

# Induced-pluripotent stem cells seeded acellular peripheral nerve graft as “autologous nerve graft”

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## ABSTRACT

**The hypothesis is that induced pluripotent stem cells (iPSC) derived Schwann cells and/or macrophages can be transplanted into acellular nerve graft in repairing injured nervous system. The efficiency of iPSC seeded acellular nerve graft may mimic the autologous peripheral nerve graft.**

**Keywords:** Induced-Pluripotent Stem Cells, Peripheral Nerve Graft; Axon Regeneration

## 1. INTRODUCTION

Brain and spinal cord injury conditions are non-reversible and current therapies are quite limited. Biomaterial transplantation, especially when combined with stem cell technology, provides one of the most attractive solutions to repair the injured nervous system, for both central and peripheral. Available biomaterials include natural sourced materials such as nerve, muscle, tendon, vein, fibronectin, collagen as well as fibronectin, and synthetic/engineered materials, such as poly-lactic acid, nanofiber scaffold, biodegradable glass and silicon [1]. However, with more than a century's laboratory and clinical trials, peripheral nerve graft is still the “gold standard”, and autologous peripheral nerve graft provided the best axonal regeneration among all these materials.

One existing problem in using peripheral nerve graft to repair the injured nerves is that the obtain of an autologous nerve graft lead to loss of sensory innervation in part of the body, while non-autologous nerve graft though is non-invasive, is of immunogen reactivity and could be expelled. The immunogenic problem could be solved with prior treatment with chemical, thermal, or liquid nitrogen freezing procedures to make the peripheral nerve graft be acellular. However the acellular grafts lost Schwann cells inside and the extracellular matrix suffers from somewhat disruption. Additionally, the acellular graft is not totally free of immunogenic activity due to the existence of non-degraded proteins [2].

## 2. THE HYPOTHESIS

We propose that the recent developed induced pluripotent stem cell (iPSC) technology combined with acellular nerve graft transplantation can provide a novel approach to repair the injured nervous system. The iPSC-seeded acellular nerve graft from other individuals can be functional similar to the autologous nerve grafts.

The induced pluripotent stem cells, genetically reprogrammed from any somatic cells can be theoretically promoted into any kinds of cells [3,4,5], including Schwann cells and macrophages. We propose that the iPSC could be generated from somatic cells of the patients, and induced into Schwann cells and macrophages before co-transplantation into the acellular allografts or even xenografts. The Schwann cell in the graft has long been found to be neuroprotective and enhancing the axonal remyelination; while macrophage can efficiently remove the remnant proteins and could be helpful in reconstructing the fine structures of extracellular matrix. During the induction of pluripotency, some further genetic modifications could be included, such as the expression of trophic factors to enhance the nerve regrowth.

## 3. TESTING THE HYPOTHESIS

It is necessary to induce iPSCs into Schwann cells and macrophages. Then the induced cells can be seeded into acellular nerve graft, potentially autologous at first, to examine their efficiency in mimicking natural and autologous Schwann cells when myelinate the regenerated nerves. With these experiences, allografts and xenografts could be tested. Finally this may bring a new avenue in clinical nerve repair procedures with ethical regulations if any are met.

## REFERENCES

- [1] Schmidt, C.E. and Leach, J.B. (2003) Neural tissue engineering: strategies for repair and regeneration. *Annu Rev Biomed Eng.*, **5**, 293-347.
- [2] Gulati, A.K. and Cole, G.P. (1994) Immuno-

- genicity and regenerative potential of acellular nerve allografts to repair peripheral nerve in rats and rabbits. *Acta Neurochir (Wien)*, **126(2-4)**, 158-64.
- [3] Yu, J. and Vodyanik, M.A., Smuga-Otto, K., Antosiewicz-Bourget, J., Frane, J.L., Tian, S., *et al.* (2007) Induced pluripotent stem cell lines derived from human somatic cells. *Science*, **318(5858)**, 1917-20.
- [4] Takahashi, K., Tanabe, K., Ohnuki, M., Narita, M., Ichisaka, T., Tomoda, K., *et al.* (2007) Induction of pluripotent stem cells from adult human fibroblasts by defined factors. *Cell*, **131(5)**, 861-72.
- [5] Takahashi, K. and Yamanaka, S. (2006) Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. *Cell*, **126(4)**, 663-76.