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A Cell Electrofusion Chip for Somatic Cells Reprogramming

Wei Wu[1,2], Ya Qu[1,2☯], Ning Hu[2,3☯], Yuxiao Zeng[1,2], Jun Yang[2,3], Haiwei Xu[1,2]*, Zheng Qin Yin[1,2]*

1 Southwest Eye Hospital, Southwest Hospital, Third Military Medical University, Chongqing, P.R. China,
2 Key Lab of Visual Damage and Regeneration & Restoration of Chongqing, Chongqing, P.R. China,
3 Bioengineering College of Chongqing University, Chongqing, P.R. China

☯ These authors contributed equally to this work.
* haiweixu2001@163.com (HX); qinzyin@aliyun.com (ZQY)

Abstract

Cell fusion is a potent approach to explore the mechanisms of somatic cells reprogramming. However, previous fusion methods, such as polyethylene glycol (PEG) mediated cell fusion, are often limited by poor fusion yields. In this study, we developed a simplified cell electrofusion chip, which was based on a micro-cavity/ discrete microelectrode structure to improve the fusion efficiency and to reduce multi-cell electrofusion. Using this chip, we could efficiently fuse NIH3T3 cells and mouse embryonic stem cells (mESCs) to induce somatic cells reprogramming. We also found that fused cells demethylated gradually and 5-hydroxymethylcytosine (5hmC) was involved in the demethylation during the reprogramming. Thus, the cell electrofusion chip would facilitate reprogramming mechanisms research by improving efficiency of cell fusion and reducing workloads.

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Introduction

Differentiated somatic cells can be reprogrammed into pluripotent stem cells by nuclear transfer into enucleated oocytes [1], co-culture with stem cell extract [2], transcription factor transduction [3] or by cell fusion [4], which has a great prospect in regenerative medicine. Through years of researches, it is shown that reprogramming is influenced by the DNA methylation status [4–6]. Ten-Eleven Translocation (TET) enzymes can convert 5-methylcytosine (5mC) to 5hmC or further oxidize 5hmC to 5-formylcytosine (5fC) and 5-carboxylcytosine (5caC) [7–9]. 5hmC, which is a new epigenetic marker, plays a crucial role in DNA demethylation [10, 11]. To advance the clinical application of induced pluripotent stem cells (iPSCs) and further elucidate reprogramming mechanisms, a multitude of studies focus on enhancing reprogramming efficiency and speed. Cell fusion has been demonstrated to be a potent way of illuminating the mechanisms of somatic cells reprogramming due to its high efficiency and celerity [12]. Although PEG is notoriously inefficient and toxic [13], it is still the most commonly utilized cell fusion reagent to study reprogramming mechanisms because PEG is easy-to-get. Besides, traditional electrofusion method is also applied in reprogramming research occasionally [14,