EXAMINATION OF THE ETHICAL IMPACTS ON RESOURCE ALLOCATION TO ORGANOID AND ADULT STEM CELL RESEARCH

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On my honor as a University Student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments

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INTRODUCTION

Organoids are three-dimensional tissue constructs derived from stem cells that have the ability to replicate both the functional and structural properties of in vivo human organs (de Souza, 2018). Organoids are primarily made from embryonic stem cells (ESCs), as opposed to adult stem cells (ASCs), because of ESC's pluripotency or ability to differentiate into any cell type, thus giving organoids potentially endless applications (De Los Angeles et al., 2015). The benefits of using ESCs do not come without some consequences as the harvesting of ESCs is seen as ethically concerning, particularly when compared to ASCs. The harvesting of ESCs is seen by some groups, particularly religious organizations, as the ending of a human life, leading to the controversy surrounding organoid research (Mollaki, 2021). Conversely, ASC harvesting is not ethically concerning as the process just involves taking out blood, separating the stem cells, and then returning the blood, thus not involving embryos or what can be seen as human lives (Schreml et al., 2009).

A possible result of this difference that will be investigated in this paper is that these ethical concerns involved in ESC harvesting lead to more resources being allocated to ASC research than to organoid or ESC research, despite the theoretically greater potential of ESCs and organoids. Through this concept, the question of how have the ethical concerns involved in organoid research impacted the development of organoids as a technology through the vector of investment and resource allocation to ASC and organoid research will be investigated throughout this paper. To better grasp these interactions, this topic will be investigated through the use of the social construction of technology (SCOT) framework, initially pioneered by Trevor Pinch and Wiebe Bijker in 1984 (Pinch & Bijker, 1984). This framework suggests the idea that technology and society are not separate entities, but instead influence the development of each other.

BACKGROUND AND SIGNIFICANCE

Human stem cells were first successfully collected in 1998, but the first derivation of these stem cells into organoids did not occur until 2009 when Sato et al. (2009) was able to derive an organoid by seeding a human stem cell into Matrigel, which is a gel made of proteins, laminin, and other growth factors. This research displayed a key factor in stem cell differentiation and therefore organoid derivation, that being the ability of hydrogels containing decellularized extracellular matrices to promote the differentiation of stem cells (Magno et al., 2020). As a result of this discovery, the field of organoid research has grown, with many different types of organoids being developed to mimic the function of different human organs. Since organoids have this ability to mimic in vivo organs, they have applications in the study of disease effects on human tissue, drug testing and development, molecular medicine, and even organ transplantation (De Souza, 2018). While ASCs have had a similar progression in terms of development up to this point, the fact that they cannot differentiate into any cell type limits their versatility and thus their applications in the medical field in comparison to ESCs and organoids.

The potential life-saving applications of organoids are what make this topic such a significant issue to investigate, as more investment could lead to treatments and cures for diseases that are currently untreatable. This results in conflict between the ethical concerns involved with organoids and its potentially live saving applications, leading to the questions: How can the benefits of organoids be realized while still remaining ethically sound? And is it worth sacrificing lives now for the potential of saving more lives later? These questions will be investigated in this paper in process of determining how the ethical concerns involved with organoids have impacted its development as a medical technology.

METHODOLOGY

The overarching question of this paper has been split into three parts, each with its own methodology of research. The first part is investigating whether there is a significant difference in the investment towards ASC research vs. organoid and ESC research. Since this question is predominately statistic-based, publicly available databases will be used to provide a baseline for the resource allocation between the two fields. The second part is determining whether the difference in resource allocation is due to the ethical concerns that are involved with organoid and ESC research. This question is more complex and there is currently not a lot of research done on the topic, therefore it requires more in-depth research, including both semi-structured interviews with medical investors as well as literature review on the development of the idea of "ethical investment". The purpose of these interviews will be to determine how much these investors take ethics into account when deciding on what fields of research to invest in. The final part is investigating how the investment difference between the two fields of research has translated into a difference in technological development, thus completing the question of how ethics can influence technological development. This question will be mainly answered through semi-structured interviews with researchers involved with stem cell research. These interviews will attempt to gain information of how members of these fields feel that the amount of investment they receive have helped or hindered their research progress and to gain quantitative information of how their technologies have developed. Some advanced analytics, such as Solow residuals, also have potential to be used as a quantitative answer to this question, although the details of their use in this context have yet to be completely realized.

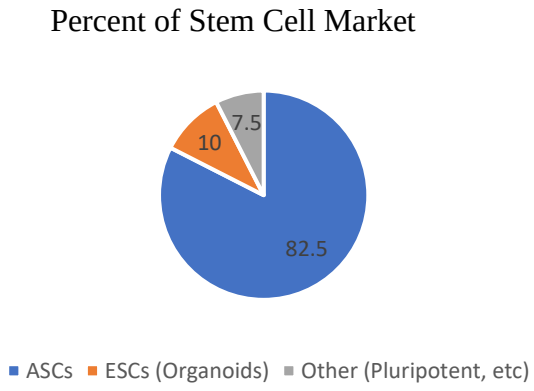
DISCUSSION AND RESULTS

Distribution of Investment in Stem Cell Research

Stem cell research is a rapidly growing field in the medical science community with a global market size of around $11.89 billion in 2021 (Grand View Research, 2021, p. 1). However, there is a significant disparity in how the market share of stem cells is distributed. Currently, as seen in Figure 1, 82.5% of the market is being allocated to research using ASCS, while only around 10% of the market has been allocated to research involving ESCs, which includes most of organoid research (Grand View Research, 2021, p. 2). While this data demonstrates the existence of a clear difference in resource allocation between ASCs and ESCs, it does not show that ethics are a significant factor in why this disparity exists. There are a variety of potential reasons to why there is a difference in investment, such as, ease of use, ease of acquisition, cost, ethics, etc. (Boffo & Patalano, 2020). The research shown in the next section aims show that the ethical concerns in ESC research are a significant factor in this discrepancy in investment between the two fields of research.

Figure 1

Distribution of Investment in Stem Cell Research (Hoffman 2023).



Impact of Ethical Concerns on the Discrepancy in Investment between ASCs and AECs

The concept of ethical investment has been gaining momentum over the last few decades as public views on ethics have changed. As of 2001, 13% of all investment dollars are going to ethical investment funds (Michelson et al., 2004), which is a value that has increased since then as society has evolved, up to potentially 33% as of 2020 according to Deborah Nanson of CNBC

(2020). This increase indicates that investors are beginning to take the ethics of what they are investing in into account more and more as indicated by this substantial and increasing percent of money being put into these ethical investment funds. While this provides some evidence to the idea that ethics have led to the difference in resource allocation between ASCs and ESCs, it is too general and does not outright prove that ethics is the main reasons behind the disparity in resource allocation. This also does not display the impact that this has had on the technological development of organoids. Through structured interviews with researchers and investors, this interaction will be further investigated.

To further show the impact that ethics has on the difference in investment between ASCs and ESCs, interviews were conducted with various researchers that use ESCs or organoids to gain a first-hand perspective on how they feel the ethical concerns have impacted the investment they have received for their research. Each of the researchers was asked the same questions for the investment portion of the interview, those being: Question 1: To what extent do you think embryonic stem cells pose significant ethical concerns? Question 2: To what extent do you feel that your research has received less investment as a result of ethical concerns? Question 3: To what extent do you feel that your field as a whole has lost potential investment as a result of ethical concerns? There are a few disclaimers to this data: All researchers were from UVA, all of the interviews are not complete yet so the dataset is still small (10 researchers so far) but will be filled out overt time as more and more interviews are completed (goal of 25 interviews), and the researchers are likely biased towards saying that they should have more investment and this may skew the data. To help account for the last disclaimer, investors that invest in stem cell technology were also interviewed in order to get the perspective from other side of the situation and those

results are shown later in this section. The data from the researchers is shown in the tables below, all values are shown in percentages:

Table 1

Researcher Interviewer Data for Investment Discrepancy

	None	Low	Medium	High
Q1	0	20	70	10
Q2	20	10	40	30
Q3	0	30	20	50

As mentioned earlier, this data is inherently biased since the researchers will most likely tend to believe that they are not receiving as much investment into their research as they believe they should be. To attempt to remedy this bias, investors in the field of stem cells were also interviewed to see how they view ethics when choosing whether or not to invest in a research project or technology. Each investor was asked the same questions for the investment portion of the interview, those being: Question 1: To what extent do you think embryonic stem cells pose significant ethical concerns? Question 2: To what extent do you take ethics into account when choosing whether or not to invest in stem cell research? Question 3: To what extent do you think others in your profession take ethics into account when choosing whether or not to invest in stem cell research? As before, there are some disclaimers with this data, the first being that like with the researcher interviews, this dataset is still small (7 investors so far) as not all the interviews have been completed, but there should be 15-20 total interviews by the end. All of the investors were also from the Virginia area, so it is not completely representative of all investors. The investors answers may also be biased since they might not want to actually state that they don't take ethics into account when investing, which could give them a bad reputation in the eyes of the public. The data from these interviews is shown below, all values are in percentages:

Table 2

Investor Interview Data for Investment Discrepancy

	None	Low	Medium	High
Q1	0	29	42	29
Q2	0	14	57	29
Q3	0	14	57	29

Since the datasets for both of the interviews is so small, it is impossible to make an actual determination of the effect that the ethical concerns of ESCs have on investment decisions. However, based on the data displayed above, there seems to be a trend that both the researchers and investors believe that ethics have at least some impact on the amount of investment that ESC and organoid research are receiving. Both sets of data showed that a majority of investors and researchers believe that the ethical concerns involved with ESCs have a medium or high effect on the investment that is received. As described before, this data is far from complete and merely shows a possible trend for this subject. More interviews will need to be conducted in order to show significant results and future interviews will ASC researchers will also need to be completed in order to show contrast from the ESC researchers.

Ethical Impact on the Technological Development of Organoids/ESCs

With the seemingly present trend of ESCs and organoids receiving less investment as a result of ethical concerns, as discussed in the previous section, it is important to also investigate how this lack of investment has affected the technologies' development over time. To investigate the impact of ethics on technological development, the researchers that were interviewed for the previous section and said that they believed the ethical concerns with organoids had a medium to high effect on investment (7 of the 10 interviewed so far) were also asked a second series of questions regarding how the lower investment has impacted their ability to further the current state

of organoid technology. These questions were: Question 1: To what extent do you believe that the lack of investment that you have received as a result of ethical concerns has impacted your labs' ability to progress organoids as a technology? Question 2: To what extent do you believe that the universal development of organoids as a technology has been hindered by its ethical concerns and thus lower investment? Question 3: If possible, describe the specific ways that the lower investment has impacted your lab. The same disclaimers that were noted for the first set of researcher questions still apply to these questions and this data as a whole. The results from the first 2 questions are shown below, with all values being in rounded percents, and the responses to the final question will be discussed after.

Table 3

Researcher Interview Data for Impact on Technological Development

	None	Low	Medium	High
Q1	14	29	29	29
Q2	0	29	42	29

In regards to Question 3, a variety of answers were received from the researchers. The most common answer was that lower investment often leads to trials taking longer for reasons such as not having the highest tier equipment or needing to buy raw materials, which leads to advancements in the technology coming much slower than would happen with more investment. Overall, even though it is again impossible to make any concrete conclusions based on such a small dataset, the results do show a slight trend towards the lack of investment affecting how quickly organoids can develop as a technology, with 71% of the researchers believing that it has a medium to high impact on development.

While these interviews do show trends in how people in the field feel the ethics involved with organoids affect its development, they do not show any quantitative data on how much it

actually affects the development of organoids. Some methods of gaining quantitative data on technological progress such as Solow Residuals are being investigated for this topic to see if they can provide useful information on how ethics has impacted the technological development of organoids (Kenton, 2021). So far, no concrete data has been collected that is specifically related to this topic and thus cannot be used as evidence for the ethical considerations with organoids affecting or slowing the development of organoids as a technology. However, as more information comes out, Solow residuals and other similar analytics could prove to be a powerful indicator of the progress that organoids have made as a technology and the extent to which their ethical concerns have hindered this progress in comparison to ASCs.

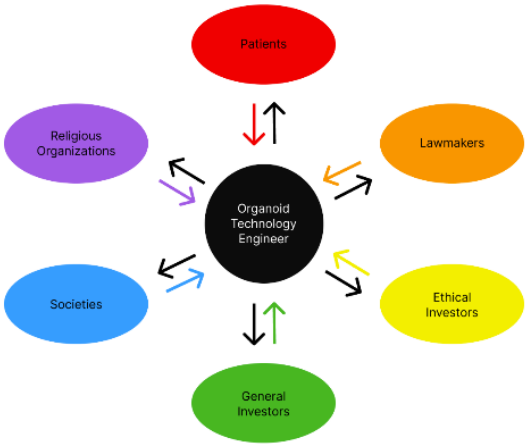
Viewing this Topic Through the SCOT Framework

The SCOT framework can be seen as a critique of the idea of technological determinism, which is the idea that technology and its development control how society progresses. Instead, SCOT argues that there is a more mutual relationship in which the societal factors and technology evolve together and each of their factors or innovations influences the progression of the other (Pinch & Bijker, 1984). This idea can be clearly seen in this topic, with the societal factor being ethics and the technology being organoids. Ethics are of course not the other social factor involved with organoid technology as there are a variety of different interactions that influence the development of both organoid technology and social factors as seen in Figure 2. As described in Johnson (2005), investment and resource allocation are some of the most recognizable and direct methods by which societal values can influence the development of a technology (p. 1793). When

a developing technology is endorsed by society it tends to receive a greater amount of investment from both private organizations and federal agencies. This increase in funding typically leads to greater rates of development of technology, as well as a higher chance of successful results (Johnson, 2005, p. 1793). This interaction is illustrated in the case of organoids as ESCs and organoids have not been completely endorsed by society because of the need to destroy human embryos in order to harvest the ESCs, thus making it unethical in some regards. As a result, these technologies tend to get less investment than they would otherwise get if not for the ethical concerns as displayed in the previous sections, which can thus lead to slower or different technological development as illustrated by the researchers' responses in the previous section. This chain represents the idea behind SCOT as the societal factor of ethics is controlling how the technology of organoids is able to develop instead of the reverse, as it would have in technological determinism.

Figure 2

Organoid research SCOT model. (Adapted by Hoffman (2022) from Carlson, 2008).



Note. This figure displays the influence that societal factors such as investment have on the development of organoid technology.

CONCLUSION

As a result of the incomplete data collection and thus small sample sizes from the interviews discussed in this paper, it is not possible to give a definite answer to the research question of this paper. However, the results still show a trend that not only is there a significant difference in the resource allocation between ASCs and ESCs/organoids, but that it seems like this difference is due at least in part due to the ethical concerns involved with ESCs and that this lower investment may have at least some effect on the speed at which organoids have developed

as a technology. This falls in line with the SCOT theory in which the social factor of ethics has influenced the development of technology, which in this case is the organoids, as opposed to the reverse. As these claims continue to be solidified through further research and interviews, the question then becomes: How do we allow organoids to get the investment needed for them to reach their potential as a potentially life-saving technology, while still maintaining ethics? This is an essential question because of the potential benefits that organoids have in the medical field. Since the ethical concerns with organoids come from the acquisition of ESCs, the change needs to be at that point in order to maintain functionality, while still making the technology more ethical. This would likely have to involve a new method of ESC farming that doesn't require actual human DNA so that the destruction of the embryo to acquire the stem cells could no longer be seen as the ending of a human life.

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