consumers at ridiculously high price. No one is looking seriously at whether the drug-like claims that are being made for these technologies are truly accurate or if their long-term use would put the consumer's health and safety at risk.

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3. Investigation, micromanagement, M. Bullock, *Elle,* Dec. 2007.