



Skin Stem Cells in Iran

Mohammad Ali Nilforoushzadeh ^{1,2}, Mohammad Amir Amirkhani ^{1,3}, Farnoosh Seirafianpour ⁴, Farzaneh Mashayekhi ⁴, Pardis Hejazi ^{5,1,*} and Azadeh Goodarzi ^{6,1,**}

¹Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran

²Jordan Dermatology and Hair Transplantation Center, Tehran, Iran

³Stem Cell and Regenerative Medicine Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran

⁴Student Research Committee, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

⁵Department of Dermatology, Autoimmune Bullous Diseases Research Center, Razi Hospital, Tehran University of Medical Sciences, Tehran, Iran

⁶Department of Dermatology, Rasool Akram Medical Complex Clinical Research Development Center, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

* Corresponding author: Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran. Email: pardis.hejazi@gmail.com

** Corresponding author: Skin and Stem Cell Research Center, Tehran University of Medical Sciences, Tehran, Iran. Email: dr.azadehgoodarzi@gmail.com

Received 2022 April 03; Revised 2022 April 20; Accepted 2022 April 20.

Keywords: Skin Stem Cell, Iran, Dermatology

Dear Editor,

During the recent decade, Iran has been keeping pace with the exponentially growing field of stem cell research and therapy, with skin-related investigations constituting a considerable share of the contributions of Iranian researchers to the field. It is thanks to immense collaborations at various levels among regulatory and administrative bodies, as well as enormous drive at the level of individuals, that the advancements have been realized. In many of the projects, the collaborations extended beyond the geographical borders to research centers all over the world.

Owing to a collective will to expedite the science of stem cells and also support from the Council for Development of Stem Cell Sciences and Technologies, increasingly more related research facilities are being established and equipped in the country. Royan Institute for Stem Cell Biology and Technology was the center that took the lead in the science of stem cells in Iran. Subsequently, several universities and academic centers, such as Tehran, Iran, Tabriz, Shiraz, Mashhad, Kerman, and Yazd universities of medical sciences, came aboard. The National Cell Bank of Iran (Pasteur Institute), Tarbiat Modares University, Cell Therapy and Regenerative Medicine Research Center affiliated with Endocrinology and Metabolism Research Institute of Tehran University of Medical Sciences are other centers active in the field. The Skin and Stem Cell Research Center, supported by the Tehran University of Medical Sciences, was established in 2011 and has been entirely dedicated to applying the science to cutaneous disorders (1).

For skin-related purposes in Iran, stem cells are obtained from a variety of sources, such as adipose tis-

sue, hair follicles, menstruation blood, placenta, amniotic membrane, endometrial tissue specimens, umbilical cord Wharton's jelly, and bone marrow aspirates (2-9). Reprogramming of differentiated somatic cells to pluripotent stem cells, performed by the Royan Institute, offers another valuable source for the cells.

Stem cells have been experimentally put into use by Iranian researchers for many dermatologic purposes, including wound repair, wrinkle, and scar enhancement (10), hair loss treatment (11, 12), and the improvement of conditions such as scleroderma (13), chronic graft versus host disease (14), and atopic dermatitis (15). Ulcers caused by diabetes (16) or burns (17) have been the most common subjects of these studies. Stem cells obtained from different sources are loaded onto a variety of natural/bioengineered scaffolds as wound dressings (18-22), spread onto the wounds (23), or delivered in injectable forms (24-28) into them. Several researchers have been seeking methods for increasing the viability of the cells and the overall efficacy of the treatments (25-33). Furthermore, the cell-free method is a novel therapeutic approach in the field of cellular therapy that is actively performed in Iran. In this method, exosomes are used to convey stem cell signals to target cells and tissues without delivering the actual cells, whereby many of the issues associated with cell-based therapies are avoided (9, 33, 34).

The many capacities of stem cells have given them great commercialization potential. Several knowledge-based companies in Iran have already joined the industry. Royan Institute for Stem Cell Biology and Technology and its spin-off companies (Royan Stem Cell Technology Com-

pany, Cell Tech Pharmed Company, Royan Biotech Company, and Royan ATMP-TDC) are actively engaged in producing stem cell products. Human Induced Pluripotent Stem Cells, Human Embryonic Stem Cells, Mouse Embryonic Stem Cells, Bone Marrow/Adipose-derived Mesenchymal Stem Cells, etc, are some examples. Cell-Amniosin™, produced by SinaCell Company, is a biologic wound dressing made from the amniotic membrane and its associated stem cells. The company also offers mesenchymal stem cell production services. Several more knowledge-based companies also cooperate with the abovementioned universities and institutes.

Stem cell science opens doors to numerous possibilities for the treatment of hard-to-manage medical conditions. Given enough expertise and financial support, it can turn into a huge industry that benefits not only patients but the investors and all other involved parties. Iranian researchers have great enthusiasm for advancing the field and eagerly look for opportunities to collaborate with their peers from all over the world.

Acknowledgments

The authors would like to express their gratitude to the Dermatology and Stem Cell Research Center at Tehran University of Medical Sciences, colleagues and staff in Jordan Clinic, Tehran University of Medical Sciences, Tehran, Iran, and the authorities of Rasool Akram Medical Complex Clinical Research Development Center for their technical and editorial assistance.

Footnotes

Authors' Contribution: It was not declared by the authors.

Conflict of Interests: We declare no competing interests.

Funding/Support: None.

References

1. Nilforoushzadeh MA, Amirkhani MA, Hamidieh AA, Seifalian AM, Sisakht MM. Skin regenerative medicine advancements in the Islamic Republic of Iran: a concise review. *Regen Med.* 2019;**14**(11):1047-56. doi: [10.2217/rme-2018-0170](https://doi.org/10.2217/rme-2018-0170). [PubMed: [31718464](https://pubmed.ncbi.nlm.nih.gov/31718464/)].
2. Nazempour M, Mehrabani D, Mehdiavaz-Aghdam R, Hashemi SS, Derakhshanfar A, Zare S, et al. The effect of allogenic human Wharton's jelly stem cells seeded onto acellular dermal matrix in healing of rat burn wounds. *J Cosmet Dermatol.* 2020;**19**(4):995-1001. doi: [10.1111/jocd.13109](https://doi.org/10.1111/jocd.13109). [PubMed: [31556227](https://pubmed.ncbi.nlm.nih.gov/31556227/)].
3. Habibi M, Chehelcheraghi F. Effect of Bone Marrow Mesenchymal Stem Cell Sheets on Skin Capillary Parameters in a diabetic wound model: A Novel Preliminary Study. *Iran Biomed J.* 2021;**25**(5):334-42. doi: [10.52547/ibj.25.5.334](https://doi.org/10.52547/ibj.25.5.334).
4. Zafari F, Shirian S, Sadeghi M, Teimourian S, Bakhtiyari M. CD93 hematopoietic stem cells improve diabetic wound healing by VEGF activation and downregulation of DAPK-1. *J Cell Physiol.* 2020;**235**(3):2366-76. doi: [10.1002/jcp.29142](https://doi.org/10.1002/jcp.29142). [PubMed: [31549396](https://pubmed.ncbi.nlm.nih.gov/31549396/)].
5. Samani S, Shokrgozar MA, Zamini A, Majidi M, Tavassoli H, Aidun A, et al. Preparation of skin tissue engineering scaffold based on Adipose-derived Tissue. *J Tissues Mater.* 2019;**2**(1):47-54.
6. Farzamfar S, Salehi M, Ehterami A, Naseri-Nosar M, Vaez A, Zarnani AH, et al. Promotion of excisional wound repair by a menstrual blood-derived stem cell-seeded decellularized human amniotic membrane. *Biomed Eng Lett.* 2018;**8**(4):393-8. doi: [10.1007/s13534-018-0084-1](https://doi.org/10.1007/s13534-018-0084-1). [PubMed: [30603224](https://pubmed.ncbi.nlm.nih.gov/30603224/)]. [PubMed Central: [PMC6209087](https://pubmed.ncbi.nlm.nih.gov/PMC6209087/)].
7. Zare S, Ahmadi R, Mohammadnia A, Nilforoushzadeh MA, Mahmoodi M. Biological Characteristics and Optical Reflectance Spectroscopy of Human Placenta Derived Mesenchymal Stem Cells for Application in Regenerative Medicine. *J Lasers Med Sci.* 2021;**12**. e18. doi: [10.34172/jlms.2021.18](https://doi.org/10.34172/jlms.2021.18). [PubMed: [34733741](https://pubmed.ncbi.nlm.nih.gov/34733741/)]. [PubMed Central: [PMC8558699](https://pubmed.ncbi.nlm.nih.gov/PMC8558699/)].
8. Zare S, Ahmadi R, Mohammadnia A, Nilforoushzadeh MA, Mahmoodi M. The efficacy of isolation and culture of human amniotic mesenchymal stem cells in cell culture medium. *Daneshvar Med.* 2021;**28**(6):1-11. doi: [10.22070/DANESHMED.2021.12957.0](https://doi.org/10.22070/DANESHMED.2021.12957.0).
9. Nooshabadi VT, Khanmohamadi M, Valipour E, Mahdipour S, Salati A, Malekshahi ZV, et al. Impact of exosome-loaded chitosan hydrogel in wound repair and layered dermal reconstitution in mice animal model. *J Biomed Mater Res A.* 2020;**108**(11):2138-49. doi: [10.1002/jbm.a.36959](https://doi.org/10.1002/jbm.a.36959). [PubMed: [32319166](https://pubmed.ncbi.nlm.nih.gov/32319166/)].
10. Nilforoushzadeh MA, Heidari-Kharaji M, Alavi S, Mahmoudbeyk M, Nouri M, Peyrovan A, et al. Transplantation of autologous fat, stromal vascular fraction (SVF) cell, and platelet-rich plasma (PRP) for cell therapy of atrophic acne scars: Clinical evaluation and biometric assessment. *J Cosmet Dermatol.* 2020. doi: [10.21203/rs.3.rs-57442/v1](https://doi.org/10.21203/rs.3.rs-57442/v1).
11. Nilforoushzadeh MA, Aghdami N, Taghiabadi E. Human Hair Outer Root Sheath Cells and Platelet-Lysis Exosomes Promote Hair Inductivity of Dermal Papilla Cell. *Tissue Eng Regen Med.* 2020;**17**(4):525-36. doi: [10.1007/s13770-020-00266-4](https://doi.org/10.1007/s13770-020-00266-4). [PubMed: [32519329](https://pubmed.ncbi.nlm.nih.gov/32519329/)]. [PubMed Central: [PMC7392975](https://pubmed.ncbi.nlm.nih.gov/PMC7392975/)].
12. Nilforoushzadeh M, Jameh ER, Jaffary F, Abolhasani E, Keshtmand G, Zarkob H, et al. Hair follicle generation by injections of adult human follicular epithelial and dermal papilla cells into nude mice. *Cell J (Yakhteh).* 2017;**19**(2):259. doi: [10.22074/cellj.2016.3916](https://doi.org/10.22074/cellj.2016.3916).
13. Azhdari M, Baghaban-Eslaminejad M, Baharvand H, Aghdami N. Therapeutic potential of human-induced pluripotent stem cell-derived endothelial cells in a bleomycin-induced scleroderma mouse model. *Stem Cell Res.* 2013;**10**(3):288-300. doi: [10.1016/j.scr.2012.12.004](https://doi.org/10.1016/j.scr.2012.12.004). [PubMed: [23396195](https://pubmed.ncbi.nlm.nih.gov/23396195/)].
14. Norooznezhad AH, Yarani R, Payandeh M, Hoseinkhani Z, Kiani S, Taghizadeh E, et al. Human placental mesenchymal stromal cell-derived exosome-enriched extracellular vesicles for chronic cutaneous graft-versus-host disease: A case report. *J Cell Mol Med.* 2022;**26**(2):588-92. doi: [10.1111/jcmm.17114](https://doi.org/10.1111/jcmm.17114). [PubMed: [34873830](https://pubmed.ncbi.nlm.nih.gov/34873830/)]. [PubMed Central: [PMC8743661](https://pubmed.ncbi.nlm.nih.gov/PMC8743661/)].
15. Davoudi Y, Mahmoodi M, Ghorbani M. Acceptance and Commitment Therapy: Human Adipose Tissue-Derived Mesenchymal Stem Cells Alleviate Atopic Dermatitis via Decreased Serum Level of IgE and Number of Mast Cells. *Open J Pharma Sci.* 2021;**1**:1-8.
16. Ebrahimpour-Malekshah R, Amini A, Zare F, Mostafavinia A, Davoody S, Deravi N, et al. Combined therapy of photobiomodulation and adipose-derived stem cells synergistically improve healing in an ischemic, infected and delayed healing wound model in rats with type 1 diabetes mellitus. *BMJ Open Diabetes Res Care.* 2020;**8**(1). doi: [10.1136/bmjdr-2019-001033](https://doi.org/10.1136/bmjdr-2019-001033). [PubMed: [32098898](https://pubmed.ncbi.nlm.nih.gov/32098898/)]. [PubMed Central: [PMC7206914](https://pubmed.ncbi.nlm.nih.gov/PMC7206914/)].
17. Roshangar L, Rad JS, Kheirjou R, Khosroshahi AF. Using 3D-bioprinting scaffold loaded with adipose-derived stem cells to burns wound healing. *J Tissue Eng Regen Med.* 2021;**15**(6):546-55. doi: [10.1002/term.3194](https://doi.org/10.1002/term.3194). [PubMed: [33779071](https://pubmed.ncbi.nlm.nih.gov/33779071/)].

18. Lotfi M, Naderi-Meshkin H, Mahdipour E, Mafinezhad A, Bagherzadeh R, Sadeghnia HR, et al. Adipose tissue-derived mesenchymal stem cells and keratinocytes co-culture on gelatin/chitosan/beta-glycerol phosphate nanoscaffold in skin regeneration. *Cell Biol Int*. 2019;**43**(12):1365–78. doi: [10.1002/cbin.11119](https://doi.org/10.1002/cbin.11119). [PubMed: [30791186](https://pubmed.ncbi.nlm.nih.gov/30791186/)].
19. Mardani M, Sadeghzadeh A, Tanideh N, Andisheh-Tadibir A, Lavaee F, Zarei M, et al. The effects of adipose tissue-derived stem cells seeded onto the curcumin-loaded collagen scaffold in healing of experimentally-induced oral mucosal ulcers in rat. *Iran J Basic Med Sci*. 2020;**23**(12):1618–27. doi: [10.22038/ijbms.2020.48698.11171](https://doi.org/10.22038/ijbms.2020.48698.11171).
20. Ferdowsi Khosroshahi A, Soleimani Rad J, Kheirjou R, Roshangar B, Rashtbar M, Salehi R, et al. Adipose tissue-derived stem cells upon decellularized ovine small intestine submucosa for tissue regeneration: An optimization and comparison method. *J Cell Physiol*. 2020;**235**(2):1556–67. doi: [10.1002/jcp.29074](https://doi.org/10.1002/jcp.29074). [PubMed: [31400002](https://pubmed.ncbi.nlm.nih.gov/31400002/)].
21. Golchin A, Hosseinzadeh S, Jouybar A, Staji M, Soleimani M, Ardeshiry-lajimi A, et al. Wound healing improvement by curcumin-loaded electrospun nanofibers and BFP-MSCs as a bioactive dressing. *Polym Adv Technol*. 2020;**31**(7):1519–31. doi: [10.1002/pat.4881](https://doi.org/10.1002/pat.4881).
22. Hashemi SS, Mohammadi AA, Moshirabadi K, Zardosht M. Effect of dermal fibroblasts and mesenchymal stem cells seeded on an amniotic membrane scaffold in skin regeneration: A case series. *J Cosmet Dermatol*. 2021;**20**(12):4040–7. doi: [10.1111/jocd.14043](https://doi.org/10.1111/jocd.14043). [PubMed: [33656768](https://pubmed.ncbi.nlm.nih.gov/33656768/)].
23. Hashemi SS, Pourfath MR, Derakhshanfar A, Behzad-Behbahani A, Moayedi J. The role of labeled cell therapy with and without scaffold in early excision burn wounds in a rat animal model. *Iran J Basic Med Sci*. 2020;**23**(5):673–9. doi: [10.22038/ijbms.2020.34324.8156](https://doi.org/10.22038/ijbms.2020.34324.8156).
24. Nilforoushzadeh MA, Sisakht MM, Amirkhani MA, Seifalian AM, Banafshe HR, Verdi J, et al. Engineered skin graft with stromal vascular fraction cells encapsulated in fibrin-collagen hydrogel: A clinical study for diabetic wound healing. *J Tissue Eng Regen Med*. 2020;**14**(3):424–40. doi: [10.1002/term.3003](https://doi.org/10.1002/term.3003). [PubMed: [31826321](https://pubmed.ncbi.nlm.nih.gov/31826321/)].
25. Panahi M, Rahimi B, Rahimi G, Yew Low T, Saraygord-Afshari N, Alizadeh E. Cytoprotective effects of antioxidant supplementation on mesenchymal stem cell therapy. *J Cell Physiol*. 2020;**235**(10):6462–95. doi: [10.1002/jcp.29660](https://doi.org/10.1002/jcp.29660). [PubMed: [32239727](https://pubmed.ncbi.nlm.nih.gov/32239727/)].
26. Mousavifard A, Najafabadi EP, Rahnama MA, Anbarlou A, Atashi A. Elevated expression of stemness genes in adipose-derived mesenchymal stem cells cultured on fibrin scaffold. *J Biosci*. 2020;**45**. doi: [10.1007/s12038-020-00050-5](https://doi.org/10.1007/s12038-020-00050-5). [PubMed: [32554906](https://pubmed.ncbi.nlm.nih.gov/32554906/)].
27. Samadikuchaksaraei A, Nasiri N, Sharifi MJ, Chauhan NPS, Farhadi-hosseineabadi B, Fatemi Sovini S, et al. Intravenous Administration of Granulocyte-Colony Stimulating Factor for Stem Cells Mobilization and Third Degree Burn Wound Healing in Rats. *J Appl Biotechnol Rep*. 2019;**6**(3):83–7. doi: [10.29252/jabr.06.03.01](https://doi.org/10.29252/jabr.06.03.01).
28. Babakhani A, Hashemi P, Mohajer Ansari J, Ramhormozi P, Nobakht M. In vitro Differentiation of Hair Follicle Stem Cell into Keratinocyte by Simvastatin. *Iran Biomed J*. 2019;**23**(6):404–11. doi: [10.29252/ibj.23.6.404](https://doi.org/10.29252/ibj.23.6.404). [PubMed: [31104417](https://pubmed.ncbi.nlm.nih.gov/31104417/)]. [PubMed Central: [PMC6800537](https://pubmed.ncbi.nlm.nih.gov/PMC6800537/)].
29. Zare F, Moradi A, Fallahnezhad S, Ghoreishi SK, Amini A, Chien S, et al. Photobiomodulation with 630 plus 810nm wavelengths induce more in vitro cell viability of human adipose stem cells than human bone marrow-derived stem cells. *J Photochem Photobiol B*. 2019;**201**:111658. doi: [10.1016/j.jphotobiol.2019.111658](https://doi.org/10.1016/j.jphotobiol.2019.111658). [PubMed: [31710923](https://pubmed.ncbi.nlm.nih.gov/31710923/)].
30. Hormozi Moghaddam Z, Mokhtari-Dizaji M, Nilforoushzadeh MA, Bakhshandeh M, Ghaffari Khaligh S. Low-intensity ultrasound combined with allogenic adipose-derived mesenchymal stem cells (AdMSCs) in radiation-induced skin injury treatment. *Sci Rep*. 2020;**10**(1):1–19. doi: [10.1038/s41598-020-77019-9](https://doi.org/10.1038/s41598-020-77019-9). [PubMed: [33203925](https://pubmed.ncbi.nlm.nih.gov/33203925/)]. [PubMed Central: [PMC7673019](https://pubmed.ncbi.nlm.nih.gov/PMC7673019/)].
31. Ahmadi H, Amini A, Fadaei Fathabady F, Mostafavinia A, Zare F, Ebrahimpour-Malekshah R, et al. Transplantation of photobiomodulation-preconditioned diabetic stem cells accelerates ischemic wound healing in diabetic rats. *Stem Cell Res Ther*. 2020;**11**(1):1–4. doi: [10.1186/s13287-020-01967-2](https://doi.org/10.1186/s13287-020-01967-2). [PubMed: [33239072](https://pubmed.ncbi.nlm.nih.gov/33239072/)]. [PubMed Central: [PMC7688005](https://pubmed.ncbi.nlm.nih.gov/PMC7688005/)].
32. Rafie M, Meshkini A. Tailoring the proliferation of fibroblast cells by multiresponsive and thermosensitive stem cells composite F127 hydrogel containing folic acid.MgO:ZnO/chitosan hybrid microparticles for skin regeneration. *Eur J Pharm Sci*. 2021;**167**:106031. doi: [10.1016/j.ejps.2021.106031](https://doi.org/10.1016/j.ejps.2021.106031). [PubMed: [34601068](https://pubmed.ncbi.nlm.nih.gov/34601068/)].
33. Pesaraklou A, Mahdavi-Shahri N, Hassanzadeh H, Ghasemi M, Kazemi M, Mousavi NS, et al. Use of cerium oxide nanoparticles: a good candidate to improve skin tissue engineering. *Biomed Mater*. 2019;**14**(3):35008. doi: [10.1088/1748-605X/ab0679](https://doi.org/10.1088/1748-605X/ab0679). [PubMed: [30754036](https://pubmed.ncbi.nlm.nih.gov/30754036/)].
34. Nilforoushzadeh MA, Aghdami N, Taghiabadi E. Effects of Adipose-Derived Stem Cells and Platelet-Rich Plasma Exosomes on The Inductivity of Hair Dermal Papilla Cells. *Cell J (Yakhteh)*. 2021;**23**(5):576–83. doi: [10.22074/cellj.2021.7352](https://doi.org/10.22074/cellj.2021.7352).