'Rejuvenated' stem cells coaxed from centenarian

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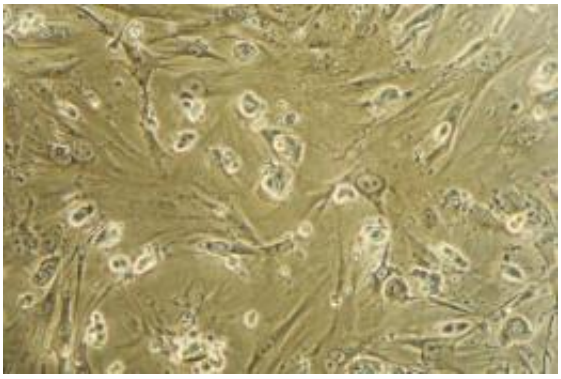

Embryonic stem cells are pictured through a microscope viewfinder in a laboratory, in 2008. Scientists said Tuesday they had transformed age-worn cells in people over 90 -- including a centenarian -- into rejuvenated stemcells that were "indistinguishable" from those found in embryos.

Scientists said Tuesday they had transformed age-worn cells in people over 90 -- including a centenarian -- into rejuvenated stemcells that were "indistinguishable" from those found in embryos.

The technical feat, reported in the peer-reviewed journal Genes & *Development*, opens a new path toward regenerative medicine, especially for the elderly, the researchers said.

"This is a new paradigm for cell rejuvenation," said Jean-Marc Lemaitre, a researcher at the Institute of Functional Genomics at the University of

Montpellier and the main architect of the study.

"The age of cells is definitely not a barrier to reprogramming," he told AFP by phone.

That human embryonic stem cells (ESC) can potentially become any type of cell in the body has long held out the tantalizing promise of diseased organs or tissue being repaired or replaced with healthy, lab-grown cells.

But the leap from theory to practice has proven difficult, and fraught with ethical and moral concerns because any such procedure requires the destruction of a human embryo.

The discovery in 2007 that it is possible to coax certain adult cells back into their immature, pre-specialised state has fuelled renewed efforts to generate brand new muscle, heart or even brain cells, this time from raw material provided by the patient.

Experiments to date, however, have shown that the usual chemical recipe for generating these so-called induced pluripotent stem cells (iPSC) works less well or not at all with the elderly and very elderly -- precisely the cohort with the most to gain from regenerative therapies.

The barrier was cellular senescence, a natural process linked to ageing that can trigger cell death when certain mechanisms within the cell become too degraded to function properly.

Lemaitre and colleagues decided to alter the standard genetic starter kit used to generate adult stemcells by adding two new ingredients -- known as transcription factors -- called NANOG and LIN28.

Experiments with human subjects ranging in age from 74 to 101 showed

that the new cocktail worked.

Several critical markers of ageing in cells were "reset", including the size of telomeres, the tiny protective caps found on the ends of chromosomes that wear down with age, the researchers reported.

Telomeres and telomerase, the enzyme that control them, are a key agent in longevity.

Every time a cell divides, the telomeres get worn down a little bit. The enzyme's job is to partially rebuild them. Eventually, when the telomeres are worn beyond repair, a cell dies.

Gene expression profiles, levels of oxidative stress, and the metabolism of the cell's energy-generating mitochondria were all likewise rejuvenated, according to the study.

"The age markers in the cell has been erased," said Lemaitre. "The iPSC stemcells we got can produce functional cells of all types with a capacity to proliferate and enhance longevity."

By reversing the age-altered physiology of the cells, he added, the new reprogramming technique "may constitute an optimal strategy for developing cell-based therapies for aged patients."

A large gap remains between this "proof-of-concept" study and therapeutic applications, the researchers cautioned.

And recent experiments with mice suggests that generating adult stemcells may yet face unexpected barriers.

Certain kinds of iPSC may be rejected by the immune system even if they are derived from the same organism, the experiments showed.

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