Creating human organs using stem cells

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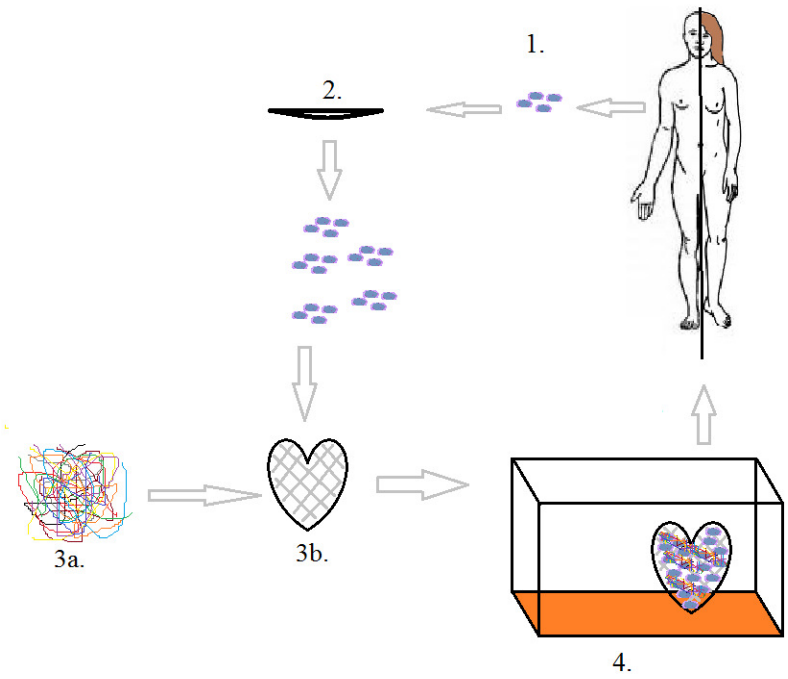
A lot of people are kept alive by machines or live a lower quality of life because they are in need of an organ, for example a heart. Because of the great need for these vital organs and the fact that organs need to match fairly well between donors and hosts there is a large shortage of these organs. There are animals that can regenerate entire limbs if they lose them. A salamander called axolotl (Ambystoma mexicanum) can even regenerate its brain or heart if half of it were to be damaged. So why cannot humans do this? The truth is we can, just not to the same extent as the axolotl. And that is what regenerative medicine revolves around. Researchers within this field try to find ways for humans to regenerate damaged tissue and organs so that we are independent of donated organs from fellow humans. Or if we cannot regenerate like the axolotl, at least we can create organs in labs by using your own stemcells. As fantastic as this subject seems, there are a lot of obstacles to overcome.

Introduction

When creating human organs there are a large variety of things that have to come together to finally produce the completed organ which is ready for transplant. First off all one needs a scaffold on which the cells of the organ-to-be are to be grown on. After that cells from the patient need to be harvested. Depending on which organ is trying to be engineered this is done by different means. More simple organs like the bladder allow for a biopsy to be taken and the uroteliala cells to be multiplied *in vitro*. However since the biopsy takes quite a big sample, roughly the since of a stamp, this cannot be done on for example an heart since this will cause significant, maybe even lethal, damage to the patient. In these cases stem cells are needed instead that can be differentiated into the desired cell type. When the scaffold and the cells are ready they are brought together in a bio chamber. The cells are applied to the scaffold by different means depending on the organ. Skin only requires cells to be grown in layers which is relatively easy compared to for example a highly vascularised organ like the heart or liver which require cells not only to be spread onto but also throughout the whole organ. This requires special demands on the scaffold like it being bio degradable and also highly vascularized. When the tissue that is being engineered is thicker than a centimetre or two, diffusion is not enough to keep the tissue oxygen rich. Even though the process sounds easy it is highly complicated and several obstacles exist. Cells do not always grow the way one wants and scaffolds do not fill all the criteria required. However considering the benefits in being able to create organs, the benefits outweigh the costs. In just the USA thirty million people suffer from liver disorders and 27,000 deaths occur every year. This is only from liver related disorders, if the other organs are also taken into account the number rises drastically. With this much loss not only in lives but in economic costs this is surely a science worth investing in.



The picture shows the principle of creating an organ and transplanting it to a patient. Cells are first harvested from the patient (1.) and the grown and manipulated *in vitro* (2.). Thereafter the now greatly increased number of cells are coated together with mechanical and molecular signaling (3a.) on the extracellular matrix (3b.). The scaffold with the seeded cells and signal molecules are placed in a bio chamber to allow growth (4.). Lastly the completed organ is transplanted into the patient.

Stem cells

There are different kinds of stem cells that are divided into two groups: the embryonic stem cells and the adult stem cells. The embryonic stem cells are too little surprise found in the early embryo. Adult stem cells can be harvested from three different parts of the body. These are the blood, bone marrow and adipose tissue. Adipose tissue are the fat cells of the body. The different stem cells differ in potency, meaning that they differ in how much they can differentiate. Totipotent cells have the highest ability of differentiation and can differentiate into any of the cell types in the organism. These cells are the result of a fusion between an egg and a sperm, but also the first rounds of cellular division result in totipotent cells. The totipotent stem cells give rise to the pluripotent stem cells. Pluripotent stem cells can differentiate into almost all the kinds of cells except for the extra embryonic tissue like the placenta. Pluripotent stem cells in turn give rise to multipotent stem cells. These stem cells can differentiate into only certain close family of cells. For example one has multipotent stem cells in the brain that produce only different types of neural cells. Since adult stem cells only produce limited types of cells they are considered multipotent. Multipotent stem cells can be found in most tissues in the body, repairing one or two particular organs.

Scaffold & Seeding

Creating the perfect scaffold that enables good adhesion possibilities and also a way to supply the tissue with oxygen and removing carbon dioxide and other cellular by-products is the ideal. Up until recently this was done by creating scaffolds of polyglycolic acid (PGA). For hollow organs like the bladder this is easy and works since you basically only need a ball to grow cells on but for complex vascularised organs like the liver this was done by 3D-printing. A 3D painting of a scaffold was created in a computer and then printed. To further improve scaffold adhesion and vascularisation researchers thought of already using live organs and taking their scaffold. Dead organs would be harvested and then rinsed of cellular matter by use of different chemicals. With all the cells gone all that was left was a clear supportive skeleton made of collagen and other proteins. Since the organ had been in a living creature before it already had the canals where blood vessels had been. This is a great advance since it allows for the use of organs that otherwise would be lost. If the patient dies and too long time passes without organs being harvested the organs themselves too die and go to waste. But with this method even the organs that would go to waste can be used. The scaffold is just recellurarized with the organ receivers own cells.

With a scaffold ready and cells harvested and multiplied the issue of distributing cells throughout the organ arose. When making bladders researchers would just pipette on cells onto the scaffold. But to create a solid organ like the liver 10^{11} cells have to be transferred throughout the organ. This presents a great challenge that is yet to be overcome. Attempts have been made were cells have been flushed through the scaffold vascular system and this has been successful with small animal organs like the rat liver. With human organs only smaller organoids have been created. More and more researchers are now following this procedure of seeding.

The number one obstacle with organ creation has been recellurarizing the organs since such a large quantity of cells need to be seeded throughout the scaffold. However other obstacles exist as well. Depending on which organ one is working with the cell type of that organ react differently. Liver cells for example do not grow that well *in vitro*. Other types of cells tend to change their morphology when grown *in vitro* which leads to them not adhering to the scaffold or other cells. Even though there are a lot of obstacles research has come far and when complete human organs are created they will be transplanted into humans without a chance of organ rejection since this will technically be one's own organ, only grown in the lab. This will not only save many human lives but also remove a great economic cost for the governments that decide to invest in this fantastic part of science.

"Never has there been a more exciting time to be involved in surgical science."
-Hollander et al. Regen Med 2009; 4: 147.

More information

If you have found this article interesting and you wish to find out more, then reading the essay "Framställning av mänskliga organ" by Dardan Konjusha can give further insight. Also Anthony Atala is one of the foremost regenerative medicine scientist out there so his work is very interesting.