UC SANTA BARBARA

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Keep the Lights On

Immortal in the lab, pluripotent stem cells divide and grow indefinitely under the right conditions. This ability may also exist further down the development path with the workhorse progenitor cells — the “sons and daughters” of stem cells responsible for creating specific tissues.

Now, stem cell pioneer James A. Thomson and his research team have discovered a way to impose an immortal-like state on mouse progenitor cells responsible for producing blood and vascular tissue. By regulating a small number of genes, the cells became “trapped” in a self-renewing state and capable of producing functional endothelial, blood and smooth muscle cells.

The findings, to be published in the Dec. 9, 2014, issue of Stem Cell Reports appear online today, point to a potential new approach to developing cells in the lab environment for use in drug screening and therapies and as a basic research tool.

“The biggest takeaway for me is the ability to arrest development of these cells,” said lead author David Vereide, a Morgridge fellow in regenerative biology. “Normally, these cells are ephemeral and get used up while differentiating into specific cell types, but we found a way to interrupt that.”

“It is possible we will find a variety of progenitor cells that intrinsically behave this way under the right conditions,” said Thomson, a professor in UC Santa Barbara’s Department of Molecular, Cellular and Developmental Biology and co-director of the campus’s Center for Stem Cell Biology and Engineering.

“This approach could have particular value for cell types that we are currently unable to maintain in culture,” he added. Thomson is also a professor at the University of Wisconsin-Madison (UWM) and director of regenerative biology at the Morgridge Institute for Research at UWM.

During development, blood and vascular cells are thought to originate from a progenitor cell known as a hemangioblast. Thomson’s research project identified and imposed six transcription factors on the cells that allowed hemangioblasts to continue proliferating over multiple generations. Transcription factors are proteins that regulate which genes get turned on or off in a genome.

In this case, the transcription factors act to “keep the lights on” in these cellular factories that kept them dividing and expanding, Vereide said.

One exciting element of this research, he continued, is it could greatly improve the efficiency of creating cell types that have research and therapeutic value. Progenitor cells are the end point in the production of the key building-block cells for the body — brain, vasculature, bone.

Embryonic stem cells are far removed from functional cell types, Vereide says. For example, when embryonic stem cells differentiate into a muscle cell or a neuron, they go through many steps over a period of several weeks to months and each step creates inefficiencies and the possibility of mutations.

“The value of having these culturable progenitors is you don’t have to go through all those steps, you are that much closer to the functional cell type that could have medical value,” Vereide said. “Instead of having 20 steps, you can have one or two. If you can cut back some of those steps, it becomes much more attractive for cell-based strategies.”

Vereide said this research offers “proof of principle” that the immortal-like state is not unique to stem cells. The next step will be to transition to human stem cells and to make progenitor cells that could have a variety of applications that advance human health.

Vereide expressed optimism that this same principle can be demonstrated in other cell types. “I’m hoping that other scientists who see this get inspired,” he said. “If you dig into the progenitor state of any tissue, you will probably find core factors that will drive the expansion of those progenitors in a dish.”

In addition to Thomson, other co-authors Vernella Vickerman, Scott Swanson, Li-Fang Chu and Brian McIntosh of the Morgridge Institute regenerative biology team.

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