

## Assessment #2

### Research Assessment #2

#### Annotated Bibliography with 5 Sources

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Topic: Biomedical Engineering

KEY:

(1) - Citation, (2) - Introduction/Topic, (3) - Aims & Research Methods, (4) - Scope, (5) - Evaluation/Usefulness, (6) - Limitations, (7) - Conclusions, (8) - Reflection/Relation

(1) Matsuzaka, Yasunari, and Ryu Yashiro. "Therapeutic Strategy of

Mesenchymal-Stem-Cell-Derived Extracellular Vesicles as Regenerative Medicine."

*International Journal of Molecular Sciences*, vol. 23, no. 12, June 2022, p. 6480.

<https://doi.org/10.3390/ijms23126480>.

(2) In this peer-reviewed research paper, Matsuzaka et al. specifically talk about the role of mesenchymal stem cell-derived vesicles (MSC-EVs) in regenerative medicine. They specifically talk about how MSC-EVs are very good at intercellular communication and the ability to integrate well into the cellular environment. MSC-EVs are used by transplantation into the body, when transplanted they transfer proteins, lipids, nucleic acids, and bioactive molecules to the site intended. (3) this paper aims to give general background about the MSC-EVs and their use in regenerative medicine. Researchers talk about how this therapy can be an alternative to cell-based therapy. Moreover, they discuss

how it has an edge over traditional stem cell therapy as it doesn't deal with factors like immune rejection and tumorigenicity. The researchers formed this argument from many preclinical and clinical studies on various disease models. (4) The researchers cover a wide range of applications of MSC-EVs; for example, they talk about its use in heart disease, renal injury, neural damage, and lung disorders. (5) This review is very useful for conducting research as it goes over a comprehensive review of the benefits of using MSC-EVs over traditional therapies because of their lower risk and ability to serve as an efficient drug delivery system. Moreover, it gives more background on ongoing clinical trials and future directions of this type of therapy. (6) One limitation of this paper is that it is a review paper, so it covers a lot of topics in one research paper. This means that it can only cover so many topics by being a little more general in each part. So, compared to a research paper that only conducts experiments on one specific topic, this provides a bit less information and may limit the strength of the author's argument. Moreover, the fact that this research paper only uses information from other studies and trials means it has no first-hand experience with experiments. (7) The authors conclude that MSC-EVs have a lot of potential in the field of regenerative medicine because of their benefits and ability to avoid risks associated with traditional methods. However, they do add that more research must be done before this treatment can be used in the real world. I can use this research in many parts of my project as there is a lot of background information. It can help build an idea of where exactly I want to go with my topic for my research project this year. (8) The information in this article is very interesting as well as useful; it thoroughly reviews the benefits and the application of MSC-EVs which gives a lot of

clarity on building a research project. This paper can give an individual a greater understanding when it comes to first learning about the MSC-EVs.

(1) McKinley, Kara L., et al. “Emerging Frontiers in Regenerative Medicine.” *Science*, vol. 380, no. 6647, May 2023, pp. 796–98. <https://doi.org/10.1126/science.add6492>.

(2) In a peer-reviewed research paper, McKinley et al. examine the current research in the field of regenerative medicine and specifically looks at the advances and challenges in the field. They specifically highlight the need for regenerative medicine in the context of replacing damaged tissue but they also look at challenges such as fibrosis, inadequacy of progenitor cells and inflammation. (3) The author's main aim is to explore the recent advances in this field while also looking at the gaps in the research. The authors review the potential and limitations of many therapeutic strategies such as cell therapy, in vivo programming and synthetic biology. Essentially, they aim to highlight the idea that though there is a lot of potential in this field there needs to be more done to fill the gaps in the research. (4) The paper specifically focuses on major advances in the use of cell-based therapies. They use many examples of clinical trials, pre-clinical trials, and more innovation in synthetic biology in the context of tissue regeneration. (5) This paper is very useful for understanding the current state of regenerative medicine. As it is a review paper it has a wide scope of different clinical trials and practice substances that are present in the field. It is very useful in this instance as it can give an easy summary of the whole field of regenerative medicine. However the limitation for this paper is that since it has such a wide scope it does not have the specifics of each topic they introduce. (6) One limitation of this paper is that it is a review paper, which means it depends on resources from other studies and experiments. The authors do not have first-hand experience with

conducting an experiment, so they have to form their arguments based on other research, which may be detrimental to their whole paper. (7) The authors conclude with the idea that though regenerative medicine is a rapidly growing field, it is not yet a clinical reality. There are many challenges that researchers need to find solutions before it can be applied in the real-world. The conclusion from this paper is very helpful in that it helped me get an idea of the gaps of the research at the current state. So by blending these gaps with more information I can build a better plan for my research project. (8) This paper can be very useful for completing my own research. It describes the complexity of the field of regenerative medicine and the many challenges that researchers are facing currently. It talks about things like inflammation, fibrosis, and immune rejections which are valuable things that need to be researched before writing a paper.

(1) Qi, Xin, et al. "Exosomes Secreted by Human-Induced Pluripotent Stem Cell-Derived Mesenchymal Stem Cells Repair Critical-Sized Bone Defects Through Enhanced Angiogenesis and Osteogenesis in Osteoporotic Rats." *International Journal of Biological Sciences*, vol. 12, no. 7, Jan. 2016, pp. 836–49.

<https://doi.org/10.7150/ijbs.14809>.

(2) This research paper by Qi et al. examines how exosomes derived from human induced pluripotent stem cells (hiPSC-MSC-Exos) can be used to heal bone defects especially when it is under osteoporotic conditions. The study talks about the negative effects of osteoporosis such as delayed bone healing. They wanted to see if these exosomes can help deal with this challenge by helping promote angiogenesis and osteogenesis. (3) The aim of the study is to see if these hiPSC-MSC-Exos will aid in the regeneration of bone by helping stimulate angiogenesis and osteogenesis. They used

ovariectomized (OVX) rats which was intended to model postmenopausal osteoporosis; essentially they wanted to see if these hiPSC-MSC-Exos can be used to treat women with postmenopausal osteoporosis in the future. Their research methods involved in vitro experiments to monitor cell proliferation and differentiation and in a few in vivo tests with rats with critical-sized bone defects. They essentially argue that these exosomes will be more beneficial in treating these conditions as they have the advantages of both induced pluripotent stem cells and mesenchymal stem cells without the risks of tumorigenicity and immunogenicity. (4) The scope of this research mainly focuses on bone regeneration when using exosomes to heal critical-sized defects under osteopathic conditions. The subjects that are being studied are ovariectomized rats which are meant to simulate the similar bone degeneration seen with postmenopausal women. (5) This paper has lots of useful information for those like me researching regenerative medicine. It is very surprising and encouraging as I never thought it was possible to use exosomes in the context of bone healing with postmenopausal women. It presents a new and innovative research question and research method, which makes it interesting and motivating to read. Finally the findings as well are encouraging as they claim that these exosomes do significantly enhance angiogenesis and osteogenesis. (6) One limitation that the authors talk about is the fact that they need to do more research to understand the molecular mechanisms about why exactly these exosomes have these regenerative effects. Moreover, this study is limited to animal models which means that there needs to be more research done especially human trials that need to be done before it can be used in clinical settings. Human trials are necessary to measure the safety and efficacy of these treatments. (7) Overall the research from the paper shows that these exosomes do have

positive effects as they promote angiogenesis and osteogenesis. The conclusion from this paper is very useful as it opens up opportunities to treat bone defects with stem cell derived exosomes. Essentially by taking ideas from this paper, I can apply the same ideas of using exosomes derived from both MSCs and iPSCs due to their superior qualities. Furthermore by pairing this technique with techniques from other studies I would be able to make a more effective experiment setup. (8) This research paper and the information it talks about is directly relevant to my topic of choice which is regenerative medicine. A subtopic I want to explore for my research is tissue regeneration which directly coincides with this research paper. Moreover, the method used in this paper includes stem cell derived exosomes which is a topic I want to study more as it is safer, less invasive without the risks of traditional methods.

(1) Samsonraj, Rebekah M., et al. "Concise Review: Multifaceted Characterization of Human Mesenchymal Stem Cells for Use in Regenerative Medicine." *Stem Cells Translational Medicine*, vol. 6, no. 12, Oct. 2017, pp. 2173–85. <https://doi.org/10.1002/sctm.17-0129>.

(2) In this research paper by Samsonraj et al, the authors examine the different characteristics of mesenchymal stem cells. It talks about all the uses of missing the most stem cells, their self-renewal possibilities, their differential potential and therapeutic uses of the stem cells in various conditions. It also focuses on standardizing protocols for the preparation and characterization of the stem cells. (3) The main purpose of this research paper is to essentially give more context and background on mesenchymal stem cells. The authors thoroughly describe what exactly stem cells are, how to isolate them, how to identify tissue sources of these stem cells, and moreover, how to identify and grow them

specifically. They also talk about differentiation and how to manipulate these stem cells so that they differentiate into the type of cell that we may need for our research. They talk about MSCs in the context of tissue regeneration especially in orthopedic conditions.

Current challenges are also widely mentioned in the paper. One of the main conclusions is that there is not yet a standardized practice for experiments in this field so it is hard to compare results from different studies. Essentially, this paper thoroughly goes through every part of stem cells and describes all the most important information that we may need to know if we are using these stem cells in the context of regenerative medicine. (4)

The scope of this research is all things mesenchymal stem cells. Essentially, the researchers go through all the different parts of stem cells, and they focus on MSCs sourced from bone marrow and adipose tissues. They focus on the growth capacities, differential potential, and therapeutic applications, especially in orthopedic situations.

Moreover, it also addresses the challenges and inconsistencies that are true in mesenchymal stem cells research at the moment.. So in summary, this research has a large scope, covering a lot of information about mesenchymal stem cells.- (5) This information in my opinion was highly useful because it helped me understand a lot more on how MSCs work and function. Moreover, the argument about standardization of practices also gave me a lot of insight into the current state of the research and what needs to be improved. I was very surprised when I found out that most of these studies all use different scales of measurement since this makes it harder to compare many studies with each other. (6) One limitation I see in this specific paper is that it is a review paper, meaning it discusses many topics generally, and the researchers have not conducted their own experiments. Instead, they have analyzed other people's experiments and drawn

conclusions from those. This means that, since they do not have firsthand experimental data, they are dependent on other studies and references. (7) The authors of this research paper conclude that as we conduct more research trials on stem cells, we need to create more standardized practices. This is really important to my project because now that I have learned this valuable information, I want to try to implement a solution in my experiment. One of my goals for the research experiment I plan to do this year is to find a way to standardize procedures, possibly by developing a standardized procedure myself that other scientists and researchers can follow in the future. (8) This article is highly relevant to my topic of study as it is closely related to regenerative medicine.

Mesenchymal stem cells have been an integral part of many regenerative medicine therapies, and it is important for me to understand how they work and why they work the way they do. Moreover, the finding that there needs to be more standardized practices in these research papers is something I really needed to know, as it helps me understand the current state of the research and what I need to improve upon so that my research can be as strong as possible.

(1) Zhang, Jieyuan, et al. "Exosomes Released From Human Induced Pluripotent Stem

Cells-derived MSCs Facilitate Cutaneous Wound Healing by Promoting Collagen Synthesis and Angiogenesis." *Journal of Translational Medicine*, vol. 13, no. 1, Feb. 2015, <https://doi.org/10.1186/s12967-015-0417-0>.

(2) This research paper focuses on exosomes derived from human induced pluripotent stem cell-derived mesenchymal stem cells (hiPSC-MSC-Exos) in the context of wound healing on the skin. It examines how these exosomes help the tissue heal especially in the context of collagen synthesis and angiogenesis. The authors found that these exosomes



have positive effects and accelerate the wound healing process. (3) The main aim of this research paper is to investigate the benefits of these exosomes when used for wound healing. The researchers especially monitored collagen synthesis and angiogenesis. An animal model was used in this case a rat wound model to conduct their experiment. Researchers also simultaneously conducted in vitro experiments to further investigate the proliferation, migration, collagen secretion from the fibroblasts and the endothelial cells that these exosomes stimulate. (4) The scope of this research is specifically on the application of hiPSC-MSC-Exos for wound healing on the skin. They used human fibroblasts, umbilical vein endothelial cells (HUVECs), and a rat model. These models are studied as they are very similar to actual cutaneous wounds so they can produce better data if studied. The collagen production, fibroblast migration and angiogenesis is monitored as the main sources of data. (5) The findings from these articles are very useful and introduce a new method and context of using hiPSC-MSC-Exos. In this study especially the authors focus on using these exosomes to produce collagen synthesis. This part about collagen synthesis was one of the most surprising as this can easily be translated into many other contexts. A lot of the aging in our body occurs due to the weakening of collagen, so the findings from this study could open a lot of doors to different applications of the hiPSC-MSC-Exos. (6) A key limitation of the study is the limited number of trials done in vivo on humans. Though they do some in vitro experiments with human models they mainly focus on the animal rat model; this may not fully translate into human physiology. Moreover, the study does not talk about the long term effects the exosome therapy had on the models. Finally there is no investigation how different sources or batches of stems cells could affect the exosomes effectiveness. (7)

The study's final finding is that these hiPSC-MSC-Exos help significantly with wound healing by promoting collagen synthesis and angiogenesis, This information is very important to me as it highlights new and different ways that these exosomes can be used and the potential things they could be applied. Specifically, I want to focus on using these exosomes for the process of collagen synthesis. As I stated before collagen is a major part of our body that deteriorates over time which causes a lot of aging. By using this research and with my findings from other stem cell therapies I could try to help[ improve my project and create a better outcome. (8) Finally, I want to say that the information in this research paper is highly relevant to my research project and my learning. The findings and results from this paper are things that I found very surprising and motivating, as they helped deepen my understanding of regenerative medicine and other therapies for wound healing. The focus on exosome therapy, in particular, directly aligns with my topic and has helped guide me in planning my research paper. It has also helped me determine exactly what I want to do for my research project this year.