Preface

In this book, the authors gather and present topical research in the study of cell transplantation. Topics discussed in this compilation include cell transplantation in chronic kidney disease; dendritic cells in allogenic hematopoietic cell transplantation; islet cell transplantation replacing beta cells that produce insulin in a diabetes cure; ocular surface reconstruction using cellular therapies; cell therapy on ischemic flaps and new therapeutic strategy for veno-occlusive disease after hematopoietic stem cell transplantation.

Chapter I - Chronic kidney disease is the progressive loss of kidney function over time, which can lead to end-stage renal failure and increased cardiovascular disease and mortality. This is a major health challenge as shortage of donor, expensive dialysis, and graft failure suggesting to develop new therapies, such as cell-based therapy, which has been a promising field of study in recent years. However, the therapeutic potential of cell transplantation, particularly stem cell, for renal disorders is still an ongoing debate. Some studies showed that the bone marrow derived stem cells could generate tubular cells and improve renal function. Other studies showed that resident stem cells are able to repopulate the tubule cells after injury. Nevertheless, the cell transplantation will provide the opportunity to treat both the malignant condition and the dialysis-dependent end-stage renal disease. In this chapter, authors will discuss the cell transplantation specifically autologous stem cell transplantation as novel therapy in chronic kidney disease. Further, authors will also explore the development of novel strategies to enhance the potential success of cell-based therapy in chronic kidney disease.

Chapter II - Dendritic cells (DCs) constitute a heterogeneous population of lymphocytes, the key component to regulate and coordinate adaptive immune responses, including tolerance. Continuing studies of DC biology and function

have revealed remarkable therapeutic options for treating a variety of immune disorders. Recent studies have demonstrated that allogeneic hematopoietic cell transplantation (allo-HCT) is not only therapeutically effective for malignant diseases, but also beneficial to non-malignant situations, such as facilitating the induction of immune tolerance in patients receiving solid organ transplantations. However, applications of allo-HCT as a therapeutic approach are still limited by both the immunologic recognition and destruction of host tissues (known as graft-versus host disease, or GVHD). Despite improvements in pathophysiology, GVHD remains a major cause of morbidity and mortality following allo-HCT. This chapter reviews the research evidence regarding the role of DCs in allo-HCT. Further, DC-involved therapeutic strategies, which have demonstrated promises as a method for manipulating allo-HCT, and clinically modulating immunity, are also summarized and evaluated.

Chapter III - Currently, >70% of recipients of islet cell transplantation achieve insulin independence. However, maintaining insulin independence is difficult due to chronic rejection. In 2005, it was shown that the insulin-free rate 5 years after islet cell transplantation was <10%. This very low long-term insulin-free rate is considered chronic graft dysfunction, which is caused by allosensitization, autoimmune recurrence, and other factors. Recently, several groups demonstrated improved long-term results for islet cell transplantation after introducing a potent induction immunosuppression therapy, supplemental islet cell transplantation, and transplantation of a high quality and quantity of islets. Thus, these interventions might be key factors in overcoming chronic graft dysfunction. In this chapter, authors describe the current status of allogeneic islet transplantation for the treatment of type 1 diabetes; the possible causes of chronic graft dysfunction, including late acute rejection, allosensitization, autoimmune recurrence, and nonimmunological factors; and recent strategies to overcome chronic dysfunction, including new immune-suppression protocols, supplemental islet transplantation, the monitoring of islet graft function, immune monitoring, and an antiinflammatory strategy.

Chapter IV - The anterior surface of the eye is covered by an epithelium. The cornea forms the clear front of the eye and is covered by the corneal epithelium. The cornea is surrounded by the white of the eye (sclera) which is covered by the conjunctival epithelium. The corneal epithelium is renewed by stem cells located at the junction between the corneal and conjunctival epithelia, in a region known as the limbus. The conjunctiva on the other hand is renewed by stem cells scattered throughout the conjunctival epithelium. The corneal epithelial stem cells (or limbal stem cells as they are more commonly known) and the conjunctival epithelial stem cells can become lost or damaged

by various diseases. The result is often an inflamed and painful blind eye. In this chapter, the diseases of limbal stem cell deficiency and conjunctival stem cell deficiency are discussed as well as the conventional and more contemporary management options available for treating them. In particular, this chapter highlights the growing importance of ex vivo expanded epithelial cell therapies for the treatment of these conditions.

Chapter V - Flap surgery is one of the most important surgical techniques in reconstructive surgery. However, the failure of the flap during ischemia/reperfusion (I/R) injury after the operation has still remained an unsolved clinical problem. Despite of development of surgical techniques, an estimated 5-10% failure rate still existed among all the reconstructive procedures, which not only lead to cosmetic and functional morbidity, but also result in additional trauma to the patient. In the past decade, the study of cell therapy has gained tremendous expansion and various cell types have been proved to increase the survival of flaps. In this chapter, authors reviewed the latest studies of cell therapy on ischemic flaps, including the transplantation of Bone Marrow-Derived Mesenchymal Stem Cells (BMSCs), Endothelial Progenitor Cells (EPCs), Adipose Derived Stem Cells (ADSCs), Bone Marrow-Derived Mononuclear Cells (BMNCs), and et al. The features of different cell types as well as their therapeutic effects were summarized. The concerns of such treatment on reconstructive surgery and the clinical perspectives of the therapy were also discussed.

Chapter VI - Injury to sinusoidal endothelial cells and hepatocytes by chemotherapy appears to be the primary event in the pathogenesis of VOD. Therefore, some biomarkers of endothelial injury such as soluble (s) E-selectin and sVCAM-1 are essential for predicting the development of VOD. Authors measured sE-selectin and sVCAM-1 after hematopoietic stem cell transplantation (HSCT) using recombinant thrombomodulin (rTM) instead of heparin. The subjects were 23 patients who underwent HSCT at the institution of residence. In all patients received allogeneic HSCT. The rTM was administered as a preventive therapy for VOD. Control group was also used heparin. All the cytokines and soluble factors exhibited significant elevations on day 0 after HSCT. There were significant improvements in IL-6, TNF-α and HMGB1 after rTM treatment, but not after heparin treatment. In contrast, the levels of sE-selectin and sVCAM-1 did not show significant changes after rTM treatment. However, heparin treatment exhibited a significant elevation of these soluble factors. The present findings suggest the possibility that rTM can play a preventive role for VOD after allogeneic HSCT.

Chapter VII - Haematopoietic stem cell transplantation (HSCT) is an intensive therapy which is used with increasing frequency for a variety of paediatric malignant and non malignant diseases.

The therapeutic success of paediatric HSCT is improving and in the two last decades several studies have outlined the significance of heath status, quality of life and psychological adjustment of paediatric patients at the various time-points linked with HSCT (pre HSCT, immediate post HSCT, long term consequences).

This chapter will review the research published in the last 20 years on medical treatment late effects on health, quality of life and psycho-social sequelae, in patients who have undergone hematopoietic stem cell transplantation during their childhood. The information emerged from the review of the literature will be discussed with special attention to methodological issues. Directions for future research will be proposed.