Stem cell 'immortality' gene found

18:28 30 May 2003
NewScientist.com news service
Shaoni Bhattacharya

The key gene that keeps embryonic stem cells in a state of youthful immortality has been discovered.

The breakthrough may one day contribute to turning ordinary adult cells into those with the properties of human ESCs. This would end the need to destroy embryos to harvest the cells for new medical treatments.

ESCs are unique as they are "pluripotent" - capable of differentiating into the different cells in the body - and hold great potential for treating damaged or diseased organs. But until now scientists did not know how a stem cell renews itself or develops into an new kind of cell.

The gene found in mouse ESCs and some human equivalents appears to be the "master gene", co-ordinating other genes to allow stem cells to multiply limitlessly while still retaining their ability to differentiate. It has been christened *Nanog* after the land in Celtic myth called Tir nan Og, whose inhabitants remain forever young.

"Nanog seems to be a master gene that makes ESCs grow in the laboratory," says Ian Chambers, one of the team at the Institute for Stem Cell Research (ISCR), Edinburgh, Scotland. "In effect this makes stem cells immortal."

"This discovery is very exciting," says Austin Smith, who led the ISCR team. "If *Nanog* has the same effect in humans as we have found in mice, this will be a key step in the developing embryonic stem cells for medical treatments."

Exclusive expression

Smith's team isolated *Nanog* by screening a DNA library of mouse ESCs and then carried out a series of experiments. Importantly, the master gene appears to be expressed in ESCs only, they say.

This discovery was also made independently by another team in Japan, led by Shinya Yamanaka, at the Nara Institute of Science and Technology. The Scottish and Japanese teams published side-by-side papers in the journal *Cell*.

In one experiment, the addition of *Nanog* prevented mouse ESCs from specialising, even though they were subjected to conditions under which they would normally have been forced to become a mature cell.

Nanog is likely to direct the process of ESCs renewing themselves by switching on and off other genes, says the team. The pattern of gene activity co-ordinated by this master gene is typically seen in human ESCs about the fourth or fifth day of development, when the cells have not yet been committed to becoming any particular type of cell.

No slave

However, it probably does not act alone, Smith told **New Scientist**. It is likely to act with another known key gene called *Oct4*. "But all the evidence indicates that *Nanog* is really a central player - it's not a slave, it's a master component," he says.

Smith cautions that reprogramming ordinary adult cells to become safe and usable ESCs is a long way off: "That's an aspiration and something we are keen to investigate, but it's not going to be simple."

He says a more immediate use of the key gene would be to enable the medical profession to grow "millions and billions" of ESCs from existing samples. These could then more safely be used in humans, as they would not have been exposed to the "cocktail" of chemicals currently needed.

Journal reference: *Cell* (vol 113, p 643)