International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 750-756 www.ijprajournal.com ISSN: 2456-4494

# "How can stem cells improve the function of skin grafts"

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Date of Submission: 20-01-2025 Date of Acceptance: 30-01-2025

**ABSTRACT**: Skin grafting is a medical procedure in which a piece of skin is harvested from a donor site and surgically transplanted to a recipient's skin injury site. Although it seems like an ideal solution to heal and protect the injured region, it does have practical and physiological limitations. To address these challenges, 3D bioprinted skin grafts offer a potential solution to create new skin grafts, without the risks associated with extracting skin from donor sites. Three dimensional (3D) skin grafts can be created using a 3D bioprinter and a bioink, containing various cell types, including stem cells. The inclusion of stem cells can provide additional benefits, such as promoting vascularisation, and enhancing hair follicle regeneration at the graft site, ultimately improving the graft's long-term function and integration.

**KEYWORDS:** Skin grafts, stem cells, 3D bioprinter

## I. INTRODUCTION

The skin is the largest organ of the human body and is part of the integumentary system. It protects our internal organs and forms the first line of defence against germs and pathogens. However, due to its constant exposure to external elements, the skin is highly vulnerable to skin injury. . Severe damage can occur through burns, diseases, wounds, or infections, leading to the loss of skin layers. In such cases, skin grafts are often necessary. This procedure involves taking healthy skin from a donor area and transplanting it to cover the missing or damaged area. Skin grafts can also be used following surgery for skin cancer, whereby skin is taken from a healthy site to replace tissue removed during the excision of the tumor.

Currently, skin grafts can be transplanted using three methods: autografts, allografts and xenografts. An autograft is a procedure where the graft is taken from the same graft recipient; an allograft is a procedure where the skin is taken from another person or member of the same species; a xenograft is a procedure where the graft is taken from a species that is different from the recipient. There are two types of skin grafts; split-thickness skin grafts and full-thickness skin grafts.

Split thickness skin grafts (STSG) are skin grafts in which the medical practitioner takes out only the top layer or the epidermis which is obtained from the thigh, belly, bottom or back. While the full-thickness skin graft (FTSG) involves taking the skin from a deeper layer like the epidermis and dermis. This is usually taken from the groin, arm or collarbone. STSGs are generally faster and easier to perform, with the added benefit of faster recovery time. Moreover, revascularization is more likely to happen in this type of graft, because there are more transected vessels. On the other hand, FTSGs contain a greater number of functioning sweat glands than STSGs, and they can also match the characteristics of natural skin compared to STSGs, due to their inclusion of multiple skin layers, which offers enhanced functionality and aesthetic outcomes compared to STSGs.

## II. THE LIMITATIONS OF SKIN GRAFTS

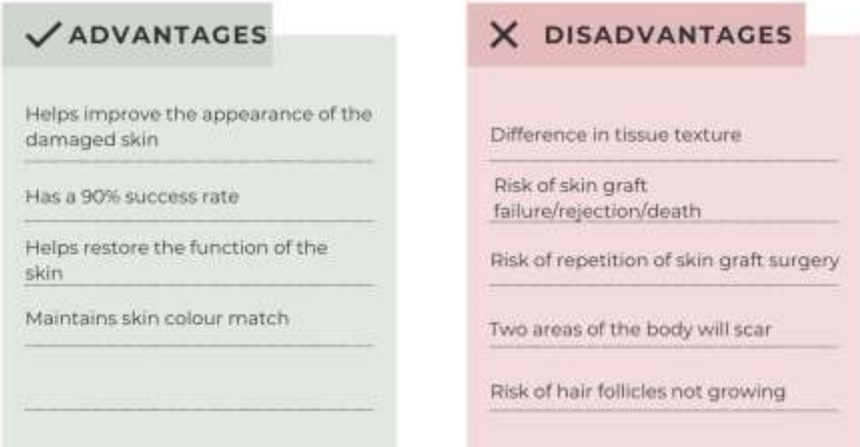
Although the success rate of skin graft surgery is generally high, with a success rate of 90%, there are some limitations [Table I]. While basic characteristics of the transplanted skin can be matched, differences in appearance may be observed. One of the primary concerns is graft failure, which may require a repeat surgery [Table I]. The risk of failure is higher for allograft procedures, while autografts have a higher success rate because of the high likelihood of compatibility. In cases of autografts where the donor of the skin is also the recipient, there are also risks associated with introducing a second area of the body to wounds or scarring. As previously mentioned, there are also significant limitations associated with the lack of availability of skin grafts for it to be a one-time procedure.

Another limitation currently facing the field of skin grafts is the lack of successful hair follicle regeneration on the skin graft area [Table I]. This is important because hair is a vital part of

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 1 Jan - Feb 2025, pp: 750-756 www.ijprajournal.com ISSN: 2456-4494

the skin for protection, temperature regulation, wound healing and skin regeneration. This means that without hair follicles, we would be more susceptible to small injuries, imbalance of temperature and our wounds will not repair after an injury and new skin won't form because of it. The primary reason for this is because hair follicles contain something called a bulge. And when this gets removed in the case of an injury, we aren't able to activate these abilities. A bulge is the site of stem cells in the hair follicle. The bulge is located between the opening of the sebaceous and the attachment site of the arrector pili muscle.

**ADVANTAGES AND DISADVANTAGES OF SKIN GRAFTS**




## III. THE USE OF 3D PRINTING TO IMPROVE SKIN GRAFTS

To improve the development of skin grafts, researchers have employed the use of 3D printing in order to artificially create and develop new skin grafts. In this regard, 3D printing has revolutionised research into skin graft development. 3D bioprinting can be described as the 'doctor' cousin of 3D printing. Normal 3D printing involves making a 3d Image of a 2D image using materials like plastic, resin and metals. 3D bioprinting involves the same principle, but instead of these materials as the ink, bioink is used instead, and a specially made substrate in the place of paper. Bioink contains cultured cells, including stem cells, using a method that supports the cells outside their natural environment, and in an environment which supports their survival. This printing method can be used to create new organs and tissues, through the use of cultured cells and specially designed nozzles to protect and guide the cells as they are printed from 3D printers. As 3D printing can be used to create new organs, it also overcomes some of the issues caused by a shortage of the issue, or not having sufficient organ donors to organ recipients.

3D bioprinting techniques are increasingly being utilized to enhance the appearance and functionality of skin grafts. Before creating the 3D printed skin, a computerized 3D model of the desired skin structure is first developed, allowing practitioners to design an accurate, custom scaffold that mimics the natural skin architecture. Then, the bioink can be formulated using a combination of skin cells, such as keratocytes, along with stem cells and other molecular components including growth factors, cell adhesion proteins and glycosaminoglycan to ensure the healthy growth and development of the skin cell. The skin scaffold is built layer by layer, alternating between bioink and printable stem cells or cytocompatible cells, such as dermal fibroblasts. This innovative approach has a higher success rate of engraftment and improves the chance of the 3D printed skin to be accepted by the body.

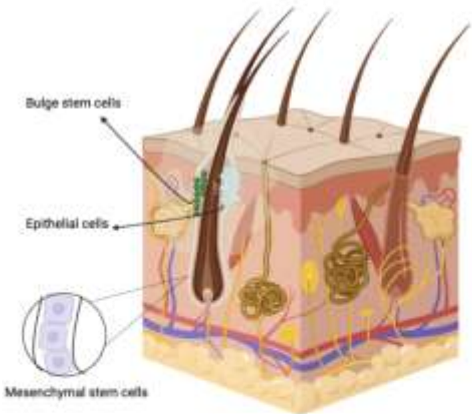
Currently, research to further advance the function of 3D printed skin grafts is being conducted. This aims to improve the integration of 3D printed skin grafts into the recipient's body. A key focus of this research is addressing the functions often lacking in traditional skin grafts but essential for optimal graft performance, such as vascularisation and hair follicle growth. Much of this research focuses on stem cells, as a tool to revolutionise graft formation.

## IV. THE USE OF STEM CELLS TO IMPROVE SKIN GRAFTS

Stem cells are unspecialised cells, which means that they don't have a specific job unlike other cells. However, they have unique properties as they can self-replicate and make more stem cells, or with the support of genetic signals and chemicals, they can replicate into other specialised cells. Because of this unique feature they can be used to repair tissues and help them grow. In particular, there are two types of stem cells: Adult stem cells and induced pluripotent stem cells (IPSC). Adult stem cells, also known as somatic stem cells, are located in areas of the bone marrow, blood vessel, skin, heart and teeth and are restricted in what type of cells they can become, but are still unspecialised. Whereas IPSC are stem cells found in embryos when they are 5-7 days old and are pluripotent, which means that they can turn into any type of cell.

Like lizards that can regenerate their body part when it has been cut off, stem cells generate new and healthy cells to replace dying ones, and are needed for the maintenance and repair of a tissue after an injury. But what makes stem cells so interesting in the field of skin graft research is their ability to fix our injuries. It's a way for medicine to be more personalized and a way for the solution to be 'within us.' Stem cells represent an optimal solution for the integration of a transplant or in this case, a skin graft or 3D printed skin, as the cells are more compatible and this reduces the risk or rejection. Stem cells are being used to improve vascularization of skin grafts, and the formation of hair follicles; both features of grafts that are currently lacking and require development.

## V. DIFFERENT STEM CELL IN THE HAIR FOLLICLE




## VI. THE USE OF STEM CELLS TO IMPROVE SKIN GRAFT VASCULARISATION.

Blood vessels are essential for the transport of crucial nutrients and oxygen around the body, so that cells can perform their functions. They also transport the waste product away from the cells through the blood. The basic process of growing these vessels is called vascularisation. Without proper vascularisation the cells will not be able to function effectively, because of insufficient oxygen and nutrient transport, and will die due to hypoxia. The dermis, which forms the second and middle layer of the skin, contains blood and lymph vessels. The blood vessels carry the blood with the nutrients and oxygen, while the lymph vessels collect the fluids from the cells and transport it back to the blood.

Vascularisation is a complex process using a combination of different cell types, growth factors and extracellular matrix proteins. Vascularisation happens because of two processes: vasculogenesis and angiogenesis. Vasculogenesis is the de novo formation of new vessels without the template of old vessels. It is performed by the endothelial cells which build a bridge that creates a connection among the vessels. On the other hand, angiogenesis is when a new vessel starts budding from an old vessel.

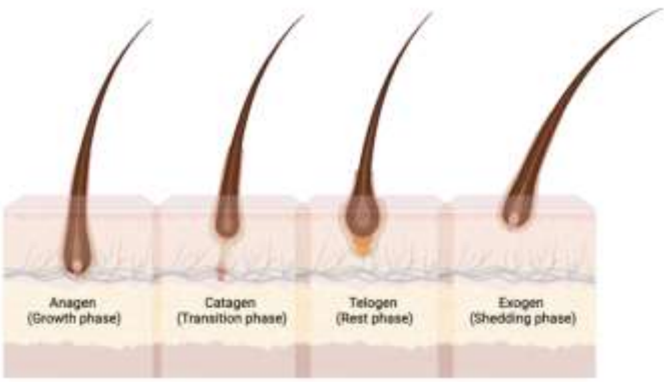
The ability for skin to heal properly depends mainly on how deep the wound is and that is determined by factors such as: the extent of the injury, the intensiveness of the surgeries and genetic abnormalities which stop or slow down the repair of the tissue. As mentioned before, the blood vessels are in the dermis, therefore second or third degree burns can damage the blood vessels. Second degree burns are those which go deep down to the epidermis and affect a part of the dermis. A common characteristic of a second degree burn is the presence of blistering and swelling. It is usually caused by touching extremely hot objects. A third degree burn reaches the epidermis and dermis and can potentially damage the muscle, tendons and bones. When that happens, it is considered a fourth degree burn. A person with a third degree burn will start losing feeling in that area because the nerves and blood vessels are also damaged.

To ensure the success of a 3D bioprinted skin graft, vascularisation is an extremely important step. As mentioned earlier, the success of a skin graft depends on the functional vascularisation as it provides essential nutrients and oxygen throughout the cells. Therefore, the lack of early and popular vascularisation could lead to graft necrosis or failure of the graft.

In a study performed for the acceleration of skin wound healing and skin regeneration of a mouse model, amniotic fluid-derived stem cells (AFSC) and mesenchymal stem cells (MSC) were used in a fibrin-collagen hydrogel. The amniotic fluid is a water-like substance that surrounds the fetus during pregnancy and plays an important role in fetal development. Along with nutrients, hormones and antibodies, the AFSCs can be identified within the amniotic fluid. Mesenchymal stem cells are derived from the bone marrow or umbilical cord and are multipotent cells which can differentiate to many somatic cells. In this study, the researchers observed that the use of the AFSCs increased microvessel density and capillary diameters in comparison to MSCs and the control cases. Since there is an increased microvessel density as well as an increase in capillary diameters, more nutrients can be delivered, and there will be less vascular pressure meaning a greater flow of blood. However, the study showed that the bioprinted cells did not survive very long and could not integrate properly into the new tissues. This demonstrates that there was some issue in the functioning of wound closure angiogenesis, as a result of the concentration of trophic factors released. In addition, the AFSCs secreted more growth factors than MSCs at a higher concentration and an AFSC-conditioned media induced more endothelial migration. This could also mean that AFSC bioprinted cells could be an optimal solution for a large wound.

## VII. THE USE OF STEM CELLS TO IMPROVE FORMATION OF SKIN GRAFT HAIR FOLLICLES

Stem cells are also being researched for their use in hair follicle formation in skin grafts. Hair follicles are pores found in the skin from where strands of hair grow. Hair follicles originate from the surface of the epidermis. They are essential for the human body as they regulate body temperature, heal wounds and regenerate skin, and are vital for protection. The skin is the first thing drugs and cosmetic touches which is protected by hair. Embedding hair follicles will allow specialists to understand how the products react with the natural skin.




## VIII. THE HAIR FOLLICLE CYCLE

Hair follicles go through a cyclical four-step process for the growth and regeneration of hair composed of; anagen (growth), catagen (transition), telogen (rest), and exogen (shedding) [Figure III]. Anagen, the first phase, takes around 3-5 years to grow, but depending on the area of hair growth, varies. The growth begins at the root so that the hair will get blood supply with the nutrients it needs to grow. It is the process where cells are rapidly dividing to form new hair. Catagen begins when anagen ends; the hair follicle shrinks and hair growth slows while also detaching off the blood supply to give place for a new hair. This tends to take around 10 days. In the telogen phase, the hair follicles don't actively grow anymore but the hair doesn't move out of the hair follicle either. The phase can take up to 4 months. The last phase in this cycle is exogen. In this stage the hair sheds from the hair follicle to allow the process to happen again. All of this is stimulated with the help of stem cells, in particular,mesenchymal stem cells, epithelial cells, and bulge cells [Figure II].

The mesenchymal stem cells are a group of pluripotent stem cells found in the bone marrow and are responsible for the differentiation of osteocytes (generates bone), chondrocytes (cartilage), cardiomyocytes (fibrous connective tissues) and adipocytes (fat). A group of mesenchymal cells in the base of the hair follicle called the dermal papilla provides crucial blood supply and nutrition for the growing hair follicle. It is embedded in the hair bulb, which is a part of the follicle that produces hair, in a circle of proliferating keratinocytes, namely the matrix progenitor cells. The dermal papilla also handles the duration of the hair growth by monitoring the activity on these progenitor cells and at the end of the anagen phase, it moderates the activity of the progenitor cells. The mesenchymal stem cells also produce a thin layer of dermal sheath cells that encloses the hair follicles during the anagen phase and also plays a vital role in hair regression.

Epithelial cells are multipotent cells,the most abundant cells, and make up the primary tissues in the body. They form the ectoderm, endoderm and mesoderm. This basically means that it covers most of the body and organ surfaces. They construct the skin, blood vessels and body cavity. In terms of the hair follicles, they are found in the bulge region of the hair follicle and contribute to the generation of new hair follicles. Since they are also multipotent, they bring about every cell in the hair and sebaceous gland.

Ultimately, bulge stem cells reside in the bulge of the hair follicle. The bulge region is based in between the opening of the sebaceous gland and the arrector pili muscle. The bulge cells are a group of undifferentiated multipotent stem cells that can regenerate into cells in the hair follicle, epidermis and sebaceous. It is also slow-cycling under regular conditions and thus has label retaining properties making it a dormant cell in the tissue. As well as possessing stem cell properties, in more specificity it is responsible for the generation of hair follicles in the hair cycle. They proliferate during the anagen phase. Additionally, they contribute in tissue regeneration and help in wound-healing in the epidermis.

Recently, the Rensselaer Polytechnic Institute has successfully been able to incorporate hair follicles in 3D printed skin grafts. Using a pneumatic-based extrusion 3D printing platform and including a bioink that contained: printed human epidermal keratinocytes, dermal papilla cells, and human umbilical endothelial cells. They printed the cells as they displayed higher cell viability in contrast to manually deposited cells. After constructing the model in the optimum spheroid, they proceeded to print the hair follicle bioink onto the crosslinked dermal layer with ingrained human dermal fibroblasts. 48 hours after this step, they observed the formation of columns growing to the height of the surface of the skin sample. This could be the first step towards the evolution of hair follicles in 3D printed skin grafts.

## IX. CONCLUSION

3D bioprinting has the potential to revolutionise the field of transplant medicine, offering new possibilities for organ recipients across a wide range of conditions. While it is currently being explored for skin grafts, the technology holds promise for a variety of other organs as well. To date, scientists have successfully bioprinted structures such as knee menisci, blood vessels, cartilage, and reconstructed ear. Researchers are also working on brain, kidney and heart models, which have been replicated in petri dishes with the hope of eventually scaling them to full size for use in organ transplantation. It is estimated that within the next 20-30 years, 3D bioprinted organs could become a viable and accessible solution for those in need of transplants, bringing a new era of medical advancements that could help countless patients.

## REFERENCES

[1]. Ong, C. S., Yesantharao, P., Huang, C. Y., Mattson, G., Boktor, J., Fukunishi, T., … Hibino, N. (2017). 3D bioprinting using stem cells. Pediatric Research, 83(1-2), 223–231. https://doi.org/10.1038/pr.2017.252

[2]. Pasierb, A., Jezierska, M., Karpuk, A., Czuwara, J., & Rudnicka, L. (2021). 3D skin bioprinting: future potential for skin regeneration. Advances in Dermatology and Allergology. https://doi.org/10.5114/ada.2021.109692

[3]. Phua, Q. H., Han, H. A., & Soh, B.-S. (2021). Translational stem cell therapy: vascularized skin grafts in skin repair and regeneration. Journal of Translational Medicine, 19(1). https://doi.org/10.1186/s12967-021-02752-2
[4]. WennersHerron, A. (2024). 3D-printed skin closes wounds and contains hair follicle precursors | Penn State University. Retrieved from Psu.edu website: https://www.psu.edu/news/research/story/3d-printed-skin-closes-wounds-and-contains-hair-follicle-precursors
[5]. Olejnik, A., Semba, J. A., Kulpa, A., Dańczak-Pazdrowska, A., Rybka, J. D., & Gornowicz-Porowska, J. (2021). 3D Bioprinting in Skin Related Research: Recent Achievements and Application Perspectives. ACS Synthetic Biology, 11(1), 26–38. https://doi.org/10.1021/acssynbio.1c00547
[6]. Ansaf, R. B., Ziebart, R., Hemanth Gudapati, Torigoe, R., Victorelli, S., Passos, J. F., & Wyles, S. P. (2023). 3D bioprinting—a model for skin aging. Regenerative Biomaterials, 10. https://doi.org/10.1093/rb/rbad060
[7]. Kejariwal, R., & Wang, Y. Q. (2024, March 10). Breakthroughs In 3D Printed Skin Grafts - Klarity Health Library. Retrieved from Klarity Health Library website: https://my.klarity.health/breakthroughs-in-3d-printed-skin-grafts/
[8]. Martel, J. L., & Badri, T. (2019, January 30). Anatomy, Hair Follicle. Retrieved from Nih.gov website: https://www.ncbi.nlm.nih.gov/books/NBK470321/
[9]. 3D bioprinting and stem cells in plastic surgery | University of Gothenburg. (2023, July 11). Retrieved from www.gu.se website: https://www.gu.se/en/research/3d-bioprinting-and-stem-cells-in-plastic-surgery
[10]. Scientists 3D-print hair follicles in lab-grown skin | News. (2023). Retrieved from Rpi.edu website: https://news.rpi.edu/content/2023/11/15/scientists-3d-print-hair-follicles-lab-grown-skin
[11]. Cleveland Clinic. (2021, July 21). Skin Graft: What Is It, Risks, Benefits & Recovery. Retrieved from Cleveland Clinic website: https://my.clevelandclinic.org/health/treatments/21647-skin-graft
[12]. Skin Graft: Purpose, Types, and Procedure. (n.d.). Retrieved from Healthline website: https://www.healthline.com/health/skin-graft#types
[13]. Split Thickness Skin Graft - an overview | ScienceDirect Topics. (n.d.). Retrieved from www.sciencedirect.com website: https://www.sciencedirect.com/topics/nursing-and-health-professions/split-thickness-skin-graft
[14]. Thourani, V. H., Ingram, W. L., & Feliciano, D. V. (2003). Factors Affecting Success of Split-Thickness Skin Grafts in the Modern Burn Unit. The Journal of Trauma: Injury, Infection, and Critical Care, 54(3), 562–568. https://doi.org/10.1097/01.ta.0000053246.04307.2e
[15]. Autograft vs Allograft: Key Differences Explained. (n.d.). Retrieved from www.gpoa.com website: https://www.gpoa.com/blog/autograft-vs-allograft-what-s-the-difference
[16]. Mahjour, S. B., Ghaffarpasand, F., & Wang, H. (2012). Hair Follicle Regeneration in Skin Grafts: Current Concepts and Future Perspectives. Tissue Engineering Part B: Reviews, 18(1), 15–23. https://doi.org/10.1089/ten.teb.2011.0064
[17]. Sanaz JOULAI VEIJOUYE, Abazar YARI, HEIDARI, F., Nayereh SAJEDI, Fatemeh GHOROGHI MOGHANI, & Maliheh NOBAKHT. (2017). Bulge Region as a Putative Hair Follicle Stem Cells Niche: A Brief Review. Iranian Journal of Public Health, 46(9), 1167. Retrieved from https://pmc.ncbi.nlm.nih.gov/articles/PMC5632317/
[18]. SPC. (2018, February 19). What Materials Are Used for 3D Printing? Retrieved from Sharretts Plating Company website: https://www.sharrettsplating.com/blog/materials-used-3d-printing/
[19]. Kang, M. S., Jang, J., Jo, H. J., Kim, W.-H., Kim, B., Chun, H.-J., … Han, D.-W. (2022). Advances and Innovations of 3D Bioprinting Skin. Biomolecules, 13(1), 55. https://doi.org/10.3390/biom13010055
[20]. José Marín-García. (2014). Molecular Determinants of Cardiac Neovascularization. Elsevier EBooks, 279–303. https://doi.org/10.1016/b978-0-12-404599-6.00009-3
[21]. Cleveland Clinic. (2022, June 18). Amniotic Fluid: Color, Smell, Function & Disorders. Retrieved from Cleveland Clinic website:

https://my.clevelandclinic.org/health/body/23310-amniotic-fluid

[22]. Subramaniam, S., Antoniadou, E., Paolo De Coppi, & David, A. L. (2018). In Utero Therapy for Congenital Disorders Using Amniotic Fluid Stem Cells. 3–20. https://doi.org/10.1016/b978-0-12-812015-6.00001-7

[23]. Srivastava, M., Ahlawat, N., & Srivastava, A. (2017). Amniotic Fluid Stem Cells: A New Era in Regenerative Medicine. The Journal of Obstetrics and Gynecology of India, 68(1), 15–19. https://doi.org/10.1007/s13224-017-1034-z

[24]. Mesenchymal Stem Cell - an overview | ScienceDirect Topics. (n.d.). Retrieved from www.sciencedirect.com website: https://www.sciencedirect.com/topics/engineering/mesenchymal-stem-cell

[25]. Cleveland Clinic. (2022b, July 8). Hair Follicle: Function, Structure & Associated Conditions. Retrieved from Cleveland Clinic website: https://my.clevelandclinic.org/health/body/23435-hair-follicle

[26]. Roland, J. (2020, September 25). Stages of Hair Growth Plus How to Maintain Hair Health in Every Stage. Retrieved from Healthline website: https://www.healthline.com/health/stages-of-hair-growth

[27]. Kingsley, A. (2022, April 11). The Hair Growth Cycle. Retrieved from https://www.philipkingsley.co.uk/ website: https://www.philipkingsley.co.uk/hair-guide/hair-science/hair-growth-cycle.html

[28]. Mehta, D. M., & Mehta, D. M. (2023, October 5). A Comprehensive Guide To The Stages Of Hair Growth | Malay Mehta Aesthetic Clinic. Retrieved from Dr Malay Mehta website: https://www.drmalaymehta.com/understanding-the-stages-of-hair-growth/

[29]. Lee, J. H., & Choi, S. (2024). Deciphering the molecular mechanisms of stem cell dynamics in hair follicle regeneration. Experimental & Molecular Medicine, 1–8. https://doi.org/10.1038/s12276-023-01151-5

[30]. Carolina Motter Catarino, Desirée Cigaran Schuck, Lexi Dechiario, & Pankaj Karande. (2023). Incorporation of hair follicles in 3D bioprinted models of human skin. Science Advances, 9(41). https://doi.org/10.1126/sciadv.adg0297

[31]. Aamar, E., Avigad Laron, E., Asaad, W., Harshuk-Shabso, S., & Enshell-Seijffers, D. (2021). Hair-Follicle Mesenchymal Stem Cell Activity during Homeostasis and Wound Healing. Journal of Investigative Dermatology, 141(12), 2797-2807.e6. https://doi.org/10.1016/j.jid.2021.05.023

[32]. Brown, T. M., & Krishnamurthy, K. (2020). Histology, Hair and Follicle. Retrieved from PubMed website: https://www.ncbi.nlm.nih.gov/books/NBK532929/

[33]. Yang, R., Zheng, Y., Burrows, M., Liu, S., Wei, Z., Nace, A., … Xu, X. (2014). Generation of folliculogenic human epithelial stem cells from induced pluripotent stem cells. Nature Communications, 5, 3071. https://doi.org/10.1038/ncomms4071

[34]. Lavker, R. M., Sun, T.-T., Oshima, H., Barrandon, Y., Akiyama, M., Ferraris, C., … Christiano, A. M. (2003). Hair follicle stem cells. The Journal of Investigative Dermatology. Symposium Proceedings, 8(1), 28–38. https://doi.org/10.1046/j.1523-1747.2003.12169.x

[35]. Christiano, A. M. (2004). Epithelial Stem Cells: Stepping out of Their Niche. Cell, 118(5), 530–532. https://doi.org/10.1016/j.cell.2004.08.024

[36]. Ohyama, M. (2007). Hair follicle bulge: A fascinating reservoir of epithelial stem cells. Journal of Dermatological Science, 46(2), 81–89. https://doi.org/10.1016/j.jdermsci.2006.12.002

[37]. Barber, C. (2023, February 15). 3D-printed organs may soon be a reality. “Looking ahead, we’ll not need donor hearts.” Retrieved from Fortune website: https://fortune.com/well/2023/02/15/3d-printed-organs-may-soon-be-a-reality/