

New study shows safer methods for stem cell culturing

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A new study led by researchers at The Scripps Research Institute (TSRI) and the University of California (UC), San Diego School of Medicine shows that certain stem cell culture methods are associated with increased DNA mutations. The study points researchers toward safer and more robust methods of growing stem cells to treat disease and injury.

"This is about quality control; we're making sure these cells are safe and effective," said Jeanne Loring, a professor of developmental neurobiology at TSRI and senior author of the study with Louise Laurent, assistant professor at UC San Diego.

Laurent added, "The processes used to maintain and expand stem cell cultures for cell replacement therapies needs to be improved, and the resulting cells carefully tested before use."

The findings were published February 25 in the open-access journal *PLOS ONE*.

Growing Stem Cells

Because these human stem cells, called "[pluripotent stem cells](#)," can differentiate into many types of cells, they could be key to reversing degenerative diseases, such as Parkinson's disease, or repairing injured tissue, such as cardiac muscle after a heart attack. Stem cells are relatively rare in the body, however, so researchers must culture them in

dishes.

While all cells run the risk of mutating when they divide, previous research from Loring and her colleagues suggested that stem cell culturing may select for mutations that favor faster cell growth and are sometimes associated with tumors.

"Most changes will not compromise the safety of the cells for therapy, but we need to monitor the cultures so that we know what sorts of changes take place," said the paper's first author Ibon Garitaonandia, a postdoctoral researcher working in Loring's lab at the time of the study.

How to Reduce Mutations

The new research shows how certain culture conditions can reduce mutations.

Loring and her colleagues tested different combinations of substrate (the layer that the stem cells grow on) and "passaging" methods, in which researchers divide up colonies of stem cells and transfer them to new culture dishes. Some substrates included "feeder" cells that provide growth factors, while others did not. Passaging was performed manually or with special enzymes.

The team cultured stem cells continuously for over almost three years and passaged them over 100 times. Over the course of the experiment, the cells were analyzed for mutations using a method to identify changes in the genome.

In the end, the researchers found the fewest mutations in [stem cells](#) grown on a feeder layer substrate with the manual passaging method.

The study also shows the importance of monitoring cell lines over time.

For example, one mutation that appeared was the deletion of TP53, a tumor suppressor gene whose absence is associated with cancer.

The take-home messages for scientists: "If you want to preserve the integrity of the genome, then grow your cells under those conditions with [feeder cells](#) and manual passaging," said Loring. "Also, analyze your cells—it's really easy."

Provided by The Scripps Research Institute

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