Skin versus nerve as a source of cells for the treatment of spinal cord injury

Following injury to the adult human spinal cord spontaneous repair processes fail resulting in life-long functional deficits below the level of injury, which can include paralysis, absent or abnormal sensory perception, chronic pain, and diminished cardiovascular, respiratory, bowel and/or bladder function. This loss of function can be quite severe, particularly in cases of high cervical (i.e., neck-level) injuries that impact lung function, such as that suffered by Christopher Reeve, which are life threatening in the absence of immediate medical intervention. Although considerable advances have been made in the management of spinal cord injury, at present there is no effective therapeutic intervention for reversing the loss of function caused by such injuries.

The transplantation of Schwann cells has emerged as one promising treatment strategy for spinal cord injury based largely on evidence that these cells promote functional recovery in a wide variety of animal models. These cells can be harvested from adults for ‘autologous’ transplantation, which means that a patient’s own cells can be harvested for transplantation, thereby eliminating the need to use harmful immunosuppressive drugs to prevent the rejection of transplanted cells, and unlike some other autologous cellular therapies (e.g., induced pluripotent stem cells), Schwann cells have a very low risk of forming tumors. There are however, drawbacks to the use of autologous human Schwann cells, as those cells are typically harvested from a peripheral nerve (i.e., the sural nerve) in the lower leg, resulting in permanent nerve injury that is associated with a loss of sensation in that region and a risk of developing chronic pain. Those issues may go unnoticed in people who lack lower limb sensation, but not all individuals with spinal cord injury have such deficits, and successful treatment may return sensation for those who do.

In light of those concerns, skin-derived precursors represent an attractive alternative source of Schwann cells (SKP-SCs) for future clinical application. The harvest of these cells involves a simple skin biopsy, which carries no risk of permanent functional deficits and could be performed during spine stabilization surgery (routinely performed after spinal cord injury), thereby avoiding an additional nerve excision surgery. Previously we showed that SKP-SCs promote functional recovery after delayed transplantation in rats with complete thoracic (lower back) spinal cord injuries. In the present work we expanded on our earlier findings considerably, by directly comparing the transplantation of Schwann cells generated from skin and nerve following a partial crush injury to the cervical spinal cord in the rat. Our results demonstrated that rats treated with Schwann cells from either source showed improved functional recovery compared to animals receiving injections without cells or with other skin cells (‘fibroblasts’), and those effects were associated with changes in the spinal cord caused by the transplanted cells. Thus, for the first time we showed that the transplantation of SKP-SCs promotes repair and functional recovery after incomplete cervical spinal cord injury, that Schwann cells from skin or nerve were both preferable to other skin cells for that purpose, and that Schwann cells from either source were equally effective as a therapy for cervical injury. These findings were very encouraging, as even a small

gain in hand/arm function could profoundly improve the performance of routine daily activities and quality of life of people living with cervical spinal cord injury. Furthermore, our findings suggest that Schwann cells generated from skin are just as effective as those harvested from nerve as a therapy for spinal cord injury, which carries implications for ongoing and future clinical trials of Schwann cells in humans.

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Publication

Schwann cells generated from neonatal skin-derived precursors or neonatal peripheral nerve improve functional recovery after acute transplantation into the partially injured cervical spinal cord of the rat.
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