CHAPTER 2

STEM CELL BASED STRATEGIES FOR SPINAL CORD INJURY REPAIR

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Abstract: As our understanding and ability to direct the differentiation of stem cells grows, specific targets and strategies to incorporate them are essential to define. Any cell-based transplantation strategy is fundamentally a combination therapy as either phenotypic or trophic mechanisms may contribute to functional recovery of the injured spinal cord. Both the transplant population as well as the recipient site will guide the growth factor expression profile and the phenotype of the transplanted cells. Although the use of high purity populations derived from stem cells will result in more regulated repair mechanisms, multiple challenges to the use of stem cell based strategies for SCI remain.

INTRODUCTION

Spinal cord injury (SCI) has been demonstrated to affect 15-40 persons per million population per annum in developed countries.1 More recent studies, such as that examining the incidence of SCI in all four branches of the United States Military between 2000-2009, revealed almost 6000 cases in a closed population of over 13 million.2 Another case series examined data about both spinal column and SCIs in mountain bikers around the Vancouver, B.C. area. They found 102 men and 5 women that fulfilled the inclusion criteria, with 64% sustaining cervical injuries and the remainder sustaining thoracic or lumbar injuries. Of that group, 40% sustained an SCI specifically. The mean age of patients at the injury was almost 33 years old. Again, young, physically active men were found to be more affected than any other group.3
None of these estimates of incidence, nor further risk factor characterization of the affected population, include SCI in under-developed nations. Undertaking a systematic survey of SCI in an impoverished nation such as Haiti, recently devastated by a large earthquake, would be not only difficult but a poor use of limited public health resources at this point in the country’s development. Nonetheless, one can conclude that the majority of persons with SCI are young active men, either at work or at play. Though the absolute number remains small, the toll on quality of life and cost to society in terms of additional care for the person and loss of productivity are huge. Investing resources in SCI should be a priority for society as a whole and especially for stem cell research, as the global pay-offs will be significant.

As the pathogenesis of SCI is described elsewhere in this text, this chapter will focus strictly on stem cell based strategies for spinal cord injury repair. It is widely accepted now that injury pathogenesis is a two-phase process: the primary event involves the deformation of tissue and the secondary event is a progressive degenerative cascade involving ongoing cellular damage and death, as well as axonal loss and demyelination.

Traditional medical approaches for SCI involve mainly symptomatic treatment and avoidance of further neurologic deficit. Most spine surgeons choose to decompress early (<24 hours), a procedure that will be proven to be useful or not useful by the ongoing Surgical Treatment of Acute Spinal Cord Injury Study (STASCIS). While these are extremely intensive and expensive surgeries, outcome measures center around length of stay in the hospital and number of days on the ventilator, as opposed to return of function. Rehabilitation services by physiatrists with aggressive physical and occupational therapy regimens also play a pivotal role, especially in the subacute phase after injury. Ultimately, palliative care physicians get involved when complications, especially for those with quadriplegia, present with insurmountable challenges such as fulminant pneumonia or sepsis from decubiti ulcers. The International Spinal Cord Society has partnered with the World Health Organization to bring further data on the needs of persons with SCI, with a view to providing improvements to their quality of life. A population once marginalized by the medical field is slowly being brought into mainstream medical care. A wiser use of resources would shift the focus of physicians and scientists toward neurologic functional recovery for the person with SCI.

CURRENT RESEARCH

Stem cell biology has boomed in both breadth and depth over the past decade. Stem cells are precursor cells with extensive renewal capacity and multi- or pluripotency. Newly identified techniques of stem cell purification and amplification permit the generation of large quantities of cells and cell products. This allows researchers to experiment with the control of proliferation, differentiation and survival, as well as investigate immunomodulation and regenerative potential of transplanted derivative populations.

iPS cells can be generated from human adult somatic tissues, most commonly fibroblasts, and carry the genetic makeup of the patient from which they were derived. They are most reliably induced by using viral-mediated transfection of transcription factors, namely Oct3/4, Sox2, c-Myc, and KLF4, to return the cells to an embryonic stem cell-like stage. Recently, Okano and colleagues demonstrated that purified mesenchymal stem cells are an efficient source for iPS cell induction. As human mesenchymal stem