Novel surface triples stem-cell growth in culture

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By irradiating typical polystyrene lab plates with ultraviolet (UV) waves, Whitehead Institute and MIT scientists have created a surface capable of tripling the number of human embryonic stem (ES) and induced pluripotent stem (iPS) cells that can be grown in culture by current methods. Use of this novel surface also eliminates the need for layers of mouse "feeder cells" to support ES- and iPS-cell growth.

"Polystyrene is the most common cell culture surface used in labs, and to be able to do a simple treatment and get something that works better than the mouse feeder layers is great and potentially has a lot of utility," says Daniel Anderson, Associate Professor in the Harvard-MIT Division of Health Sciences & Technology.

The research is published online this week in the *Proceedings of the National Academy of Sciences* (*PNAS*).

The promise of ES and iPS cells lies in their ability to regenerate and to become almost any cell type in the body. By harnessing this ability, scientists can use ES and iPS cells to create cell lines that model difficult-to-study diseases, such as Parkinson's and Alzheimer's, and screen for potential drugs for these diseases. Also, researchers may one day manipulate iPS cells into therapeutic cells for transplantation into patients with diabetes, neurodegenerative diseases, and nerve or other tissue damage.

Some scientists estimate that such techniques would require millions or

even billions of cells, but current cell cultivation methods thwart efficient production of such mass quantities. Current approaches to cell culturing also rely on supportive mouse feeder cells, which can contaminate the stem cells by transferring viruses or macromolecules from the mouse cells to the human cells. The resulting cells would be deemed unsuitable for transplantation into humans.

To address both the bottleneck in stem cell cultivation and the potential risk for contamination, Krishanu Saha and Ying Mei, co-first authors of the PNAS paper, have been investigating what ES and iPS cells require to grow quickly on a lab plate. In a Nature Materials paper in 2010, Mei and Saha reported inducing significant increases in cell growth by using synthetic polymer substrates with high content of hydrocarbon and ester groups. Although successful, that process is less practical for large-scale production because the required polymers are difficult to synthesize in various cell culture formats.

"The last paper is trying to figure out what is the correct, optimum surface chemistry to support stem cells," says Mei, a research associate in the labs of Robert Langer and Daniel Anderson in MIT's chemical engineering department. "This paper says, with the knowledge we have about this optimal surface chemistry, what is the easiest way and the most reasonable, cost-effective way to generate this surface chemistry so we can make dishes efficiently grow stem cells."

In the current paper, Saha and Mei have taken an unconventional route to producing the ideal concentration of hydrocarbon and ester groups on the surface of the polystyrene plates—irradiating them with UV waves from a UV ozone unit in the MIT chemical engineering department. Saha and Mei found that a mere 2.5 minutes of UV irradiation produced the impressive growth rates in the absence of feeder cells.

"I think it's going to be a useful technique," says Saha, who is a

postdoctoral researcher in Whitehead Member Rudolf Jaenisch's lab. "There is a lot of push, at least in the field, to [eliminate animal products]. If you were one day to inject these cells into patients, you wouldn't have to worry about as many safety risks as if you had co-cultured them with animal cells."

More information: "Surface-engineered substrates for improved human pluripotent stem cell culture under fully defined conditions" *PNAS*, published online the week of Nov. 7, 2011.

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