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Perspective

Induced pluripotent stem cells are induced pluripotent stem cell-like cells

Liting Song[1,✉], Emanuel Goldman[2]

[1]*Hope Biomedical Research, Toronto, ON M2K 2J8, Canada;*

[2]*Department of Microbiology and Molecular Genetics, New Jersey Medical School, Rutgers, The State University of New Jersey, Newark, NJ 07103, USA.*

Gold is rare and precious, while pyrite (FeS_2) is abundant and cheap. Pyrite is nicknamed fool's gold, since pyrite looks like gold and it is even shinier and brighter than gold. It is very difficult to recognize the differences between a real natural gold and a gold-like rock (pyrite) to non-professional persons[1], but we know that all that glitters is not gold.

Similar mistakes can happen in biomedical research as well. Pluripotent embryonic or adult stem cells can self-renew and proliferate into different cells, and these stem cells are very valuable in transplantation and gene therapy. Because the government of the United States of America and other governments have tight regulations restricting embryonic stem cell work, this has driven research towards finding stem cells from adult sources rather than embryos. Instead of acquiring useful adult stem cells from adult tissues, in recent years some researchers have claimed that they could magically turn adult somatic cells into induced pluripotent stem cells[2,3]. Is this real? Or is this too good to be true?

Dr. Liu has actively challenged the validity of the so-called induced pluripotent stem cells since 2008; he suspected that pre-existing adult stem cells might have played a vital and essential role in the process of producing those induced pluripotent stem cells[4]. It was later proven that only real adult stem cells (muse cells) can generate those claimed induced pluripotent stem cells[5,6]. Several research groups have found that those proclaimed induced stem cells had more abnormal chromosomes[7], more protein-coding point mutations[8], more abnormal epigenomic reprogramming and DNA methylation[9–11], and more copy number variations[12,13] than normal somatic cells or embryonic stem cells; those supposed induced pluripotent stem cells had more chances to develop tumors, and they could form tumors more rapidly than human embryonic stem cells[14]. Moreover, those hypothetical induced pluripotent stem cells caused more immune rejections in recipient mice than normal embryonic stem cells[15]. In comparison with normal embryonic stem cells, those so-called induced pluripotent stem cells had different metabolic activities[16,17]. In a major turn of events, the very same laboratory that pioneered these supposed stem cells has now reported that the believed human induced pluripotent stem cells were actually different from real human embryonic stem cells in several aspects[18].

Some researchers have claimed that they could produce mice from the putative induced pluripotent stem cells[19–22], but this is questionable. Rather, they caused confusion by using an inappropriate tetraploid complementation assay. They did not produce any mouse directly from those claimed induced pluripotent stem cells; instead, they injected those assumed induced pluripotent stem cells into a tetraploid blastocyst. Their experiments only can prove that the so-called induced pluripotent stem cells did not stop or interrupt an embryo from growing into a mouse. Therefore, those claims were misleading. It has been known since the early days of in vitro fertilization experiments that an in vitro fertilized egg can be transplanted into a womb

✉Corresponding author: Liting Song, Hope Biomedical Research, 809-50 Ruddington Drive, Toronto, ON M2K 2J8, Canada. Tel/Fax: 416-733-1573, E-mail: ltsong@yahoo.com.

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and grow into an animal or an infant[23]. Dolly the cloned sheep and several other cloned animal experiments proved that the genome of an adult cell can replace the genome of an egg, and develop into a viable animal if the egg is transplanted into an animal womb[24]. In order to prove that these putative pluripotent stem cells can generate a mouse, the researchers need to implant the putative induced pluripotent stem cells into the womb of a female mouse, and to see if indeed a mouse will grow.

It is now clear that the said human induced pluripotent stem cells (iPSCs) are not equal to human embryonic or adult stem cells. They should not have been misleadingly named induced pluripotent stem cells in the first place. To be scientifically correct, those assumed induced pluripotent stem cells should be redefined as induced pluripotent stem cell-like cells. It is not that difficult to make mutated cells from normal cells; but it is extremely hard to convert mutated/abnormal cells into normal cells; otherwise, cancer would not be a serious health problem, if we were able to treat those mutated cells efficiently and easily. We do not think that those so-called induced pluripotent stem cells will be a reliable and feasible source of stem cells for the foreseeable future. A large amount of money and extensive resources have been spent on the iPSCs research programs in the world already[25], but this is a wrong track which will never achieve our goals. This is the unfortunate consequence of politics driving the direction of research, when research on authentic stem cells would otherwise be preferable.

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