New cell line should accelerate embryonic stem cell research

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Dr. Carol Ware at work in her laboratory at the Institute for Stem Cell and Regenerative Medicine. Credit: Bryan Donohue

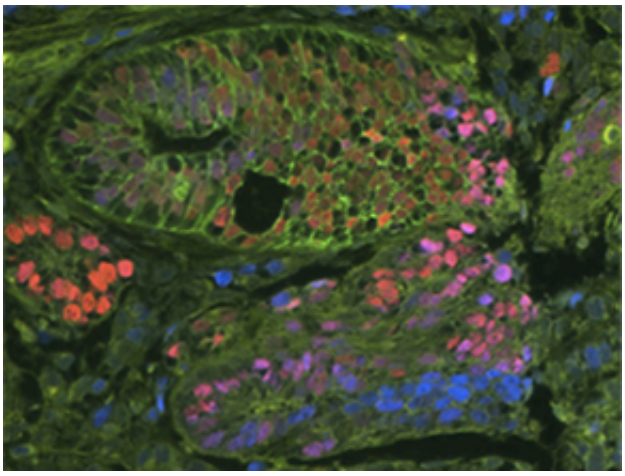
Researchers at the University of Washington have successfully created a line of human embryonic stem cells that have the ability to develop into a far broader range of tissues than most existing cell lines.

"These cells will allow us to gain a much greater understanding of normal embryonic development and have the real potential for use in developing ways to grow new tissues and organs for transplantation," said Carol Ware, a professor in the UW Department of Comparative Medicine and lead author of a paper describing the new cell line appearing in the March 10 issue of the journal *Proceedings of the National Academy of Sciences*.

The cells, called naïve embryonic stem cells, normally appear at the earliest stages of embryonic development and so retain the ability to differentiate in all the different types of cells of the human body—a capacity called pluripotency.

Researchers had been able to develop naive cells using mouse embryonic stem cells but to create naive human embryonic stem cells has required inserting a set of genes that force the cells to behave like naive cells.

While these "transgenic" cells are valuable research tools, the presence of the artificially introduced genes meant the cells will not develop as normal embryonic cells would nor could they be safely used to create tissues and organs for transplantation.



This tissue derived from the Elf1 cell line shows cells that typically develop into liver and pancreas cells. Credit: Vincenzo Cirulli

In an article, Ware and her colleagues from the UW Institute for Stem Cell and Regenerative Medicine describe how they successfully created a line of naive human embryonic stem cells without introducing an artificial set of genes.

They first took embryonic stem cells that are slightly more developed, called primed stem cells, and grew them in a medium that contained factors that switched them back—or "reverse toggled" them—to the naive state.

They then used the reverse toggled cells to develop a culture medium that would keep them in the naive state and create a stable cell line for study and research.

Then having worked out how to maintain the cells in the naive state, Ware and her colleagues harvested naive cells directly from donated human embryos and cultured them in the maintenance medium to see if they could create a stable cell line that had not undergone reverse toggling. After many tries, they succeeded.

While the "reverse toggled" cells are much easier to create and will prove valuable research tools, Ware said, the cells that were directly derived from embryos are the more important advance because they are more likely to behave, grow and develop as embryonic cells do in nature.

The new cell line is called Elf1: "El" for the Ellison Foundation, a major supporter of the lab's work; "f" for female, the sex of the stem cell; and "1" for first.