Potential Solutions to Organ Shortage for Solid Organ Transplantation

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Abstract: With advances in the medical industry, more treatments have been developed and improved time to time. One of which is called organ transplantation, the transplant of organ from a healthy recipient to a morbid patient, proofed to be efficient for many diseases like kidney failure, heart attack, skin burn and leukemia. While it is becoming more and more popular, the key problem, shortage of organs, unfolds and troubles people for decades. With some of today's technology, this problem is hoped to be dealt (at least released) by using hiPSC, xenotranplantation and mechanical organs.

1. Introduction

Since the first solid organ transplantation(SOT) was operated in 1954, Dr. Joseph Marry has opened a new horizon to treat patients who have organ failures. From the first case of the kidney transplantation, to lateral heart, pancreas, intestine, trachea and skin, organ transplantation technology has experienced many developments, achieved many improvements, and saved thousands of lives. However, an intricate challenge of the shortage of compatible organs and organ donors impedes the clinical success of this technique. Until February 2021, there are still more than 107,000 Americans on the waiting list for organ transplants, but only 39,000 cases were done in 2020[1]. Unfortunately, around 20 people died everyday for they did not receive organs needed in time[2]. This is due to the fact that most available organs come from living or dead people, and the condition of the organs donated needs to be estimated. For example, a donor's organ shown evidence of terminal cancer or strong immune responses with the organ recipient will not be considered for transplant. Meanwhile, ethical issues arise with organ donation: voluntary or monetary donation, people who have rights to sign the consent of organ donation, and whether the government can provide organs from prisoners who were executed, etc. Shortage of organs has always been a problem, thus new and effective solutions are urgently needed. So far, researchers have made progress on stem cell culturing (totipotent, pluripotent, multipotent), organ-split and organs from species besides human (xenotransplantation) that enable more available organs for urgent need. With the development of 3D printing, artificial organs would be another

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solution to cope with the dilemma.

2. Stem Cell Culturing-Solid Organ Transplantation

Stem cell culturing, a technology where the nonfunctional stem cell can be transformed into other types of cells to replace the existing abnormal cells, is an emerging technology that can customize organs by using the recipient's body cells. There are three types of stem cells: multipotent, the one found in organs that commonly replace the dysfunctioned cells in its family; pluripotent, the one found in human embryo that can convert to almost all cells; totipotent, where found similar with pluripotent, can be converted to cells of placenta especially. While multipotent used to repair a partial damage of an organ (e.g., bruise), pluripotent, especially a technology called human induced pluripotent stem cells therapy (hiPSC), is one hopeful solution to organ shortage. It works by extracting a skin cell from the recipient, adding four genes (Oct4, Sox2, c-Myc, Klf4) by using viruses or other methods, and reprogramming the cell back to a state of embryonic stem cell(ESC), and reconverting it back to needed cell types. Since its inception in 2007, the hiPSC technology has developed rapidly. With this technology, recipients can customize organs that their body would not reject. In addition to whole organs, organs parts such as cornea, trachea and bone marrow are customizable, which also helps patients with cataract, leukemia, diabetes and so forth. Besides, by customizing organs that show little or no immunoreaction to recipients, hiPSC can reduce the time recipients wait for an organ, thus less people will die on the waiting list.

Nonetheless, problems accompany with these attractive benefits. First, it is still expensive although cheaper than solid organ transplant. In general, it costs US $10,000–$25,000 to generate and validate a research grade hiPSC line[3]. Second, it is a blooming technology, meaning time must be waited before it can really apply to the public, otherwise potential and unknown complications or side-effects will emerge. Third, ethical problems occur. With the technology that can create a well-functioning organ with skin cells, people who have the access to do hiPSC may duplicate organs from their skin cells, selling them to the black market, and earning ignominious profits from it. As for career problems, if staff customized an organ with disorders, like the organ will be poorly oxygenated or can bring infectious disease to the recipient that lead to health-threatening conditions, it’s not likely for the recipient to replace his organ soon, since organs from hiPSC need to be cultured in weeks. Luckly, hiPSC will not be limited to only organ transplants, it can be utilized for other studies. For example, it can provide a tool for saving endangered species that are facing functional extinction, and instructional measures for teaching students processes of cell developments such as gastrulation and neurulation.All in all, hiPSC is facing an optimistic future, and hoping to benefit more people who need help.

3. Xenotransplantation-Solid Organ Transplantation

Other influential solutions like xenotransplantation are considered to be a possible treatment for body disorders and terminal organ failures. Xenotransplantation is a process that carries out organ transplantation by using organs from non-human beings. It directly solves the organ shortage problem due to many ideal animals which are suitable for transplantation.Pig, for example, a common livestock in people’s life, can be used for burned skin and kidney transplant. It has kidneys that are identical in size compared to human’s, and recipients with pig’s organs show least severe immune response among using other animal’s kidneys.Besides, using animal organs is much more affordable to more families. According to Caplan, operation price for a kidney transplant can be up to $400,000, $1.3 million for

heart transplant, and further mandatory medicines for counter rejection effect can take $2,500 monthly[3].Even the human skin graft with its procedures can cost up to $28,000[4]. Nevertheless, using pig's skin for skin graft can only take $400. Moreover, animal organs are so common. They are waited to be used anytime, which curtails the time an organ recipient waits, meaning less recipients will die on the waiting span.

However, xenotransplantation does have flaws. Although it deals with organ shortages, organs from animals cannot match an identical quality with organs from humans, which means that animal organs may have more drawbacks, such as limited endurance of the animal organ, serious immunoreaction in some cases that human organs do not have. Apart from this, a recipient with animal organs may have lethal inter-species diseases. Some monkey viruses-for example, herpes 8-are deadly to humans in a matter of days[5]. Meanwhile, animal organs can lead to moral and ethical issues. Bold xenotransplantation that causes severe complications would be an ethical problem. Recipient cannot survive, his family is unsatisfied, the surgeon and scientists' reputations are being questioned and the hospital will need to compensate for it. Although xenotransplantation is a revolutionary technology that seems applicable to current organ shortages, deeper efforts and practices have to be done to reduce the effect of drawbacks.

4. Mechanical Organs-Solid Organ Transplantation

Idea of using organs from other species brought insights of mechanical organs. One reason for organ failure is that the organ is aged, functioning inefficiently, but with mechanical organs, the body can function normally or even better than before. Since 1982, when Dr. Jarvik implanted an artificial heart (Jarvik-7) to a recipient and succeeded, using artificial organs has become a popular topic in bioengineering. By using non-flesh materials to build organs, the body's immune response can be reduced to a lower level. Milder or no rejection response means recipients do not need to take anti-rejection drugs after they finish implantation, lower risks of complications and possibility for death from counter-effect means the recipient will resuscitate and return to normal life quickly. Furthermore, it's cheap enough to save patients as much as possible. The average cost of an artificial organ is $20,000, and about 2% of Americans have an artificial organ or joint[6]. Apart from this, artificial organs can be saved under room temperature, which is different from organs from humans that need to be cared for meticulously under low temperature. This feature allows those artificial organs to be sent without a cold chain, so the expense on transportation is lowered, and unnecessary organ squandering can be avoided. They can even be stored in hospitals if the storage standard approaches required level. The most important thing is, the quality of such devices can be improved from time to time, providing better performance and greater safety.

But, it is absurd to assert that artificial organs are immortal, when they meet malfunctions, recipients have to go back to hospitals and places that have the ability to fix it. Since artificial organs will be a large market, means there will be many brands of artificial organs with slight differences in structures. If the recipient goes to a hospital with no ability to fix his device, he will be in a life-threatening moment, and very likely to die because of it, which brings high inconvenience. While using metal and other materials to build organs, this technology can be used to help people who have physical disabilities. For example, prosthesis, refers to an artificial limb which helped millions of people around the world who experienced limb loss. As a result, artificial organs are a blooming study with a copacetic future, flexible application and sizable population's benefits.

5. Conclusion

There are more possible solutions to organ shortages apart from these three. For example, the liver is the only organ that can regenerate, because it has a special protein called fibrinogen, which reacts with platelets. Reaction creates blood clot, and fibrinogen and platelets thus allow the regeneration process to go slowly. If scientists can gene edit a patient's DNA sequences to allow his organ probably "have" fibrinogens, or be compatible to fibrinogens and implant it from liver, it will allow patient's organs regenratable in most cases. However, there is one flaw with organ regeneration: the damaged organ must function normally before it is fully recovered. In liver's case, damaged organ can still function the way it did before it was damaged, but only the difference in efficacy before and during the regeneration; whereas if the heart is damaged and have to cut the damaged part off just like liver does, the heart might function abnormally. If the left side is cut off, then the cardiovascular muscle will not able to pump the blood into the pulmonary circulation, where the blood is being oxygenated and send oxygen throughout tissues and cells in the body. Therefore, it's necessary to later study which organs can be programmed to regeneratable. Additionally, one problem of xenotransplantation is minor qualities of animal organs. What if there is a batch of pig waiting for artificial selections? Gradually, those pigs will develop organs that are more compatible for implantation use under human factor.

By listed measures, organ shortage is hoped to become a less concerning problem. Without organ shortage, people on the waiting list will survive and return to normal life. Nevertheless, it's also necessary to notice the large population basis of organ recipients. Besides genetic issues they inherited that lead their organ failures, many causes are avoidable. In fact, diabetes is the most common cause of kidney failure in the United States. Currently, there are 34.2 million Americans, about 10.5% of the total population, either diagnosed or undiagnosed, are predicted to have diabetes [7]. If more people can have a better lifestyle and healthier diet, their body will be less likely to develop such diseases that cause organ failures, and further organ transplant. Conclusively, we are at a hopeful condition where organ transplant technology is growing rapidly, where more and more people will be saved and benefit from it. Not only will these technologies solve the current organ shortage, also can they improve health, and even lengthen the average life expectancy.

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