Male germ cells can be directly converted into other cell types

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Veterinary biosciences professor Paul Cooke and doctoral student Liz Simon led a team that found that spermatagonial stem cells can be directly converted into other cell types. Credit: Photo by Diana Yates

Researchers have found a way to directly convert spermatogonial stem cells, the precursors of sperm cells, into tissues of the prostate, skin and uterus. Their approach, described this month in the journal *Stem Cells,* may prove to be an effective alternative to the medical use of embryonic stem cells.

The hunt for alternatives to embryonic stem cells has led to some promising yet problematic approaches, some of which involve

spermatagonial stem cells (SSCs). Researchers recently observed, for example, that SSCs grown in the laboratory will eventually give rise to a few cells that look and act like embryonic stem cells. This process can take months, however, and only a small percentage of the SSCs are converted into "embryonic stem-like" cells.

Other researchers have used viruses to insert genes into SSCs that will spur them to turn into ES-like cells. But this approach is problematic and the use of viruses to ferry in the needed genes has caused concern.

The new method, recently developed at the University of Illinois, takes advantage of the unusual interaction of two tissue types: the epithelium and the mesenchyme. The epithelium lines the cavities and surfaces of glands and many organs and secretes enzymes and other factors that are essential to the function of these tissues. The mesenchyme is the connective tissue in embryos. (In adults, the connective tissue is called stroma.)

In the 1950s, scientists discovered that the epithelium takes its developmental instructions from the mesenchyme. For example, when researchers put bladder epithelial cells on the mesenchyme of a prostate gland, the bladder cells were changed into prostatic epithelium. The prostatic mesenchyme had altered the fate of the bladder epithelium.

"The mesenchyme - it's the director; it's controlling the show," said University of Illinois veterinary biosciences professor Paul Cooke, who led the new study with postdoctoral researcher Liz Simon.

Cooke began the effort with what even he considered an unlikely proposition.

"Could we take spermatagonial stem cells and cause them to directly change into other cell types by putting them with various mesenchymes

and growing them in the body?" he said. "I thought it was possible, but I didn't think it would work."

The experiment did work, however. When Simon placed SSCs from inbred mice on prostate mesenchyme and grafted the combination into living mice, the SSCs became prostatic epithelium. When combined with skin mesenchyme and grown in vivo, the SSCs became skin epithelum. The researchers were even able to convert SSCs into uterine epithelium by using uterine mesenchyme.

The newly formed tissues had all the physical characteristics of prostate, skin or uterus, and produced the telltale markers of those tissue types, Cooke said. They also stopped looking and behaving like SSCs.

To assure that their tests were not contaminated with epithelial cells from the source of the mesenchyme cells, the researchers repeated the experiments using a mouse whose cells contained a gene that fluoresces green under ultraviolet light. The SSCs were obtained from a green-fluorescing mouse, but the mesenchyme came from a non-fluorescing mouse. This enabled the researchers to trace the fate of the SSCs. If the newly formed prostatic epithelium glowed green even though the mesenchyme did not, for example, the researchers knew that the SSCs had been converted into prostatic epithelium.

Cooke hopes that a more streamlined approach can be developed that makes use of a man's own SSCs and stroma (the adult equivalent of the mesenchyme) to produce new skin cells or other tissues when needed - for example, to replace skin damaged in a burn. And his team is investigating the use of ovarian stem cells instead of SSCs to see if the same results can be obtained with ovarian tissue.

Source: University of Illinois at Urbana-Champaign (news : web)

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