Preface

The treatment of major peripheral nerve injuries represents a significant clinical challenge. Despite an intrinsic ability for regeneration in the peripheral nervous system (PNS), nerve gaps necessitate surgical repair with autologous nerve grafts. This gold-standard treatment has not been modified significantly since its routine introduction and, correspondingly, clinical outcomes remain poor. It has become clear that surgical reconstructions should be combined with novel therapies that address the problems of the limited rate and quantity of axonal regeneration, neuronal cell death and target organ atrophy. Advances in both basic neuroscience and translational medicine have highlighted that there is significant scope for the application of cellular and biological approaches towards peripheral nerve repair, the themes presented in this special topics issue of *Cells Tissues Organs*.

Schwann cells, the peripheral nerve glia, play an important role in axonal regeneration after peripheral nerve injury. In the first article, Namgung [this issue, pp. 6–12] details some of the signaling pathways underlying the remarkable plasticity of these cells and highlights how timely interaction between the Schwann cells and the axon is critical to achieving efficient axonal regeneration. However, chronically denervated Schwann cells lose their functional activity and ideally it would be possible to replace these host cells with exogenous regenerative cells. A number of different sources of stem/progenitor cells are being explored for their potential application in the treatment of peripheral nerve injuries. This special topics issue includes reviews about skin-derived precursor cells by Grochmal and Midha [this issue, pp. 13–22], adipose tissue-derived stem cells by Kingham et al. [pp. 23–30], mesenchymal stem cells by Wakao et al. [pp. 31–41] and hair follicle-accessible pluripotent stem cells contributed by Hoffman [pp. 42–47]. Each of these stem cells has been shown to differentiate towards glial cell phenotypes, produce significant quantities of neurotrophic factors and have efficacy in animal models of peripheral nerve injury.

Therapeutic cell transplantation also requires the development of suitable scaffold constructs which can support their integration into the nervous system. In an original article, Uemura et al. [this issue, pp. 78–91] describe the long-term efficacy and safety outcomes of the transplantation of induced pluripotent stem cell-derived neurospheres within bioabsorbable nerve conduits. An alternative to stem cells is to use other native neural supporting cells. Radkte and Kocsis [this issue, pp. 48–58] review recent advances in work indicating that olfactory ensheathing cells, specialized glial cells within the olfactory system, can contribute to neural repair after peripheral nerve injury.

The growth-promoting properties of Schwann cells can be counteracted by injury-induced upregulation of axon growth-inhibiting molecules. Although more commonly studied in the central nervous system, chondroitin sulfate proteoglycans are potent inhibitors of neural regeneration in the PNS. The use of chondroitinase ABC, an enzyme capable of digesting these molecules, as a treatment modality alone or in combination with other therapies for nerve repair is reviewed by Gause II et al. [this issue, pp. 59–68]. Finally, noninvasive imaging techniques need to be developed to assist in the diagnosis of nerve injuries and for the efficient analyses of these state of the art therapies. The advantages and drawbacks of various imaging applications, including MRI, ultrasound and PET, for the study of the PNS are described by Rangavajla et al. [this issue, pp. 69–77].

In summary, this issue provides an overview of how cellular and biological approaches might provide technological innovation for the treatment of peripheral nerve injuries. Encouragingly, many of the experimental approaches are now advancing towards clinical application.

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