



## Magic at McMaster: Dr. Bhatia's discovery in turning human skin cells to blood cells

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"I didn't believe it. I thought it was another cell type masquerading as blood cells". That was Dr. Mick Bhatia's reaction when he saw blood cells in a Petri dish that had previously been skin cells about a month prior. (CTV.ca News staff, 2010). Scientific director of McMaster University's Stem Cell and Cancer Research Institute; Dr. Mick Bhatia and his team have discovered a process that involves turning skin cells directly into blood cells. The process was published in the science journal: Nature officially on November 7th, 2010 and has demonstrated groundbreaking potential.

Previously, the conversion from skin to blood involved converting the skin cells back to a pluripotent (or "stem cell") intermediate state, before they were differentiated into the desired cell type (in this case blood). Dr. Bhatia's method cuts out the middle step and skin cells are turned directly into blood cells, being: white blood cells, red blood cells or platelets. (Mark Curtis, 2010). In order to form the necessary blood progenitor cells, the gene OCT4 (stem cell gene related to development and pluripotency), is transcribed via ectopic expression (a method to determine the function of a certain gene) with the help of blood transcription factors. The gene can then be transcribed (hematopoietic) with the needed blood progenitor cells being formed during this process (Mark Curtis, 2010). Depending on the transcription factors, the process can be adjusted to form red blood cells, white blood cells, or platelets. So if a patient has anaemia and only needs red blood cells, or, if they have haemophilia, in which case they would need platelets for clotting, the process is tweaked and they have the specific blood cells that are needed. The skin cells used in Dr. Bhatia's research were taken from 6 different people, who's ages varied from a newborn to 80, and it was determined that age was not a factor; the skin cells were effectively converted to blood cells regardless (Sheryl Ubelacker, 2010). Once they were completely turned to blood, the cells were injected into lab mice and the effects were observed. This showed promising results, with no evidence of tumours or complications showing thus far.

There is a multitude of opportunities and advantages to Dr. Bhatia's discovery. The first and possibly most significant is the possibility for treatment of cancers like leukemia and other blood disorders. Normally, such patients have to wait for bone marrow and blood transplants, which in itself proves difficult. First of all, the donation has to be a match to the patient, often a deciding factor as patients may die waiting for a matching donor. Second, there is always a chance of the patient's body rejecting that blood or bone marrow. (Caroline Alphonso, 2010). Dr. Bhatia's method means that rather than waiting and hoping for a donor, a patient would have a small skin graft removed, which would be converted into blood. Furthermore, that blood is still genetically theirs, so there is no risk that their body will reject it.



The process also has the potential to improve therapy for cancer patients. During treatment, patients often have to withdraw from chemotherapy/radiation because it begins to destroy the blood system. During this break in treatment there is always the possibility that the carcinogenic cells could re-grow, often resistant to the chemotherapy. However, using Dr. Bhatia's discovery, the patient could have the necessary blood to continue their therapy without having to break in between; leaving less chance the cancerous cells will grow back.

The method is overall appealing and convenient because it skips the intermediate step of converting a cell to the pluripotent stage and then differentiating it to the necessary cell type. In the latter technique, turning skin cells into cells similar to embryonic stem cells often had the negative result of the formation of uncontrolled and cancerous tumours called teratomas, which are a group of carcinogenic cells that spontaneously differentiate into random cell types. (Mark Curtis, 2010).

Furthermore, when skin cells are converted to stem cells and then differentiated into blood cells, in patients with blood cancers/ disorders the genetic mutation that cause the disorder is often present in the stem cells and is being transferred back into their bodies. However, the mutation that causes, for example leukemia, is not present in the skin; therefore the blood that is created is clean and free of the genetic mutation (Caroline Alphonso, 2010). Similarly, only adult cells are produced in this process, unlike previously in which the pluripotent cells yielded fetal blood cells, which are inadequate for use in adults (Wade Hemsworth, 2010).

This is a convenient procedure patient wise as well, as small grafts of skin would be removed, grown in vitro, trans- differentiated into blood cells, and then transfused into the patient. Because the skin is converted into blood outside of the patient's body, if something were to go wrong in the process, it would go wrong while still in the test tube, which yields the opportunity for it to be fixed and the patient is left unharmed.

On another point, the detour around stem cells, while also avoiding the possible cancerous tumours that tend to develop, also remains less controversial than using embryonic stem cells. There are several ethical, political and religious issues that surround embryonic stem cell research and this process avoids the issue completely.

The possibilities for this system are not limited to just treatment of patients. Dr. Bhatia wants to do what he refers to as "a clinical trial in a dish" and use the created cells in order to test drugs which are still in the experimental stage (Sheryl Ubelacker, 2010). The potential also exists to freeze red blood cells and megakaryocytes (the cells in bone marrow that produce platelets) to be stored and then thawed when they are needed by a patient.

The process is still in the trial stage, however the results so far look promising, and without any major setbacks Dr. Bhatia would like to begin clinical trials in humans in 2012. In light of Dr. Bhatia's discovery the Canadian Cancer Society awarded him \$423 000 in order to further his research on the subject. (McMaster University Daily news, 2011) The goal is ultimately to upscale these results to create large amounts of blood that can be used in transfusions for cancer patients. Approximate calculations show that by taking a skin graft of about 3 by 4 centimetres, enough blood can be produced to do a full human transplant (Kerry Sheridan, Agence France-Presse, 2010).



As the process moves forward, the opportunities will as well; opportunities in treatment, research, and the possibility to create more than just blood cells. There is immense potential that could come from Dr. Bhatia's research, and it could surely save the lives of countless people, so it is for that reason that this truly is Canada's top biotechnology story of the year.



## Sources

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