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Reprogrammed Cells: How Far Away from the Clinical Use?

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Currently, the discovery of Compounds induced Pluripotent Stem Cells (CiPSCs) and the Stimulus-Triggered Acquisition of Pluripotency (STAP) cells are rocking the field of stem cells [1].

In 1981, the first embryonic stem cells (ESCs) were first derived from mouse embryos by two groups respectively [2,3]. In 1998, a breakthrough occurred when Thomson group first developed a technique to isolate and grow human ESCs in cell culture [4]. The finding of ESCs, especially the human ESCs, brought the hope for the regeneration medicine. However, because of the ethic issues and potential xenograft rejection problems of human ESCs, it is very hard for the derivatives of human ESCs to go directly towards clinical application.

In 2006, Yamanaka group first showed a way of reprogramming mouse skin cells into pluripotent stem cells (induced Pluripotent Stem Cells, iPSCs) via defined transcription factors, which is a ground breakthrough in the stem cell field [5]. One year later, Yamanaka group and Thomson group successfully reprogrammed human tissues into iPSCs [6,7]. With the concept of reprogramming, more and more human somatic tissues were reprogrammed into iPSCs and adult stem cells, including Neural Stem Cells (NSCs). The somatic cell reprogrammed stem cells may potentially solve the ethic issues and the xenograft rejection problems caused by human ESCs derived cells for cell therapy, however, the traditional way of introducing reprogramming factors into somatic cells via lentivirus or retrovirus may bring another risk---tumor formation [8]. In order to overcome this problem, researchers developed several optimized approaches to reduce the risk of mutating genome, which include using plasmid DNA, RNA, RNA virus, and proteins [9-12]. In theory, after long-term passage or cellular metabolism, the induced exogenous factors could be completely removed from the cells; however, these methods are still not the best way to guarantee the safety of the introduced factors.

In front of us, it seems the better way is to find a method which could induce reprogramming without introducing any exogenous factors. In 2013, Deng group used a combination of several compounds to reprogram mouse somatic cells (both neonatal and adult) into iPSCs [3]. Right after the discovery, Obokata et al. reported a unique cellular reprogramming phenomenon, called Stilulus-Triggered Acquisition of Pluripotency (STAP), which requires neither nuclear transfer nor the introduction of transcription factors (Obokata et al., 2014). Unfortunately, it looks this method has a hard time to convert adult somatic cells. Although neither of these two factor-free methods showed any successful case in human tissues, we can believe it is a fundamental step and great advance towards the clinical use of these reprogrammed cells.

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