

Stem cells and the pursuit of youth, a tale of limitless possibilities and commercial fraud

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Abstract

This article examines the hype generated around the term “stem cell”, and the capitalization of the stem cell craze by the cosmetic industry. It started by introducing product lines containing active ingredients derived from plant stem cells. Then, evolved to using own cells for skin regeneration and hair loss treatment, and allogenic cells for the manufacturing of stem cell-derived products. This article also discusses the missing links for safe and reliable stem cell applications in cosmetics, and why local regulatory bodies, members of the industry and consumers must all work together to stop the illegitimate use of the “stem cell” good name in unsafe or fraudulent commercial practices.

Key Words: Stem cell; Stem cell-derived products; Cosmetics; Regulations

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Core Tip: The capitalization of the stem cell craze by the cosmetic industry. Products and procedures utilizing plant stem cells-extracts, a person’s own cells or allogenic laboratory grown stem-like cells, are all being offered as direct-to-consumer options for tissue regeneration. What are the missing links for safe and reliable stem cell applications in cosmetics, and why is it important to address these issues?

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INTRODUCTION

The term “stem cell” first appeared in the literature in the 1860s, in an attempt to explain the Darwinian Theory of Evolution. The German biologist Ernest Heckel constructed a phylogenetic tree, and used the term “*StammZelle*” (Stem Cell), to describe the original single cell organism from which, he suggested, all other multicellular organisms evolved[1]. Since then, the “stem cell” concept went through diligent polishing, to be crystallized in the restricted and descriptive term of a biological entity that we use now. Scanning through the history of stem cell research, a major milestone worth mentioning occurred in 2010, when embryonic stem cells were used for the first time to treat a patient with a spinal injury[2]. This marked the conquering of theoretical, technical, and ethical challenges facing the advancement of stem cell-based regenerative claims from bench to bedside. Subsequently, the transitional applications of stem cells expanded rapidly to include therapeutic and non-therapeutic applications, and stem cell research news started to be broadcasted in the mainstream media coverage. Even though specialists in the field are still contending with the evolving nomenclature of the stem cell sub-types, the general public do share a broad understanding of what a stem cell is, its functional traits and the promising potential. This has initiated a widespread capitalization of stem cells. Within the cosmetic industry, manufacturers and clinics started introducing new product lines and procedures with the term “stem cell” in the label, to capture the customer’s attention in this highly competitive market.

PLANT STEM CELL

The first consumer encounter with stem cell cosmetics began with skin and hair care products containing active ingredients derived from plant stem cells. The manufacturers of these products often failed to disclose that the term “stem cell” in the label of their under eye cream or night serum, referred to stem cell extracts of plant origin. More than a decade ago, research groups presented evidence supporting the regenerative effects of different plant stem cells and their extracts on fibroblasts, keratinocytes and isolated hair follicles[3-5]. Yet, it is doubtful whether the actual benefits of the hundreds of commercial products containing plant stem cell extracts, mixed with various ingredients and preservatives, can be consistent. The validity of the anti-aging and regenerative claims varies vastly between these products, depending on the formulation. Fortunately, the worst case scenario when buying such products is the possibility of being a victim of false advertising, as no serious side effects are caused by the plant extracts. Still, we posit that introducing the plant-based products to market as “stem cell-products” had two major consequences. Firstly, manufacturers realized that including “stem cell” in a product’s label supports a steep price increase. For example, a tomato anti-oxidant cream is 10\$, but a stem cell anti-oxidant cream, made of tomato plant stem cell extracts, can be 50\$, although both creams are made of the same basic ingredients. Such commercialization opportunities increased the industry’s appetite for developing more direct-to-consumer stem cell products and services. Secondly, flooding the market with allegedly “stem cell” containing products desensitized the public regarding the term and its significance. For example, if a person can buy a shampoo claiming to contain “stem cells” to control hair loss, this person will consent to injecting stem cells directly into his/her scalp, not realizing that the first is a plant extract, and the latter is a living biological entity. In other words, the mislabeling of plant extracts as stem cell-off-the-shelf products made the current direct-to-consumer marketing of mammalian stem cell-based products/procedures acceptable to the public, who often miss the small print.

AUTOLOGOUS STEM CELL

The next consumer encounter with stem cell-cosmetics was with mammalian stem

cells, in the form of procedures using autologous stem cells. The most promoted and widely used autologous regenerative procedure is platelet rich plasma (PRP). Although this procedure does not involve actual stem cells, it is often marketed as a stem cell-based regenerative treatment. The regulatory challenges of PRP and autologous stem cell use in cosmetic applications are similar. PRP is separated from the person's own blood *via* centrifugation, to obtain the platelets, plasma proteins and growth factor-rich fraction. Theoretically, the application of PRP to skin or hair follicles could induce cell proliferation and extracellular matrix synthesis. Current literature do report the regenerative effects of PRP on skin and hair[6-8], but large controlled clinical trials are still lacking. In addition, there is no standardization in terms of a sample collection and processing protocol, PRP volume and concentration, and the method of administration for each intended purpose, which makes consistent and reliable results unattainable. These two major concerns of PRP, a procedure that has been used for years, is a clear indication that the premature introduction of a cosmetic procedure to market is acceptable to both practitioners and consumers. The actual autologous stem cells used are mostly adipose tissue-derived mesenchymal stem cells for skin regeneration or tissue augmentation, and follicular stem cells for hair loss. As in PRP, there is evidence supporting the claims; however, large controlled clinical trials are still required[9,10]. Also required, is standardization of the procedure, as the differences in the techniques used cause significant variations in the results for patients in different clinics.

ALLOGENEIC STEM CELL

Allogenic stem cell use in cosmetics is primarily using stem cells of human or animal origin for the mass production of stem cell-derived products. Currently, there is a number of products made from stem cell condition media, or a specific fraction, in the form of topical creams or serums or intradermal injections. This is based on the claims that the constituents of the condition media, including cytokines, growth factors and exosomes, will initiate the required cellular pathways for tissue regeneration. Studies on the mechanism of action of stem cell therapies are confirming that the transplanted cells exert their regenerative effects through the release of paracrine factors. These factors stimulate endogenous cells and promote local angiogenesis at the damaged tissue site[11-13]. For skin and hair, in particular, there is a considerable number of publications supporting the claim that stem cell condition media have a measurable effect when used to treat skin damage or hair loss[14-17]. Notably, these studies also report significant inconsistencies in the outcomes depending on the method used for cell isolation, medium collection, medium processing, and mode of application[18]. On the other hand, allogenic whole-stem cell use for cosmetic applications is still in its infancy. It is projected to be laboratory grown, genetically manipulated, and ready to inject cells with stem cell characteristics. These cells will be sold by manufacturers to cosmetic clinics for "heavy duty" cosmetic applications, such as severe facial deflation or advance pattern baldness. It is projected that, similar to previous applications, implementation in practice will occur prior to the completion of appropriate clinical investigation, or establishing clear regulations. The concern is that this category has an increased risk of serious side effects, specifically different types of immune reactions. When using whole cells, an additional concern is unspecific differentiation or tumorigenicity, which occurred in stem cell therapeutics, especially when certain sub-types such as embryonic and induced pluripotent stem cells are used[19,20] (Figure 1).

STEM CELL BUSINESS

Thousands of businesses globally are engaged in direct-to-consumer marketing of stem cell-derived products or stem cell-based procedures. Some of which are mislabeled as stem cell-related, while others do involve stem cells, but are not yet clinically proven or adequately regulated. Mammalian stem cells, especially from an allogenic source, and their paracrine factors are biological products and must be considered with extreme caution. Firstly, there should be strict requirements for the laboratories that prepare stem cells for the purposes of generating cell-derived products or whole cell use. Secondly, it is crucial to establish detailed protocols for manufacturing *i.e.* tissue source and collection, cell isolation, cell culture and manipulation, phenotypic profile, concentration or number of cells administered and mode of administration for each intended purpose. Thirdly, adequate clinical trials must be

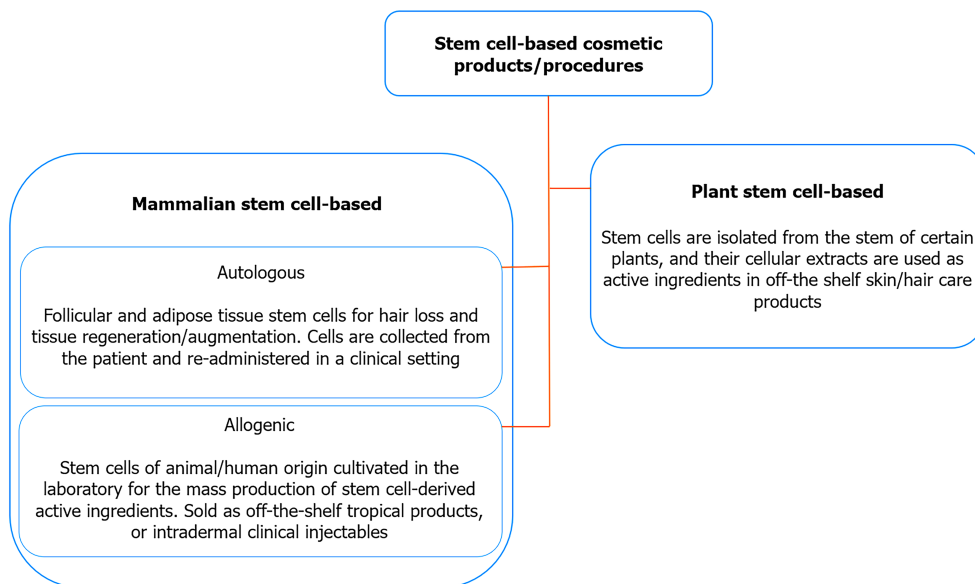


Figure 1 Categorization of currently available stem cell-based cosmetic products/procedures available through direct-to-consumer marketing.

conducted for each application, to confirm safety and effectiveness. It is crucial that providers of a given product or procedure do not cause harm to their consumers, or practice deception with unproven claims. Stem cell products and procedures must comply with both the local Drug and Medical Devices Authorities guidelines for safety, as well as the truth-in-advertising laws. It is also worth mentioning that this inadequate regulation is not unique to stem cell cosmetics. In the cosmetic industry, a procedure is frequently introduced to market prior to adequate clinical testing. This is due to the regulatory bodies' oversight being unable, or under equipped, to manage this rapidly paced industry. The cosmetic industry has to offer the latest social media cosmetic hypes, even unregulated or unproven products or procedures, to supply the demand and not lose market share. Therefore, it is vital to inform consumers about the requirements and the processes of a cosmetic product or procedure approval, as well as the gaps within the system. For example, an approved laser machine for cellulite removal indicates that the machine is relatively safe, but it does not mean that it actually eliminates cellulite! This is important so that consumers can inform and educate themselves about the product or procedure they intend to purchase, and report any suspected malpractices.

CONCLUSION

In conclusion, some final remarks. Using stem cells in cosmetic applications cannot be dismissed as trivial. Improving peoples' aesthetic concerns can significantly improve their quality of life. Conditions such as facial acne scars or lupus bald patches can be detrimental to a person's self-perception and body image, which could have serious consequences. The addition of a profitable, commercial arm will push the entire field of stem cell research forward. Due to the growing demand, companies within the cosmetic industry are investing more in research and development of new stem cell related products and applications. When the cosmetic industry becomes well regulated, and provides evidence-based claims by following proper scientific research practices, the outcomes of their research will contribute to the pool of stem cell knowledge. This means that the data from cosmetic-related research could be used as a proof-of-concept for other therapeutic applications, where funding is scarce. The second remark is that the East Asian market is the biggest market for stem cell-cosmetics. A study investigating online direct-to-consumer marketing of stem cell therapies, reported that 83% of the websites in the Japanese online stem cell market were promoting cosmetic procedures, compared to only 14% in the United States of America[21]. The Drug and Medical Devices regulatory authorities in East Asia will benefit from taking the lead in governing the market practices of manufacturing, marketing and use of stem cells for cosmetic purposes. This will not only offer safety

and avoid commercial fraud for local consumers, but will also establish East Asia as the number one destination for affordable, high quality cosmetic solutions.

REFERENCES

- 1 **Dröschner A.** Images of cell trees, cell lines, and cell fates: the legacy of Ernst Haeckel and August Weismann in stem cell research. *Hist Philos Life Sci* 2014; **36**: 157-186 [PMID: 25515356 DOI: 10.1007/s40656-014-0028-8]
- 2 **Mayor S.** First patient enters trial to test safety of stem cells in spinal injury. *BMJ* 2010; **341**: c5724 [PMID: 20940208 DOI: 10.1136/bmj.c5724]
- 3 **Schmid D, Züllli F.** Stimulating epidermal regeneration with plant-derived stem cells. *DNA* 2010; **1**: 3
- 4 **Schmid D, Schürch C, Züllli F.** Stimulation of stem cells for real rejuvenation. *Mibelle Biochemistry* 2008
- 5 **Tito A, Carola A, Bimonte M, Barbulova A, Arciello S, de Laurentiis F, Monoli I, Hill J, Gibertoni S, Colucci G, Apone F.** A tomato stem cell extract, containing antioxidant compounds and metal chelating factors, protects skin cells from heavy metal-induced damages. *Int J Cosmet Sci* 2011; **33**: 543-552 [PMID: 21609336 DOI: 10.1111/j.1468-2494.2011.00668.x]
- 6 **Wang JV, Schoenberg E, Saedi N, Ibrahim O.** Platelet-rich Plasma, Collagen Peptides, and Stem Cells for Cutaneous Rejuvenation. *J Clin Aesthet Dermatol* 2020; **13**: 44-49 [PMID: 32082473]
- 7 **Gentile P, Garcovich S.** Systematic Review-The Potential Implications of Different Platelet-Rich Plasma (PRP) Concentrations in Regenerative Medicine for Tissue Repair. *Int J Mol Sci* 2020; **21** [PMID: 32784862 DOI: 10.3390/ijms21165702]
- 8 **Dervishi G, Liu H, Peternel S, Labeit A, Peinemann F.** Autologous platelet-rich plasma therapy for pattern hair loss: A systematic review. *J Cosmet Dermatol* 2020; **19**: 827-835 [PMID: 31452328 DOI: 10.1111/jocd.13113]
- 9 **Zarei F, Abbaszadeh A.** Stem cell and skin rejuvenation. *J Cosmet Laser Ther* 2018; **20**: 193-197 [PMID: 29394110 DOI: 10.1080/14764172.2017.1383615]
- 10 **Egger A, Tomic-Canic M, Tosti A.** Advances in Stem Cell-Based Therapy for Hair Loss. *CellR4 Repair Replace Regen Reprogram* 2020; **8** [PMID: 32968692]
- 11 **Elshaer SL, Evans W, Pentecost M, Lenin R, Periasamy R, Jha KA, Alli S, Gentry J, Thomas SM, Sohl N, Gangaraju R.** Adipose stem cells and their paracrine factors are therapeutic for early retinal complications of diabetes in the Ins2^{Akita} mouse. *Stem Cell Res Ther* 2018; **9**: 322 [PMID: 30463601 DOI: 10.1186/s13287-018-1059-y]
- 12 **Li JY, Ren KK, Zhang WJ, Xiao L, Wu HY, Liu QY, Ding T, Zhang XC, Nie WJ, Ke Y, Deng KY, Liu QW, Xin HB.** Human amniotic mesenchymal stem cells and their paracrine factors promote wound healing by inhibiting heat stress-induced skin cell apoptosis and enhancing their proliferation through activating PI3K/AKT signaling pathway. *Stem Cell Res Ther* 2019; **10**: 247 [PMID: 31399039 DOI: 10.1186/s13287-019-1366-y]
- 13 **Sun H, Pratt RE, Hodgkinson CP, Dzau VJ.** Sequential paracrine mechanisms are necessary for the therapeutic benefits of stem cell therapy. *Am J Physiol Cell Physiol* 2020; **319**: C1141-C1150 [PMID: 33026832 DOI: 10.1152/ajpcell.00516.2019]
- 14 **Fukuoka H, Suga H.** Hair Regeneration Treatment Using Adipose-Derived Stem Cell Conditioned Medium: Follow-up With Trichograms. *Eplasty* 2015; **15**: e10 [PMID: 25834689]
- 15 **Kim YJ, Seo DH, Lee SH, An GH, Ahn HJ, Kwon D, Seo KW, Kang KS.** Conditioned media from human umbilical cord blood-derived mesenchymal stem cells stimulate rejuvenation function in human skin. *Biochem Biophys Res* 2018; **16**: 96-102 [PMID: 30417126 DOI: 10.1016/j.bbrep.2018.10.007]
- 16 **Wang L, Abhange KK, Wen Y, Chen Y, Xue F, Wang G, Tong J, Zhu C, He X, Wan Y.** Preparation of Engineered Extracellular Vesicles Derived from Human Umbilical Cord Mesenchymal Stem Cells with Ultrasonication for Skin Rejuvenation. *ACS Omega* 2019; **4**: 22638-22645 [PMID: 31909348 DOI: 10.1021/acsomega.9b03561]
- 17 **Kim SN, Lee CJ, Nam J, Choi B, Chung E, Song SU.** The Effects of Human Bone Marrow-Derived Mesenchymal Stem Cell Conditioned Media Produced with Fetal Bovine Serum or Human Platelet Lysate on Skin Rejuvenation Characteristics. *Int J Stem Cells* 2021; **14**: 94-102 [PMID: 33377452 DOI: 10.15283/ijsc20070]
- 18 **Kim HJ, Min SJ, Yu KH, Jung AH.** A study on clinical effectiveness of cosmetics containing human stem cell conditioned media. *Bio Dermatol* 2020; **4**: 1-11 [DOI: 10.1186/s41702-020-0056-9]
- 19 **Tompkins BA, Balkan W, Winkler J, Gyöngyösi M, Goliash G, Fernández-Avilés F, Hare JM.** Preclinical Studies of Stem Cell Therapy for Heart Disease. *Circ Res* 2018; **122**: 1006-1020 [PMID: 29599277 DOI: 10.1161/CIRCRESAHA.117.312486]
- 20 **Lukomska B, Stanaszek L, Zuba-Surma E, Legosz P, Sarzynska S, Drela K.** Challenges and Controversies in Human Mesenchymal Stem Cell Therapy. *Stem Cells Int* 2019; **2019**: 9628536 [PMID: 31093291 DOI: 10.1155/2019/9628536]
- 21 **Munsie M, Lysaght T, Hendl T, Tan HL, Kerridge I, Stewart C.** Open for business: a comparative study of websites selling autologous stem cells in Australia and Japan. *Regen Med* 2017; **12**: 777-790 [PMID: 29125016 DOI: 10.2217/rme-2017-0070]



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