

Induced Pluripotent Stem Cells—Bringing Humanity One Step Closer to Curing Cancer

ARTICLE INFORMATION

Received: 15 October 2019
Accepted: 10 November 2019
Published: 29 November 2019

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ABSTRACT

Cancer develops when healthy cells experience a mutation, allowing for rapid and abnormal growth. Mutagens, such as radiation and carcinogens, allow fast-growth variant cells to be positively selected and thus propagate the development of cancer. Radiation and chemotherapy are prevailing, but non-ideal forms of cancer treatment as they can harm healthy cells in the body. Stem cells can be used to replace the healthy cells that were lost, but there are ethical concerns regarding the acquisition of embryonic stem cells (ESCs), or technicalities in obtainment and usage of adult stem cells (ASCs). Thus, the discovery of induced pluripotent stem cells (iPSCs) allows for the use of ASCs that are given the pluripotent characteristics of ESCs. In 2018, Kooreman and his colleagues from Stanford University coaxed iPSCs to display the epitopes of breast cancer. After exposing mice with breast cancer to iPSCs, 70% of the mice had a decreased tumour size compared to control mice. Thus, iPSCs may work as a vaccine for cancer and potentially treat and cure the disease. Further research is required to study the feasibility of the use of iPSCs for human breast cancer.

Keywords: iPSCs, breast cancer, vaccine, adaptive immunity

When one thinks of a cure for cancer, one tends to imagine a miraculous medication discovered in an exotic rainforest or a unique concoction invented by a genius. What if a part of the answer was not as far as one tends to perceive it to be; what if the path towards a cure was right under one's nose in the form of stem cells? In order to harness the full potential of these cells, it is beneficial to first understand how cancer cells develop into a tumour.

Tumours are initiated by a genetic mutation that allows for the development of abnormal cells and rapid rates of cell division.¹ A mutation can occur randomly or can be induced by radiation or carcinogens that damage DNA.¹ Other carcinogens can be tumour promoters, like phorbol esters, which increase the rate of cell proliferation by activating proteins such as protein kinase C.¹ A tumour progresses as more mutations accumulate in the population of tumour cells. Some of these mutations may provide the selective advantage of faster growth to the cell and a possibility to invade nearby tissues.¹ From this, variants of a tumour are

grown which result in a transition from a benign to a malignant tumour, as the cells confined to its original location begin to invade surrounding tissue, representative of cancer.¹

Currently, chemotherapy and high doses of radiation therapy are used to target and eliminate cancerous cells.² A drawback of this treatment method is that some of the non-cancerous but rapidly dividing healthy cells are also eradicated in the treatment process. As such, both of these therapeutic options seem to be less desirable, especially chemotherapy, as the medicine may be ingested or administered intravenously and thus, has the potential to affect any cell in the body. For recovery from the loss of healthy cells in the body due to aforementioned treatments, stem cells are injected into a vein, allowing them to implant in the bone marrow to form blood cells and platelets.² Most stem cells are taken from the patient's bone marrow as these cells have a lower likelihood of being rejected by the body after transplantation.³ Unlike embryonic stem cells (ESCs), adult stem cells (ASCs) are

harder to isolate due to their scarcity and poor differentiation capacity.³ The lack of pluripotency of ASCs means that they cannot differentiate into multiple cell types. Although ESCs have more technical advantages than ASCs, they are not used due to the ethical concerns involved, such as the destruction of a potential human life and the infliction of pain to the embryo during this process. As such, ASCs are usually the default cells of choice.

To continue using ASCs while harvesting the advantages of ESCs, induced pluripotent stem cells (iPSCs) can be used for cancer treatment. iPSCs are formed through somatic cell nuclear transfer, in which three transcription factors that allow ESCs to be pluripotent are introduced to the nucleus of ASCs.⁴ iPSCs are useful as they can be used to battle cancer.

control group. Furthermore, two of the treated mice completely rejected breast cancer cells.⁵ Hence, it appears that iPSCs have a substantial likelihood of being able to prevent breast cancer in humans.

Overall, a cure for cancer may be closer than anticipated, as treatment techniques are currently exploring the use of induced pluripotent stem cells, reaping the benefits of both adult and embryonic stem cell characteristics. If so far, the use of these cells can evolve from controlling the repercussion of cancer to reducing its growth, it is only natural to wonder whether future developments in stem cell research hold the key to a cure for cancer. Future research should be directed towards determining whether it is feasible to use iPSCs for treating human breast cancer through the possibility of eventually administering clinical trials.

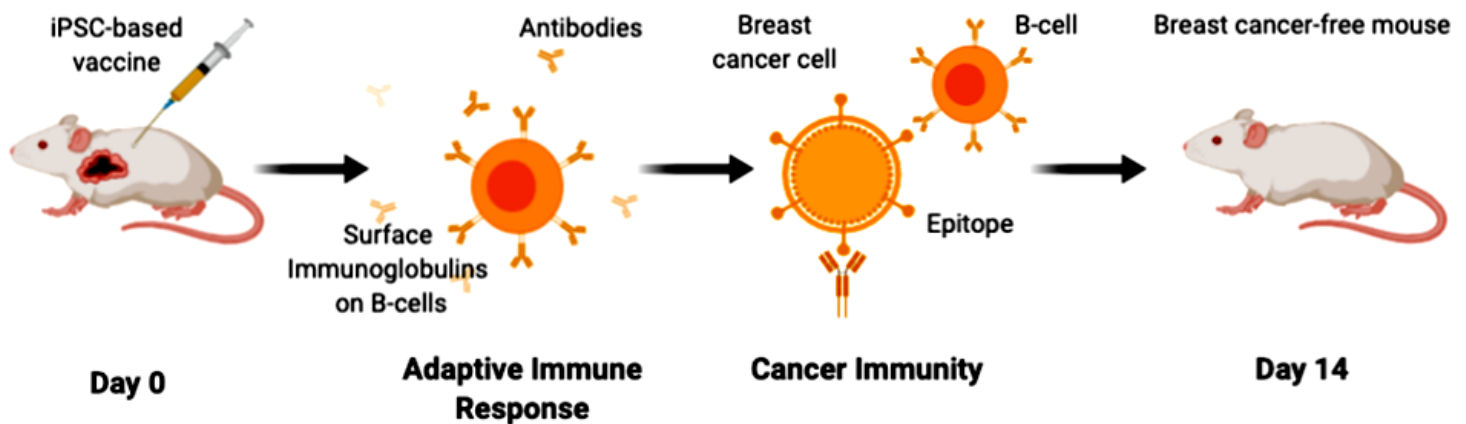


Figure 1. Overview of iPSC-mediated cancer treatment. The mice were injected with an iPSC-based vaccine. T-cell-activated B-cells from the immune system were exposed to the epitopes on iPSCs. This allowed them to recognize the same protein on cancer cells and reduce cancer growth over 14 days via memory-based mechanisms of adaptive immunity.⁵ Figure created using BioRender.

Using appropriate laboratory techniques, iPSCs can form a teratoma, which is a tumour composed of different cell types.⁵ As such, both iPSCs and cancer cells have the same protein on their surface, termed epitopes.⁵ These two characteristics of iPSCs can be used to develop a vaccine that will train the immune system to fight against cancerous cells.

Using this information, Kooreman and his colleagues from Stanford University used iPSCs to train the immune system of mice to attack tumours. This was done by introducing breast cancer cells in mice after the injection of iPSCs and an immune-stimulating agent called adjuvants (refer to Figure 1).⁵ iPSCs work as vaccines by exposing the adaptive immune system to antigens so that the body can prepare antibodies without the concomitant effect of the cancer cells. This leads to memory formation through effector B-cell and T-cell responses, which allows for the recognition of the antigen almost immediately upon exposure to a true cancer cell.⁵ After experimenting on mice, it was found that cancer in seven of the ten mice in the treatment group decreased in size when compared to the

ACKNOWLEDGEMENTS

This work did not receive funding. There are no conflicts of interests.

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