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Adipose-Derived Stem cell Therapy for Acetic Acid Induced Ulcerative Colitis in Adult Male Albino Rat

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ABSTRACT

Ulcerative colitis (UC) is a chronic, relapsing inflammatory gastrointestinal condition. The patient's quality of life may be directly impacted by UC activity, which can range from mild to severe. Anemia, gastrointestinal tract obstruction, and nutritional deficiencies caused by the intestines' inability to absorb food are the most harmful and serious adverse effects of this inflammatory disease. However, it was shown that these patients had a significant risk of developing diseases like lymphoma and colorectal cancer, which may account for the higher death rates among those affected patients.
Current treatments are known to have serious adverse effects. Due to the high rates of side effects and the overall ineffectiveness of existing medicines, new treatment approaches must be investigated.
Stem cell therapy has become a promising area of treatment due to its high rate of proliferation, minimally invasive process, and lack of ethical concerns.

KEYWORDS: ulcerative colitis, acetic acid, stem cells.

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INTRODUCTION

Relapse and remission are hallmarks of ulcerative colitis, a chronic inflammatory disease of the mucosa lining the colon. Ulcerative colitis (UC) is distinct from Crohn's disease, which may affect any part of the gastrointestinal system and causes transmural inflammation in patches, by affecting just the colon and causing surface inflammation that lasts for a long time [1].

Idiopathic means that the specific reason someone gets UC is still a mystery. Several factors contribute to the onset and progression of colitis, including genetic vulnerability, environmental variables, and an enhanced host immunological response. A study conducted by Ho et al. [2] in 2019 indicated... Alterations to the structure and function of the mucosal barrier are indicated by changes in the quantity and diversity of the microbiota. Preliminary data suggests that UC patients have drastically altered gut flora compared to the general population. [3]

Despite our limited understanding of ulcerative colitis's pathogenesis, it is often associated with reduced antioxidant capacity and elevated production of free radicals such reactive oxygen species (ROS) [4].

The overproduction of reactive oxygen species (ROS) leads to lipid peroxidation, which in turn decreases the antioxidant capacity of cells and, in the end, produces noticeable inflammation in the colon [5].

The gut mucosal tissue is visited by macrophages and lymphocytes in UC. Lipid peroxidation, increased blood vessel permeability, neutrophil entrance, and enhanced intestinal mucosal inflammation are all caused by free radicals produced by activated white blood cells in the mucosal tissue of the intestines [6].

Both the innate and adaptive immune systems may be dysregulated, either before or after the macroscopic lesions. As a result of direct cytotoxicity against the epithelial cells, interleukin-13 production stands out as a key marker of the immune response in ulcerative colitis [7].

Tenesmus, stomach discomfort, urgency, and bloody diarrhea are classic symptoms of UC. In very rare cases, individuals may exhibit systemic symptoms including a low-grade fever or a decrease in body weight. It usually takes a few weeks for the illness to set in and worsen [8].

The most typical extraintestinal symptoms impact the heart, lungs, skin, and eyes. Included in this category of extraintestinal symptoms are conditions such as anemia, mouth sores, arthritis, osteoporosis, skin problems, liver illnesses, and cancer. Sulima et al. [9] published the following.

It is impossible for a single diagnostic test to provide conclusive evidence of ulcerative colitis. The patient's intestinal mucosa biopsy, together with endoscopic and clinical results, forms the basis of this. To further evaluate and track the progression of the illness, as well as to distinguish UC from other types of colitis that have similar symptoms, diagnostic tests such as ultrasonography, radiographs, and laboratory measures might be helpful. Methods that evaluate the degree and intensity of inflammation are often the foundation of an accurate UC diagnosis [10].

Treatment for ulcerative colitis is often based on the patient's severity of sickness and the extent to which the disease has progressed. At first, medication is used to promote remission, which involves alleviation of symptoms and restoration of the colon's mucosal lining. To keep the disease at bay and prevent a return, patients are given medication for an extended period of time [11]. Remission induction and maintenance is a crucial concept. Acute severe ulcerative colitis requires hospitalization, infection exclusion, and corticosteroids [12].

As a medical issue, ulcerative colitis has proven to be challenging. Up until this point, it has remained a mystery. Presently, immunosuppressants, corticosteroids, and anti-inflammatory medications such aminosalicylates (sulfasalazine) are the mainstays of UC treatment. According to Siddiqui et al. [13], these treatments mostly address the disease's symptoms.

As a first line of defense against moderate to severe rectal and colon inflammation, aminosalicylates are often used. The possible negative effects of long-term usage of corticosteroids make them only appropriate for short-term use in the treatment of flare-ups. In order to halt the immunological response that causes inflammation, immunosuppressants lower the immune system's activity. Mild to moderate flares or maintenance of remission may be achieved with their help [14].

Biologics are an advanced kind of medicine that attack inflammatory-promoting immune system proteins. According to Ferretti et al. [15], antibiotics such as ciprofloxacin or metronidazole may be used to address bacterial overgrowth.

Major adverse effects, including as infection and an increased risk of cancer, are known to occur with these pharmaceuticals, and they may not necessarily alleviate patients' symptoms in the long run. Because of the high frequency of adverse effects, current therapies are often unsuccessful, necessitating the exploration of new therapeutic techniques. Thus, novel remedial drugs are critically required to address these challenges [16].

When medicine fails to alleviate symptoms or causes difficulties, surgery becomes a possibility. It is usual practice to do a colectomy. In order to avoid the necessity for a permanent stoma, a surgeon may construct a J-pouch after a colectomy. This pouch is constructed from the small intestine attached to the anus. Stomas, which are abdominal incisions that hold a bag for waste collection, may be required temporarily or permanently in some instances [17].

Stem cell treatment is one promising field of medicine. Due to their fast rate of multiplication, absence of ethical difficulties, and less invasive method, mesenchymal stem cells (MSCs) have garnered interest [18].

ACETIC ACID

Simple form of acetic acid:
An acidic, colorless liquid and organic substance with the molecular formula CH3COOH, acetic acid is also known as ethanoic acid (Kobayashi, 2023). Among carboxylic acids, acetic acid ranks second in simplicity, only after formic acid [19].

It is a fermentation byproduct that gives vinegar its signature aroma. A solution of acetic acid in water makes up about 4-6% of vinegar [20].

Acetic acid is a key ingredient in many common household products, including rubber, plastics, dyes, and insecticides [21]. Another commercial usage is in the manufacture of chemical compounds, vitamins, antibiotics, and hormones [22].

In the manufacturing of cellulose acetate for photographic film, polyvinyl acetate for wood glue, and synthetic fibers and textiles, it plays a significant role as both a reagent and an industrial chemical [23].

Descaling treatments generally include diluted acetic acid, which is often used in houses. According to Kobayashi et al. [24], acetic acid is regulated in the food sector for its use as a condiment and acidity regulator. The acetyl group, which is a building block of all biological molecules, is essential in biochemistry. According to Zeidan and Marti [19], it plays a crucial role in the metabolism of carbohydrates and lipids when attached to coenzyme A.

There should be no negative health consequences from consuming small amounts of acetic acid via food or using acetic acid-containing home goods properly [25]. Damage from corrosion may occur when exposed to solutions of acetic acid at higher concentrations. At concentrations commonly used in laboratories and factories, acetic acid is very irritating to the skin, eyes, and mucous membranes. According to Abbas et al. [26], prolonged exposure to concentrated acetic acid on the skin may lead to burns, ulcers, pain, and harm to surrounding tissues.

When exposed to excessive levels of acetic acid vapors by inhalation, one may experience a variety of symptoms such as eye, nose, throat, cough, chest tightness, headache, fever, and disorientation. Workplace infections such as pharyngitis, bronchitis, and conjunctivitis are not uncommon in highly exposed individuals [27].

Urinary tract burns, trouble breathing, gag reflexes, nausea, vomiting (with or without blood), and stomach aches are also symptoms of ingesting larger quantities [28].

The release of protons to the epithelium causes an acidic environment that damages the colonic epithelium and increases inflammation; as a result, acetic acid may promote ulcerative colitis in rats [29]. So, the contents of the intestines come into contact with the lamina propria, which in turn triggers the generation of cytokines that promote inflammation [3].

stem cells:
In addition to differentiating into other cell types, stem cells may self-renew and generate an infinite number of identical daughter cells [30] .

Stem cells are a kind of immature cell that may be sourced from many tissues; they possess the ability to proliferate and regenerate over an extended period of time [31]. These stem cells have the remarkable ability to develop into any kind of cell in the body, depending on their origin (Poliwoda et al., 2022).

Properties of stem cells

1) the ability to renew one's own cells—that is, to divide many times while maintaining their undifferentiated state [32].
2) Poliwoda et al. [33] defined "potency" as "the capacity of a cell to differentiate into other cell types." Stem cells are classified into the following categories based on their potency:
3) Transdifferentiation is possible between embryonic and extraembryonic cell types in totipotent stem cells. These cells are created when an egg and sperm fuse. The cells that are created during the first rounds of cell division in a fertilized egg are also considered totipotent [34].
4) Almost every kind of cell may be differentiated from pluripotent stem cells [35].
5) According to Rosner et al. [36], multipotent stem cells have the ability to develop into many cell types that belong to a closely related family.
6) Myeloid and lymphoid stem cells are two of the few cell types that oligopotent stem cells may develop into [33].
7) The number of cell types that can be differentiated from unipotent stem cells is one. What sets stem cells apart from other types of cells is their ability to replenish themselves [37].

Types of stem cells
1-Emberyonic stem cells
The inner cell mass of a blastocyst, an early stage preimplantation embryo, is the source of human embryonic stem cells, which are pluripotent (Park et al., 2024). In the first week after fertilization, embryonic cells are extracted from the egg cells. All cell types may be differentiated from them [38]. Nevertheless, an immunological response might develop as a side effect of embryonic stem cell treatment. Furthermore, their origins in developing embryos make their usage contentious [39]

2- Induced pluripotent stem cells (IPSCs)
An artificial method of producing IPSCs involves reprogramming adult somatic cells via the forced expression of certain genes [40]. Mesodermal, endodermal, and ectodermal cells are all within their range of possible differentiation. Patients' own somatic cells may be used to create IPSCs, which eliminates immunogenic rejection and ethical concerns [41].

3- **Umbilical cord blood stem cells**
One potential place to find mesenchymal stem cells is in the human umbilical cord. Human umbilical cord mesenchymal stem cells have quicker self-renewal capabilities and are collected painlessly, in contrast to bone marrow stem cells [42].

4- **Adult stem cells (Somatic stem cells)**
Adult stem cells are ubiquitous, unspecialized cells that may divide endlessly to repair injured tissues [43]. According to de Morree and Rando [44], these cells have the remarkable ability to proliferate and produce every kind of cell in the organ from where they originated.

There are no moral issues with using them in research. Most research on them has been conducted on rats and mice, which are used as models for people [45]. Adult stem cells come in a wide variety, including:

Neural stem cells
They self-renew and are found in the central nervous system. Both in vivo and in vitro proliferation is within their capabilities. Human neural stem cells that have been transplanted travel to different parts of the brain and develop into neurons [46].

Mammary stem cells
According to Liu et al. [47], stem cells found in the breast can self-renew in both living organisms and laboratory settings. In addition to producing new luminal and myoepithelial cells, they can also restore the mammary gland [48].

Haematopoietic stem cells
Bone marrow and blood from the umbilical cord both include haematopoietic stem cells, which have the ability to develop into any kind of blood cell [49].

Mesenchymal stem cells (MSCs)
Isolating mesenchymal stem cells (MSCs) from many tissues such as the umbilical cord, adipose tissue, olfactory mucosa, lungs, bone marrow, and placenta is possible [50].

Subcutaneous adipose tissue is a rich source of MSC, and it is readily accessible by liposuction and other minimally invasive surgical procedures. Because of their minimal donor site morbidity and ease of accessibility, ASCs are great choices for many cell-based therapies [51].

Medical professionals are showing a growing interest in these cells because of their potential for in-situ or intravenous transplantation, immunosuppressive effects that lessen graft failure, and capacity to differentiate into targeted cells in response to local conditions and culture conditions [52, 53].

Relevant sections
Morphology of mesenchymal stem cells
Mesenchymal stem cells are characterized by a tiny cell body and many long, thin processes. There is a huge, spherical nucleus in the middle of the cell body, and its nucleolus is quite visible. The nucleus seems transparent because it is encased in finely scattered chromatin particles. Golgi apparatus, rough endoplasmic reticulum, polyribosomes, and mitochondria are also present in modest quantities inside the cell body [54].

Application of stem cell therapy in management of diseases
Stem cells for cardiovascular diseases:
Heart conditions, both old and new, may be safely and effectively treated with adult stem cell treatment. Potential pathways for stem cell-mediated cardiac disease recovery include myocardial cell regeneration, increased angiogenesis, and growth factor release [55].

Stem cells for liver diseases:
Cirrhosis of the liver due to alcoholic liver disease, hepatitis C and B, and end-stage liver disease have all been treated using stem cells [56]. Stem cell infusion was administered to patients with decompensated cirrhosis via a peripheral vein. According to Zheng et al. [57], there are no reported negative effects in patients throughout the follow-up period.

Stem Cells for Treatment of Wounds:
Scar tissue often replaces the disordered collagen structure, hair follicle loss, and abnormal vascular structure that develops in injured tissue. According to Riha et al. [58], stem cells play a crucial role in facilitating the regeneration of injured tissues.

Stem Cells for Diabetes:
When the pancreas stops making enough insulin, the result is diabetes, which is characterized by an imbalance in blood insulin levels. There have been several attempts to find a way to stop needing insulin shots by transplanting either the pancreas or the islet of Langerhans. Following implantation, the recipient often rejects the pancreas and islet cells [59].

Because stem cells do not cause rejection, they are a viable option [60].

Stem cells for renal diseases:
One treatment option for chronic renal failure is stem cell therapy, which has the potential to aid in cellular repair and remodeling of the kidneys [61]. Administered stem cells have the potential to enter the bloodstream and go to injured areas inside the kidneys when the patient is in acute renal failure. Therefore, they are able to respond to various local stimuli, such as hypoxia or ischemia, and subsequently secrete chemokines, growth factors, immunomodulatory cytokines, and vasoactive factors. Therefore, MSCs and other stem cells may aid in the full recovery of patients with acute renal failure. This information is sourced from Kanduri et al. [62].

Stem cells for inflammatory bowel diseases
Animal and human studies have shown that MSC have more therapeutic promise than conventional drugs for treating UC in mouse models and in people [63].

Due to their ability to decrease inflammation in the intestines, stimulate long-term repair of the intestinal mucosa, and substantially enhance patient quality of life, stem cells have emerged as a promising alternative therapy for inflammatory bowel diseases [64].

DISCUSSION:

According to studies on stem cells, mesenchymal stem cells (MSCs) have the ability to divide themselves and replenish themselves. They can house the injured area, reduce inflammation by secreting cytokines, promote healing by expressing growth factors, and release anti-apoptotic substances; these characteristics give them therapeutic effects in various inflammatory diseases, including ulcerative colitis.

CONCLUSION
Results from this meta-analysis support the use of stem cells in the treatment of ulcerative colitis.

FUTURE DIRECTIONS
Overall, it seems that the research approach was solid and appropriate. Stem cell therapy for ulcerative colitis was defined in a clear and concise review. The study's findings provide a streamlined and current synopsis of stem cell treatment for ulcerative colitis.

Research should focus on enhancing stem cell effectiveness and delivery, developing new cell types and engineering strategies, and standardizing protocols for personalized treatment.

LIST OF ABBREVIATIONS
UC: ulcerative colitis.
MSCs: Mesenchymal stem cells.
IPSCs: Induced pluripotent stem cells.

CONFLICT OF INTEREST
The writers have stated that they have no competing interests. The final version of the manuscript was reviewed and approved by all authors.

AUTHORS CONTRIBUTION
In this study, each author had an equal say.

REFERENCES

1. Nakase, H., et al., The influence of cytokines on the complex pathology of ulcerative colitis. Autoimmunity Reviews, 2022. 21(3): p. 103017.
2. Ho, S.-M., et al., Challenges in IBD Research: Environmental Triggers. Inflammatory Bowel Diseases, 2019. 25(Supplement_2): p. S13-S23.
3. hussein, m.n., et al., Assessment of the Prophylactic Effect of Probiotics in an Experimental Model of Ulcerative Colitis in Male Albino Rat: Histological and Immunohistochemical Study. Egyptian Journal of Histology, 2023. 46(1): p. 33-48.
4. Jarmakiewicz-Czaja, S., K. Ferenc, and R. Filip Antioxidants as Protection against Reactive Oxidative Stress in Inflammatory Bowel Disease. Metabolites, 2023. 13, DOI: 10.3390/metabo13040573.
5. Wan, Y., et al., Excessive Apoptosis in Ulcerative Colitis: Crosstalk Between Apoptosis, ROS, ER Stress, and Intestinal Homeostasis. Inflammatory Bowel Diseases, 2022. 28(4): p. 639-648.
6. Ashique, S., et al., Recent updates on correlation between reactive oxygen species and synbiotics for effective management of ulcerative colitis. Frontiers in Nutrition, 2023. Volume 10 - 2023.
7. Du, L. and C. Ha, Epidemiology and Pathogenesis of Ulcerative Colitis. Gastroenterology Clinics, 2020. 49(4): p. 643-654.
8. Garnica Camacho, C.E., Differential Diagnosis of Ulcerative Colitis, in Unveiling Ulcerative Colitis - A Comprehensive Approach to Understanding and Management, D.C. Lazar, Editor. 2025, IntechOpen: London.
9. Sulima, O. and V. Sulyma, Extraintestinal Manifestations of Ulcerative Colitis: The Opinion of a Rheumatologist and Proctologist. The Eurasia Proceedings of Science, Technology, Engineering & Mathematics (EPSTEM), 2020. 11: p. 159-162.
10. Hassanshahi, N., et al., The Healing Effect of Aloe Vera Gel on Acetic Acid-Induced Ulcerative Colitis in Rat. Middle East J Dig Dis, 2020. 12(3): p. 154-161.
11. Ko, C.W., et al., AGA Clinical Practice Guidelines on the Management of Mild-to-Moderate Ulcerative Colitis. Gastroenterology, 2019. 156(3): p. 748-764.
12. Calméjane, L., et al., Review article: Updated management of acute severe ulcerative colitis: From steroids to novel medical strategies. United European Gastroenterology Journal, 2023. 11(8): p. 722-732.
13. Tausif Siddiqui, M., R. Kasiraj, and M. Naseer, Medical Management of Ulcerative Colitis and Crohn’s Disease—Strategies for Inducing and Maintaining Remission. Surgical Clinics, 2025. 105(2): p. 435-454.
14. Gros, B. and G.G. Kaplan, Ulcerative colitis in adults: a review. Jama, 2023. 330(10): p. 951-965.
15. Ferretti, F., et al. An Update on Current Pharmacotherapeutic Options for the Treatment of Ulcerative Colitis. Journal of Clinical Medicine, 2022. 11, DOI: 10.3390/jcm11092302.
16. Aslam, N., et al., A review of the therapeutic management of ulcerative colitis. Therapeutic Advances in Gastroenterology, 2022. 15: p. 17562848221138160.
17. Dai, N., et al., Colectomy rates in ulcerative colitis: A systematic review and meta-analysis. Digestive and Liver Disease, 2023. 55(1): p. 13-20.
18. Golchin, A., E. Seyedjafari, and A. Ardeshirylajimi, Mesenchymal Stem Cell Therapy for COVID-19: Present or Future. Stem Cell Reviews and Reports, 2020. 16(3): p. 427-433.
19. Zeidan, H. and M.E. Marti, Selective and efficient separation of levulinic, acetic and formic acids from multi-acid solutions by adjusting process parameters. Journal of Water Process Engineering, 2023. 56: p. 104299.
20. Husain, A., EXPERIMENTAL PHARMACEUTICAL ORGANIC CHEMISTRY. Vol. 1. 2021: DARSHAN

PUBLISHERS.
21. Ayres, D.C. and D.G. Hellier, Dictionary of environmentally important chemicals. 2022: Routledge.
22. Deshmukh, G. and H. Manyar, Production pathways of acetic acid and its versatile applications in the food industry, in Biomass. 2020, IntechOpen.
23. Coban, H.B., Organic acids as antimicrobial food agents: applications and microbial productions. Bioprocess and Biosystems Engineering, 2020. 43(4): p. 569-591.
24. Kobayashi, N., et al., The Roles of Peyer's Patches and Microfold Cells in the Gut Immune System: Relevance to Autoimmune Diseases. Frontiers in Immunology, 2019. Volume 10 - 2019.
25. Additives, E.Panel o., et al., Safety and efficacy of a feed additive consisting of acetic acid for all animal species. EFSA Journal, 2021. 19(6): p. e06615.
26. Abbas, A., A.Y. Adesina, and R.K. Suleiman, Influence of organic acids and related organic compounds on corrosion behavior of stainless steel—a critical review. Metals, 2023. 13(8): p. 1479.
27. Suzuki, N., et al. Concentrations of Formic Acid, Acetic Acid, and Ammonia in Newly Constructed Houses. International Journal of Environmental Research and Public Health, 2020. 17, DOI: 10.3390/ijerph17061940.
28. Uygun, I. and S. Bayram, Corrosive ingestion managements in children. Esophagus, 2020. 17(4): p. 365-375.
29. Shahid, M., et al. Sinapic Acid Ameliorates Acetic Acid-Induced Ulcerative Colitis in Rats by Suppressing Inflammation, Oxidative Stress, and Apoptosis. Molecules, 2022. 27, DOI: 10.3390/molecules27134139.
30. Shah, A.A. and F.A. Khan, Types and Classification of Stem Cells, in Advances in Application of Stem Cells: From Bench to Clinics, F.A. Khan, Editor. 2021, Springer International Publishing: Cham. p. 25-49.
31. Tkemaladze, J., Reduction, proliferation, and differentiation defects of stem cells over time: a consequence of selective accumulation of old centrioles in the stem cells? Molecular Biology Reports, 2023. 50(3): p. 2751-2761.
32. Chhabra, S.N. and B.W. Booth, Asymmetric cell division of mammary stem cells. Cell Division, 2021. 16(1): p. 5.
33. Poliwoda, S., et al., Stem cells: a comprehensive review of origins and emerging clinical roles in medical practice. Orthop Rev (Pavia), 2022. 14(3): p. 37498.
34. Cai, J., et al., Research Progress of Totipotent Stem Cells. Stem Cells and Development, 2022. 31(13-14): p. 335-345.
35. Gordeev, M.N., E.I. Bakhmet, and A.N. Tomilin, Pluripotency Dynamics during Embryogenesis and in Cell Culture. Russian Journal of Developmental Biology, 2021. 52(6): p. 379-389.
36. Rosner, M., et al., Multipotent fetal stem cells in reproductive biology research. Stem Cell Research & Therapy, 2023. 14(1): p. 157.
37. Laplane, L., Stem cell epistemological issues. Stem cell biology and regenerative medicine, 2022: p. 693-712.
38. Moris, N., Stem cells used to model a two-week-old human embryo. 2023, Nature Publishing Group UK London.
39. Habib, O., et al., Comprehensive analysis of prime editing outcomes in human embryonic stem cells. Nucleic Acids Research, 2022. 50(2): p. 1187-1197.
40. Kim, J.Y., et al., Review of the Current Trends in Clinical Trials Involving Induced Pluripotent Stem Cells. Stem Cell Reviews and Reports, 2022. 18(1): p. 142-154.
41. Cerneckis, J., H. Cai, and Y. Shi, Induced pluripotent stem cells (iPSCs): molecular mechanisms of induction and applications. Signal Transduction and Targeted Therapy, 2024. 9(1): p. 112.
42. Shi, P.A., et al., Umbilical cord blood: an undervalued and underutilized resource in allogeneic hematopoietic stem cell transplant and novel cell therapy applications. Current Opinion in Hematology, 2022. 29(6): p. 317-326.
43. Mannino, G., et al., Adult stem cell niches for tissue homeostasis. Journal of Cellular Physiology, 2022. 237(1): p. 239-257.
44. de Morree, A. and T.A. Rando, Regulation of adult stem cell quiescence and its functions in the maintenance of tissue integrity. Nature Reviews Molecular Cell Biology, 2023. 24(5): p. 334-354.
45. Gopalarethinam, J., et al., Advantages of mesenchymal stem cell over the other stem cells. Acta Histochemica, 2023. 125(4): p. 152041.
46. Willis, C.M., et al., Soluble factors influencing the neural stem cell niche in brain physiology, inflammation, and aging. Experimental Neurology, 2022. 355: p. 114124.
47. Liu, C., et al., Procr functions as a signaling receptor and is essential for the maintenance and self-renewal of mammary stem cells. Cell Reports, 2022. 38(12).
48. Martignani, E., et al., Whole transcriptome analysis of bovine mammary progenitor cells by P-Cadherin enrichment as a marker in the mammary cell hierarchy. Scientific Reports, 2020. 10(1): p. 14183.
49. Yamashita, M., et al., Dysregulated haematopoietic stem cell behaviour in myeloid leukaemogenesis. Nature Reviews Cancer, 2020. 20(7): p. 365-382.
50. Kouchakian, M.R., et al., The Clinical Trials of Mesenchymal Stromal Cells Therapy. Stem Cells International, 2021. 2021(1): p. 1634782.
51. Li, C.-W., et al., Low-glucose culture environment can enhance the wound healing capability of diabetic adipose-derived stem cells. Stem cell research & therapy, 2023. 14(1): p. 236.
52. Miceli, V., et al. Therapeutic Properties of Mesenchymal Stromal/Stem Cells: The Need of Cell Priming for Cell-Free Therapies in Regenerative Medicine. International Journal of Molecular Sciences, 2021. 22, DOI: 10.3390/ijms22020763.
53. Yang, X., et al., Mesenchymal stem cell therapy for liver disease: full of chances and challenges. Cell & Bioscience, 2020. 10(1): p. 123.
54. Yim, E.K.F. and K.W. Leong, Significance of synthetic nanostructures in dictating cellular response. Nanomedicine in Cancer, 2017: p. 129-158.
55. Chang, D., et al., Application of mesenchymal stem cell sheet to treatment of ischemic heart disease. Stem Cell Research & Therapy, 2021. 12(1): p. 384.

56. Zhang, S., et al., The clinical application of mesenchymal stem cells in liver disease: the current situation and potential future. Ann Transl Med, 2020. 8(8): p. 565.
57. Zheng, S.P., et al., Endoscopic ultrasound-guided intraportal injection of autologous bone marrow in patients with decompensated liver cirrhosis: A case series. World J Gastrointest Surg, 2023. 15(4): p. 655-663.
58. Riha, S.M., M. Maarof, and M.B. Fauzi Synergistic Effect of Biomaterial and Stem Cell for Skin Tissue Engineering in Cutaneous Wound Healing: A Concise Review. Polymers, 2021. 13, DOI: 10.3390/polym13101546.
59. Shapiro, A.M.J., M. Pokrywczynska, and C. Ricordi, Clinical pancreatic islet transplantation. Nature Reviews Endocrinology, 2017. 13(5): p. 268-277.
60. Hogrebe, N.J., M. Ishahak, and J.R. Millman, Developments in stem cell-derived islet replacement therapy for treating type 1 diabetes. Cell Stem Cell, 2023. 30(5): p. 530-548.
61. Almeida, A., et al., Bone marrow-derived mesenchymal stem cells transplantation ameliorates renal injury through anti-fibrotic and anti-inflammatory effects in chronic experimental renovascular disease. Biomedical Journal, 2022. 45(4): p. 629-641.
62. Kanduri, S.R., et al., Kidney recovery from acute kidney injury after hematopoietic stem cell transplant: a systematic review and meta-analysis. Cureus, 2021. 13(1).
63. Jiang, X., et al., Umbilical cord mesenchymal stem cells in ulcerative colitis treatment: efficacy and possible mechanisms. Stem Cell Research & Therapy, 2024. 15(1): p. 272.
64. Wang, R., et al., Stem cell therapy for Crohn's disease: systematic review and meta-analysis of preclinical and clinical studies. Stem Cell Research & Therapy, 2021. 12(1): p. 463.