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What Skin Cells Can Tell Us About Huntington's Disease

In the United States, 30,000 individuals currently suffer from Huntington's disease (HD), a neurodegenerative disease that is always lethal and causes death 15-20 years after diagnosis [1] [2] [3]. HD causes uncontrolled movements, cognitive impairment, and emotional problems [4]. Diagnosis typically occurs either in adulthood or childhood, depending on the type of genetic mutation involved [4]. Currently, treatments are limited and there is no cure.

But what if the key to treating HD could be found in the cells of our body?

Emerging research suggests that cells found in the dermis of our skin may have therapeutic potential for this devastating condition [5]. The specific cells are called fibroblasts and they normally function to make proteins like collagen, which give skin its elastic nature [6]. Unlike most cells, fibroblasts are unusually easy to grow in a petri dish in the lab, making them an ideal research tool.

But how can fibroblasts help with a brain disease? Huntington's disease is caused by a genetic mutation of a gene that is required in neurons; when this mutation is present it ultimately causes neurons to die [4]. It turns out that the fibroblasts in the dermis of a person with HD will carry the exact same genetic mutation. Therefore, by studying the fibroblasts from HD patients we can perhaps dissect the molecular mechanism of the HD mutation to learn how it destroys neurons. In addition to being easily grown in the lab, the ability of fibroblasts to model genetic mutations is another advantage of using these cells in research.

One way scientists are studying fibroblasts from HD patients involves the use of gene-editing techniques. Such techniques allow researchers to edit genes in different ways, most commonly by removing a gene altogether, changing its genetic sequence, or by turning it on. In the case of HD, gene-editing tools have been used to turn off the mutated gene in order to assess if limiting the function of the mutant gene in fibroblasts is possible [4].

Some gene-editing tools can be used to facilitate reprogramming of patient-derived fibroblasts to induced pluripotent stem cells (iPSCs), a type of artificially created stem cell that resembles embryonic stem cells [7]. These iPSCs can tell us a lot about disease pathology; there are established methods for inducing iPSCs to form neurons—meaning fibroblasts taken from a skin sample of an HD patient can ultimately show scientists how HD neurons are impaired [5]. This is a major advantage given that skin cells are easily obtained, whereas brain tissue from a live patient is obviously not. And because that fibroblast has the HD gene, the iPSCs and induced neurons will have it, too.

These induced neurons are similar to the neurons dying in HD patients. Therefore, induced neurons can help scientists develop treatments that will improve HD patient health. Treatments given to a HD patient should not put their neurons at additional risk, which makes knowing how a drug will affect neurons important. Studying the induced neurons' response to varying types and amounts of drugs, can help scientists determine if a drug is toxic and likely to kill the neurons in a HD patient's body. Using induced neurons to advance treatment options

does not have to be limited to drug testing outside the body, as these cells can potentially be a therapy injected back into the patient [5].

When a patient's own induced neurons are administered as a therapy it decreases the likelihood of death by host-graft rejection. Host-graft rejection occurs when the host's immune system has recognized the donor's cells as foreign invaders, which can lead to severe inflammation and prevent the body from working properly. Preventative measures for host-graft rejection are immunosuppressant drugs that leave the host more susceptible to life-threatening infections [7]. If induced neurons are injected into a HD patient, an immune response is less likely to occur because the induced neurons are not foreign invaders to the immune system.

Our body is programmed to defend itself against diseases. However, our body is not always successful in doing so when the disease is caused by a genetic mutation. It is truly remarkable that scientists can use skin cells themselves and ones reprogrammed to induced neurons to advance understanding on HD and develop treatments for patients with Huntington's disease.

References

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