Cutting out the middle man

Using transdifferentiation as a means of regenerating specific cell types.

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Stem cell research has been the cornerstone of scientific endeavors in a decade of history. Recently, scientists may have discovered a way to genuinely reprogram cells to serve an uncanny regenerative purpose. The purpose of this research was to find an alternative method of reprogramming cells so that any and all inconveniences during future procedures can be avoided. In a study recently published in the Proceedings of the National Academy of Sciences of the United States of America, Tanabe and colleagues (2018) explore the future possibility of reprogramming specific cells to change from one cell type to another, all whilst avoiding the unnecessary steps in between[1]. The regenerative applications that humans could harness go as far as possible treatments for several illnesses like liver disease or brain related diseases[2]. But first, we must first take a look at the history of transdifferentiation to understand its progression throughout the years.

One of the earliest applications of transdifferentiation was an experiment testing the role of laminin (a protein), and basement membrane that separates tissue during differentiation of endothelial cells to produce capillary like structures[3]. In 2004, scientists explored tissue plasticity in mice to see how transdifferentiation can be used to reverse engineer epithelial cells into adipocytes in the mammary gland and vice versa[4]. After 2010, there was a significant growth in differentiation research in humans and animals. Recently, scientists have been able to experiment with tumor cells and explore future therapeutic remedies that involve transdifferentiation of the tumor cells[5].

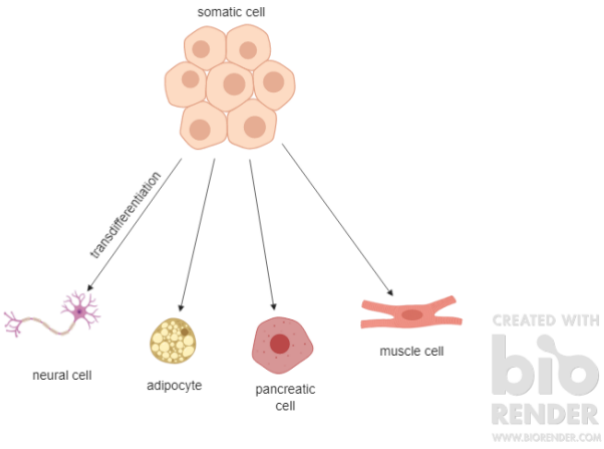

Figure 1. Potentials for transdifferentiation.

Tanabe and colleagues (2018) lab test the limits of transdifferentiation. Fibroblasts (a common cell type found in connective tissue) were obtained with a minimal invasive biopsy. One of the main tools used for inducing transdifferentiation to occur is CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats). CRISPR has the ability to silence specific genes and prevent them from expressing them ever again[6]. Due to their scarce supply and the amount of time needed to regenerate, neuronal cells are a huge target for transdifferentiation. Tanabe, et al., were able to execute an experiment in which peripheral blood cells could potentially be transdifferentiated into brain cells. They were able to accomplish this through centrifugation of

adult blood and introduced four DNA transcription factors by electrically stimulating the blood cells. These DNA transcription factors were transfected (injected into a eukaryotic cell), in order for transdifferentiation to occur[7].

The remarkable discovery that had been made in the Tanabe, et al., lab was that just from 1 mL of peripheral blood, greater than 50,000 brain cells were generated within one step. The brain cells that were generated from this experiment displayed great efficacy in firing action potentials and formation of fully-functional synapses. Other data that has been gathered was that these transdifferentiated brain cells derived from blood cells only obtain excitatory properties[1].

As a student of neuroscience, I find this type of research to be incredibly fascinating. The possibility to change the function of certain cells to do whatever we want seems like a dream. This type of research opens up so many new avenues in developing a treatment for terminal cases of cancer, and/or neurodegenerative diseases such as Alzheimer's, multiple sclerosis, and Parkinson's disease. There have been experiments that simply leave me dumbfounded such as using transdifferentiation to turn human dermal cells into viable skeletal muscle tissue[8], or transdifferentiating specific cells to attain an immune response to harmful foreign bacteria[9]. Regardless of the infinite possibilities in the realm of transdifferentiation, I think it's important to remember that this type of research is still in its premature phase, and that the likelihood of these procedures being conducted on the public anytime soon is very little. I believe that though this type of research is very interesting, there may also be risks involved. Recently in an article by Cohen (2018)[10], Dr. He Jiankui created the very first gene-manipulated babies (a set of twins) by using CRISPR to wipe out the genomic receptor for HIV in an attempt to make the fetuses resistant to the virus during their lifetime. This was countered with extreme backlash by the scientific community, and rightfully so in my opinion. There is still a lot we do not know about the future of transdifferentiation. There will have to be experiments that go throughout generations of offspring before we can even begin thinking about testing on humans.

If you took all of the knowledge that could possibly be collected about the human brain, and limited it so the length of one mile, it is in my humble opinion that we have achieved no further than 10 feet in that mile as scientists. I am very excited to learn more about this topic as it develops in the scientific community, and what treatments arise as a result of it.

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