

# TABLE OF CONTENTS

<b>0. Executive Summary .....</b>	<b>21</b>
<b>1. Introduction to Cell Therapy .....</b>	<b>25</b>
<b>Introduction .....</b>	<b>25</b>
<b>Historical landmarks of cell therapy .....</b>	<b>25</b>
<b>Interrelationship of cell therapy technologies .....</b>	<b>27</b>
<b>Cells and organ transplantation .....</b>	<b>27</b>
<b>Cells and protein/gene therapy .....</b>	<b>28</b>
<b>Cell therapy and regenerative medicine.....</b>	<b>29</b>
<b>Cells therapy and tissue engineering .....</b>	<b>29</b>
<b>Therapy based on cells involved in disease.....</b>	<b>30</b>
<b>Advantages of therapeutic use of cells .....</b>	<b>30</b>
<b>Use of cells for improving drug delivery.....</b>	<b>31</b>
<b>2. Cell Therapy Technologies .....</b>	<b>33</b>
<b>Introduction .....</b>	<b>33</b>
<b>Cell types used for therapy .....</b>	<b>33</b>
<b>Sources of cells.....</b>	<b>33</b>
Xenografts .....	34
Cell lines.....	34
<i>Immortalized cells.....</i>	<i>34</i>
Blood component therapy .....	34
<i>Therapeutic apheresis.....</i>	<i>34</i>
<i>Leukoreduction .....</i>	<i>35</i>
<i>Platelet therapy .....</i>	<i>35</i>
<b>Basic technologies for cell therapy .....</b>	<b>36</b>
Cell culture .....	36
<i>Observation of stem cell growth and viability.....</i>	<i>36</i>
<i>Companies involved in cell culture.....</i>	<i>37</i>
Cell sorting .....	38
<i>Flow cytometry.....</i>	<i>38</i>
<i>A dielectrophoretic system for cell separation .....</i>	<i>39</i>
<i>Molecular beacons for specific detection and isolation of stem cells .....</i>	<i>39</i>
<i>Multitarget magnetic activated cell sorter.....</i>	<i>40</i>
<i>Nanocytometry .....</i>	<i>40</i>
<i>Companies supplying cell sorters .....</i>	<i>40</i>
<i>Dynabead technology for cell sorting .....</i>	<i>41</i>
<i>ALDESORTER system for isolation of stem cells.....</i>	<i>42</i>
<i>Adult stem cell sorting by identification of surface markers .....</i>	<i>42</i>
Cell analysis .....	42
Preservation of cells .....	43
<i>Innovations in cryopreservation.....</i>	<i>43</i>
Packaging of cells .....	43
Selective expansion of T cells for immunotherapy .....	44
Cloning and cell therapy .....	44
Techniques for cell manipulation .....	45
<b>Cell-based drug discovery.....</b>	<b>45</b>
<b>Cells as vehicles for drug delivery.....</b>	<b>48</b>
<b>Drug delivery systems for cell therapy .....</b>	<b>48</b>
Intravenous delivery of stem cells.....	48
Pharmacologically active microcarriers.....	49
Devices for delivery of cell therapy.....	49
<b>Artificial cells.....</b>	<b>50</b>
Applications of artificial cells.....	50
<b>Cell encapsulation.....</b>	<b>51</b>
Diffusion capsule for cells.....	51
Encapsulated cell biodelivery .....	52
Therapeutic applications of encapsulated cells .....	52
Nitric oxide delivery by encapsulated cells.....	53
Implantation of microencapsulated genetically modified cells .....	54
Ferrofluid microcapsules for tracking with MRI .....	54
Companies involved in encapsulated cell technology.....	55
<b>Electroporation .....</b>	<b>55</b>
<b>Gene therapy .....</b>	<b>56</b>
Cell-mediated gene therapy .....	56
<i>Fibroblasts .....</i>	<i>56</i>
<i>Chondrocyte.....</i>	<i>57</i>

<i>Skeletal muscle cells</i> .....	57
<i>Vascular smooth muscle cells</i> .....	58
<i>Keratinocytes</i> .....	58
<i>Hepatocytes</i> .....	59
<i>Lymphocytes</i> .....	59
<i>Mammalian artificial chromosomes</i> .....	59
<b>In vivo tracking of cells</b> .....	<b>59</b>
Molecular imaging for tracking cells .....	60
<i>MRI technologies for tracking cells</i> .....	60
<i>Superparamagnetic iron oxide nanoparticles as MRI contrast agents</i> .....	61
<i>Visualization of gene expression in vivo by MRI</i> .....	61
<b>Role of nanobiotechnology in development of cell therapy</b> .....	<b>61</b>
<b>Cell transplantation for development of organs</b> .....	<b>62</b>
<b>Cells transplantation and tolerance</b> .....	<b>62</b>
Strategies to improve tolerance of transplanted cells .....	63
<i>Encapsulation to prevent immune rejection</i> .....	63
<i>Prevention of rejection of xenotransplants</i> .....	63
<i>Expansion of allospecific regulatory T cells</i> .....	64
<b>Removal and replacement of pathogenic cells of the body</b> .....	<b>64</b>
Therapeutic leukocytapheresis .....	64

### **3. Stem Cells**..... **65**

<b>Introduction</b> .....	<b>65</b>
<b>Biology of stem cells</b> .....	<b>66</b>
Embryonic stem cells .....	66
Growth and differentiation of ESCs .....	66
<i>Regulation of stem cell self-renewal and differentiation</i> .....	67
<i>Role of Pax3 in stem cell differentiation</i> .....	67
<i>ESCs and signaling pathways</i> .....	68
<i>Genetic signature of stem cells</i> .....	68
<i>Epigenetics of hESCs</i> .....	68
<i>Chromatin as gene regulator for ESC development</i> .....	69
<i>Mechanism of differentiation of ESCs</i> .....	69
<i>Chemical regulation of stem cell differentiation</i> .....	70
<i>Comparison of development of human and mouse ESCs</i> .....	70
<i>In vitro differentiation of hESCs</i> .....	70
<i>Global transcription in pluripotent ESCs</i> .....	71
<i>Signaling pathways and transcription factors in ESCs</i> .....	71
<i>Stem cells in the pituitary gland</i> .....	71
<i>hESCs in stead of oocytes for reprogramming human somatic nuclei</i> .....	72
Mechanism of regulation of stem cells for regeneration of body tissues .....	72
<i>Role of microenvironments in the regulation of stem cells</i> .....	72
<i>Regulation and regeneration of intestinal stem cells</i> .....	73
Parthenogenesis and human stem cells .....	73
<i>Uniparental ESCs</i> .....	74
Bone marrow stem cells .....	74
<i>Hematopoietic stem cells</i> .....	74
<i>Role of HSCs in the immune system</i> .....	76
<i>Derivation of HSCs from ESCs</i> .....	76
<i>Mesenchymal stem cells</i> .....	77
<i>Multipotent adult progenitor cells</i> .....	78
<i>Side population (SP) stem cells</i> .....	79
Differentiation of adult stem cells .....	79
Growth and differentiation of HSCs .....	80
<i>Signaling pathways in the growth and differentiation of HSCs</i> .....	80
<i>Mathematical modeling of differentiation of HSCs</i> .....	80
<i>Role of prions in self renewal of HSCs</i> .....	81
<b>Sources of stem cells</b> .....	<b>81</b>
Sources of human embryonic stem cells .....	81
Nuclear transfer to obtain hESCs .....	82
Direct derivation of hESCs from embryos without nuclear transfer .....	83
Alternative methods of obtaining hESCs .....	83
<i>Establishing hESC lines without destruction of embryo</i> .....	83
<i>Altered nuclear transfer</i> .....	84
<i>Small embryonic-like stem cells</i> .....	85
Advantages and disadvantages of ESCs for transplantation .....	85
Use of ESC cultures as an alternative source of tissue for transplantation .....	85
Spermatogonial stem cells .....	86
Amniotic fluid as a source of stem cells .....	87
Placenta as source of stem cells .....	87
<i>Amnion-derived multipotent progenitor cells</i> .....	87

<i>Placenta as a source of HSCs</i> .....	88
<i>Umbilical cord as a source of MSCs</i> .....	88
Umbilical cord blood as source of neonatal stem cells .....	89
<i>Cryopreservation of UCB stem cells</i> .....	90
<i>UCB as source of MSCs</i> .....	90
<i>Applications of UCB</i> .....	90
<i>Advantages of UCB</i> .....	91
<i>Limitations of the use of UCB</i> .....	91
<i>Licensing and patent disputes involving UCB</i> .....	92
<i>Infections following UCB transplants</i> .....	93
<i>Unanswered questions about UCB transplantation</i> .....	93
<i>Companies involved in UCB banking</i> .....	93
<i>UCB banking in the UK</i> .....	95
<i>US national UCB banking system</i> .....	95
<i>Future prospects of UCB as a source of stem cells</i> .....	96
<b>Induced pluripotent stem cells derived from human somatic cells</b> .....	<b>97</b>
Characteristics of iPSCs .....	97
DNA methylation patterns of iPS cells .....	98
iPSCs derived from blood .....	98
iPSCs derived from skin .....	98
Use of retroviral vectors for generation of iPSCs .....	98
Use of non-integrating viral vectors for generation of iPSCs.....	99
Clinical relevance of iPSCs.....	99
<b>Sources of adult human stem cells</b> .....	<b>100</b>
Adipose tissue as a source of stem cells.....	101
<i>Transforming adult adipose stem cells into other cells</i> .....	101
<i>iPSCs derived from adult human adipose stem cells</i> .....	102
Skin as a source of stem cells.....	102
<i>Controlling the maturation of embryonic skin stem cells</i> .....	102
<i>Epidermal neural crest stem cells</i> .....	102
<i>Follicle stem cells</i> .....	103
<i>Mesenchymal stem cells in skin</i> .....	103
<i>Regulation of stem cells in hair follicles</i> .....	104
<i>Skin-derived precursor cells</i> .....	104
Stem cells in teeth .....	104
Peripheral blood stem cells.....	105
Spleen as a source of adult stem cells .....	106
Search for master stem cells .....	106
<b>Adult stem cells vs embryonic stem cells</b> .....	<b>106</b>
Transdifferentiation potential of adult stem cells .....	107
Neural crest stem cells from adult hair follicles .....	108
Stem cells obtained from blood in adults.....	108
<b>VENT cells</b> .....	<b>109</b>
<b>Stem cell banking</b> .....	<b>109</b>
<b>Stem cell technologies</b> .....	<b>109</b>
Analysis of stem cell growth and differentiation .....	109
Tracking self-renewal and expansion of transplanted muscle stem cells .....	110
Stem cell biomarkers.....	110
<i>Endoglin as a functional biomarker of HSCs</i> .....	110
<i>STEMPRO® EZChek™ for analysis of biomarkers of hESCs</i> .....	111
<i>SSEA-4 as biomarker of MSCs</i> .....	111
<i>p75NTR as a biomarker to isolate adipose tissue-derived stem cells</i> .....	111
<i>Neural stem cell biomarker</i> .....	111
<i>Protein expression profile as biomarker of stem cells</i> .....	112
<i>Real-time PCR for quantification of protein biomarkers</i> .....	112
Study of stem cell pathways.....	112
Study of stem cell genes .....	113
Gene inactivation to study hESCs.....	113
<i>RNAi to study gene inactivation in hESCs</i> .....	113
<i>Study of ESC development by inducible RNAi</i> .....	114
<i>Targeting Induced Local Lesions in Genomes</i> .....	115
<i>Homologous recombination of ESCs</i> .....	115
<i>Immortalization of hESCs by telomerase</i> .....	115
Gene modification in genomes of hESCs and hiPSCs using zinc-finger nuclease.....	116
miRNA and stem cells.....	116
<i>Role of miRNAs in gene regulation during stem cell differentiation</i> .....	116
<i>Influence of miRNA on stem cell formation and maintenance</i> .....	117
<i>Transcriptional regulators of ESCs control miRNA gene expression</i> .....	117
Stem cells and cloning.....	118
<i>Cell nuclear replacement and cloning</i> .....	118
<i>Nuclear transfer and ESCs</i> .....	118

Cloning from differentiated cells.....	119
Cloning mice from adult stem cells .....	120
Creating interspecies stem cells .....	120
Cloned cells for transplantation medicine .....	121
Claims of cloning of hESCs .....	121
Cytogenetics of embryonic stem cells .....	122
Engraftment, mobilization and expansion of stem cells .....	123
Adipogenesis induced by adipose tissue-derived stem cells.....	124
Antisense approach for preservation and expansion of stem cells.....	124
Chemoattraction of neuronal stem cells through GABA receptor.....	125
Enhancement of HSC engraftment by calcium-sensing receptor .....	125
Enhancement of stem cell differentiation by Homspera .....	125
Ex vivo expansion of human HSCs in culture .....	126
Ex vivo expansion of MSCs.....	126
Expansion of HSCs in culture by inhibiting aldehyde dehydrogenase.....	127
Expansion of adult stem cells by activation of Oct4 .....	127
Expansion of transduced HSCs in vivo .....	127
Mobilization of HSCs by growth factors .....	128
Mobilization of stem cells by cytokines/chemokines.....	128
Mobilization of adult human HSCs by use of inhibitors .....	129
Mobilization of stem cells by HYC750.....	129
Mobilization of stem cells by hyperbaric oxygen .....	130
Mobilization by adenoviral vectors expressing angiogenic factors .....	130
Selective mobilization of progenitor cells from bone marrow.....	131
Selective Amplification.....	131
Stem cell mobilization by acetylcholine receptor agonists.....	131
Use of parathyroid hormone to increase HSC mobilization.....	132
Expansion of stem cells in vivo by Notch receptor ligands .....	132
Technologies for inducing differentiation of stem cells.....	132
Use of lineage selection to induce differentiation of hESCs.....	132
Growth factor-induced differentiation of MAPCs.....	132
Neurotrophin-mediated survival and differentiation of hESCs.....	133
Generation of RBCs from hematopoietic stem cells .....	133
Generation of multiple types of WBCs from hESCs and iPSCs.....	133
Use of RNAi to expand the plasticity of autologous adult stem cells .....	134
Use of carbohydrate molecules to induce differentiation of stem cells .....	134
Mechanical strain to induce MSC differentiation.....	134
Limitations of the currently available stem cell lines in the US .....	135
Contaminating material in stem cell culture and measures to eliminate it.....	135
Stem cell separation.....	136
Stem cell culture.....	137
Conversion of stem cells to functioning adipocytes .....	137
Mass production of ESCs.....	138
Promoting survival of dissociated hESCs .....	138
Analysis and characterization of stem cells.....	138
Harvesting and identification of EPCs.....	139
Labeling of stem cells .....	139
Quantum dots for labeling hMSCs .....	140
Imaging and tracking of stem cells in vivo.....	140
Quantum dot imaging for ESCs.....	140
Perfluorocarbon nanoparticles to track therapeutic cells in vivo.....	140
Project for imaging in stem cell therapy research .....	141
<b>Applications of stem cells .....</b>	<b>141</b>
Controlling the maintenance process of hematopoietic stem cells .....	142
Self renewal and proliferation of HSCs .....	142
Aging and rejuvenation of HSCs.....	142
Peripheral blood stem cell transplantation .....	142
Complications of PBSC transplantation in children .....	143
Stem cell transplantation for radiation sickness.....	143
Stem cells and human reproduction .....	143
Expansion of spermatogonial stem cells .....	143
Conversion of ESCs into spermatogonial stem cells .....	144
Conversion of stem cells to oocytes.....	144
ESCs for treatment of infertility in women .....	145
Cloning human embryos from oocytes matured in the laboratory .....	145
In utero stem cell transplantation .....	146
Innovations in delivery of stem cells.....	146
Immunological aspects of hESC transplantation .....	147
Immunosuppression to prevent rejection of hESC transplants.....	147
Histocompatibility of hESCs.....	147
Strategies for promoting immune tolerance of hESCs .....	148

Stem cells for organ vascularization .....	149
<i>Activation of EphB4 to enhance angiogenesis by EPCs</i> .....	149
Advantages and limitations of clinical applications of MSCs .....	150
Biofusion by genetically engineering stem cells .....	150
Stem cell gene therapy .....	150
<i>Combination of gene therapy with nuclear transfer</i> .....	151
<i>Gene delivery to stem cells by artificial chromosome expression</i> .....	151
<i>Genetic manipulation of ESCs</i> .....	151
<i>Genetic engineering of human stem cells for enhancing angiogenesis</i> .....	152
<i>HSCs for gene therapy</i> .....	152
<i>Helper-dependent adenoviral vectors for gene transfer in ESCs</i> .....	153
<i>Lentiviral vectors for in vivo gene transfer to stem cells</i> .....	153
<i>Linker based sperm-mediated gene transfer technology</i> .....	153
<i>Mesenchymal stem cells for gene therapy</i> .....	154
<i>Molecular vibration for gene transfer</i> .....	154
<i>Regulation of gene expression for SC-based gene therapy</i> .....	154
<i>Stem cells and in utero gene therapy</i> .....	154
<i>Therapeutic applications for hematopoietic stem cell gene transfer</i> .....	155
<i>The future of hematopoietic stem cell gene therapy</i> .....	155
Stem cell pharmaceuticals .....	155
<i>Stem cells for drug discovery</i> .....	155
<i>Advantages of using stem cells for drug discovery</i> .....	156
<i>Role of stem cells in therapeutic effects of drugs</i> .....	157
<i>Hepatocytes derived from hESCs</i> .....	157
<i>Cardiomyocytes derived from hESCs</i> .....	157
<i>ESCs as source of models for drug discovery</i> .....	158
<i>Engineered stem cells for drug delivery to the brain</i> .....	159
<i>Use of ESCs for toxicology and drug safety studies</i> .....	159
<i>European projects for safety testing of drugs using ESCs</i> .....	160
<i>Pharmaceutical manipulation of stem cells</i> .....	161
<i>Adverse effects of drugs on stem cells</i> .....	163
<b>Future challenges for stem cell technologies .....</b>	<b>163</b>
Study of the molecular mechanism of cell differentiation .....	163
MBD3-deficient ESC line .....	164
In vivo study of human hemopoietic stem cells .....	164
Stem cell biology and cancer .....	164
Research into plasticity of stem cells from adults .....	165
Stem cells and aging .....	165
Activation of bone marrow stem cells into therapeutic cells .....	166
Role of nitric oxide in stem cell mobilization and differentiation .....	167
Stem cell genes .....	167
<i>Gene expression in hESCs</i> .....	167
<i>The casanova gene in zebrafish</i> .....	168
<i>Nanog gene</i> .....	168
Stem cell proteomics .....	169
<i>hESC phosphoproteome</i> .....	170
<i>Proteomic studies of mesenchymal stem cells</i> .....	170
<i>Proteomic profiling of neural stem cells</i> .....	170
<i>Proteome Biology of Stem Cells Initiative</i> .....	171
Genomic alterations in cultured hESCs .....	171
Hybrid embryos/cybrids for stem cell research .....	171
Generation of patient-specific pluripotent stem cells .....	172
Markers for characterizing hESC lines .....	173
Switch of stem-cell function from activators to repressors .....	173
<b>Stem cell research at academic centers .....</b>	<b>174</b>
International Regulome Consortium .....	175
<b>Companies involved in stem cell technologies .....</b>	<b>175</b>
<b>Concluding remarks about stem cells .....</b>	<b>180</b>
<b>Challenges and future prospects of stem cell research .....</b>	<b>180</b>
<b>4. Clinical Applications of Cell Therapy .....</b>	<b>183</b>
<b>Introduction .....</b>	<b>183</b>
<b>Cell therapy for hematological disorders .....</b>	<b>183</b>
Transplantation of autologous hematopoietic stem cells .....	183
Hemophilias .....	183
<i>Ex vivo cell/gene therapy of hemophilia B</i> .....	183
<i>Cell/gene therapy of hemophilia A</i> .....	184
Hematopoietic stem cell therapy for thrombocytopenia .....	185
Stem cell transplant for sickle cell anemia .....	185
Treatment of chronic acquired anemias .....	186
<i>Implantation of genetically engineered HSCs to deliver rhEpo</i> .....	186

<i>Drugs acting on stem cells for treatment of anemia</i> .....	186
Stem cell therapy of hemoglobinopathies .....	187
Stem cells for treatment of immunoglobulin-light chain amyloidosis .....	187
Future prospects of cell therapy of hematological disorders .....	187
<b>Cell therapy for immunological disorders .....</b>	<b>188</b>
Role of dendritic cells in the immune system .....	188
Modifying immune responses of DCs by vaccination with lipiodol-siRNA mixtures .....	188
Stem cell therapy of chronic granulomatous disease.....	189
Stem cell therapy of X-linked severe combined immunodeficiency.....	189
Stem cell therapy of autoimmune disorders.....	190
<i>Treatment of Crohn's disease with stem cells</i> .....	190
<i>Treatment of rheumatoid arthritis with stem cells</i> .....	190
<i>Stem cell transplants for scleroderma</i> .....	191
Role of T-Cells in immunological disorders.....	191
<i>Autologous T-cells from adult stem cells</i> .....	192
Cell therapy for graft vs host disease.....	192
<b>Cell therapy for viral infections.....</b>	<b>193</b>
<i>T-cell therapy for CMV</i> .....	193
<i>T-cell therapy for HIV infection</i> .....	194
<i>T-cell immunity by Overlapping Peptide-pulsed Autologous Cells</i> .....	194
<i>Anti-HIV ribozyme delivered in hematopoietic progenitor cells</i> .....	195
<i>Dendritic-cell targeted DNA vaccine for HIV</i> .....	195
<b>Cell therapy of lysosomal storage diseases.....</b>	<b>195</b>
Niemann-Pick disease.....	196
Gaucher's disease .....	196
Fabry's disease.....	197
<b>Cell therapy for diabetes mellitus .....</b>	<b>197</b>
Limitations of current treatment .....	198
<i>Limitations of insulin therapy for diabetes mellitus</i> .....	198
<i>Limitations of pancreatic transplantation</i> .....	198
Islet cell transplantation .....	199
<i>Autologous pancreatic islet cell transplantation in chronic pancreatitis</i> .....	199
<i>Clinical trials of pancreatic islet cell transplants for diabetes</i> .....	199
<i>Drawbacks of islet cell therapy</i> .....	200
<i>Use of an antioxidant peptide to improve islet cell transplantation</i> .....	200
<i>Cdk-6 and cyclin D1 enhance human beta cell replication and function</i> .....	201
<i>A device for delivery of therapeutic cells in diabetes</i> .....	201
<i>Monitoring of islet cell transplants with MRI</i> .....	201
<i>Concluding remarks about allogeneic islet transplantation for diabetes</i> .....	202
Encapsulation of insulin producing cells .....	202
<i>Encapsulated porcine pancreatic islet cells for pancreas</i> .....	202
<i>Encapsulated insulinoma cells</i> .....	203
<i>Magnetocapsule enables imaging/tracking of islet cell transplants</i> .....	203
Islet precursor cells.....	203
Dedifferentiation of $\beta$ cells to promote regeneration .....	204
Xenotransplantation of embryonic pancreatic tissue .....	204
Non-pancreatic tissues for generation of insulin-producing cells .....	205
Exploiting maternal microchimerism to treat diabetes in the child .....	205
Bio-artificial substitutes for pancreas.....	205
Role of stem cells in the treatment of diabetes .....	206
<i>Pancreatic stem cells</i> .....	206
<i>Embryonic stem cells for diabetes</i> .....	206
<i>Isolation of islet progenitor cells</i> .....	208
<i>Expansion of pancreatic progenitor cells in vitro</i> .....	208
<i>Human neural progenitor cells converted into insulin-producing cells</i> .....	208
<i>Insulin-producing cells derived from UCB stem cells</i> .....	208
<i>Stem cell injection into portal vein of diabetic patients</i> .....	209
<i>HSC transplantation to supplement immunosuppressant therapy</i> .....	209
Dendritic cell-based therapy for type 1 diabetes.....	210
Gene therapy in diabetes .....	210
<i>Viral vectors for gene therapy of diabetes</i> .....	210
<i>Genetically engineered dendritic cells</i> .....	211
<i>Genetically altered liver cells</i> .....	211
<i>Genetically modified stem cells</i> .....	211
Companies developing cell therapy for diabetes.....	212
Concluding remarks about cell and gene therapy of diabetes.....	213
<b>Cell therapy of gastrointestinal disorders .....</b>	<b>214</b>
Inflammatory bowel disease.....	214
<b>Cell therapy for liver disorders .....</b>	<b>214</b>
Types of cells and methods of delivery for hepatic disorders.....	215
Bioartificial liver.....	215

<i>Limitations of bioartificial liver</i> .....	216
Stem cells for hepatic disorders .....	216
<i>Deriving hepatocytes from commercially available hMSCs</i> .....	217
<i>Implantation of hepatic cells derived from hMSCs of adipose tissue</i> .....	217
<i>MSC derived molecules for reversing hepatic failure</i> .....	218
Cell-based gene therapy for liver disorders.....	218
<i>Transplantation of genetically modified fibroblasts</i> .....	219
<i>Transplantation of genetically modified hepatocytes</i> .....	219
<i>Intraperitoneal hepatocyte transplantation</i> .....	219
<i>Genetically modified hematopoietic stem cells</i> .....	219
Clinical applications .....	219
Future prospects of cell-based therapy of hepatic disorders.....	220
<b>Cell therapy of renal disorders.....</b>	<b>220</b>
Bioartificial kidney.....	221
Bone marrow stem cells for renal disease .....	221
Human stem cells to prevent end stage renal disease.....	222
<i>Role of stem cells in renal repair</i> .....	222
<i>Cell-based repair for vascular access failure in renal disease</i> .....	222
Mesangial cell therapy .....	223
<b>Cell therapy for pulmonary disorders.....</b>	<b>223</b>
Delivery of cell therapy for pulmonary disorders .....	223
<i>Intratracheal injection of cells for pulmonary hypoplasia</i> .....	223
Role of stem cells in pulmonary disorders .....	223
<i>Lung tissue regeneration from stem cells</i> .....	224
<i>Role of stem cells in construction of the Cyberlung</i> .....	224
<i>Respiratory epithelial cells derived from UCB stem cells</i> .....	224
<i>Respiratory epithelial cells derived from hESCs</i> .....	225
<i>Lung tissue engineering with adipose stromal cells</i> .....	225
<i>Cell-based tissue-engineering of airway</i> .....	225
Pulmonary disorders that are treatable by stem cells.....	226
<i>Acute lung injury and ARDS treated with MSCs</i> .....	227
Bronchopulmonary dysplasia treated with MSCs.....	227
<i>Cystic fibrosis treatment with genetically engineered MSCs</i> .....	228
<i>Pulmonary arterial hypertension treatment with EPCs</i> .....	228
<b>Cell therapy for disorders of bones and joints .....</b>	<b>229</b>
Repair of fractures and bone defects .....	229
<i>Adult stem cells for bone grafting</i> .....	230
<i>Cell therapy for osteonecrosis</i> .....	230
<i>ESCs for bone repair</i> .....	230
<i>Intrauterine use of MSCs for osteogenesis imperfecta</i> .....	230
<i>In vivo bone engineering as an alternative to cell transplantation</i> .....	231
<i>MSCs for repair of bone defects</i> .....	231
<i>MSCs for repair of bone fractures</i> .....	234
<i>Osteoecel</i> .....	234
<i>Stem cells for repairing skull defects</i> .....	235
<i>Stem cell-based bone tissue engineering</i> .....	235
Osteoarthritis and other injuries to the joints.....	236
<i>Mosaicplasty</i> .....	237
<i>Autologous cultured chondrocytes</i> .....	237
<i>Autologous intervertebral disc chondrocyte transplantation</i> .....	238
<i>Cartilage repair by genetically modified fibroblasts expressing TGF-<math>\beta</math></i> .....	239
<i>Generation of cartilage from stem cells</i> .....	239
Role of cell therapy in repair of knee cartilage injuries .....	240
<i>Role of cells in the repair of anterior cruciate ligament injury</i> .....	242
Autologous tenocyte implantation in rotator cuff injury repair .....	243
Platelet injection for tennis elbow.....	243
Cell therapy of rheumatoid arthritis.....	243
<b>Cell therapy for diseases of the eye .....</b>	<b>244</b>
Cell therapy for corneal repair .....	244
Stem cell therapy for limbal stem cell deficiency .....	246
<b>Cell therapy for regeneration.....</b>	<b>246</b>
Stem cells for regeneration .....	246
Stem cells for regenerating organs.....	247
Umbilical cord blood for regeneration .....	248
Promotion of regeneration by Wnt/beta-catenin signaling .....	248
Role of stem cells in regeneration of esophageal epithelium .....	248
Cell therapy for regeneration of muscle wasting.....	249
MSCs for regeneration of ovaries following radiotherapy damage .....	249
<b>Wound healing: skin and soft tissue repair .....</b>	<b>249</b>
Cells to form skin substitutes for healing ulcers .....	250
CellSpray for wound repair.....	251

Role of follicular stem cells in skin and wound repair .....	251
Cell therapy for burns.....	252
Genetically engineered cells for wound repair .....	253
Closure of incisions with laser guns and cells .....	253
Repair of aging skin by injecting autologous fibroblasts .....	253
<b>Role of cells in tissue engineering and reconstructive surgery .....</b>	<b>254</b>
Stem cells for tissue repair.....	254
Scaffolds for tissue engineering .....	254
Improving vascularization of engineered tissues .....	255
Enhancing vascularization by combining cell and gene therapy .....	255
Choosing cells for tissue engineering .....	255
ESCs vs adult SCs for tissue engineering.....	256
Use of adult MSCs for tissue engineering.....	256
Nanobiotechnology applied to cells for tissue engineering .....	257
Stem cells for tissue engineering of various organs .....	258
<i>Engineering of healthy living teeth from stem cells</i> .....	258
<i>Adipose tissue-derived stem cells for breast reconstruction</i> .....	259
<i>Improving tissue engineering of bone by MSCs</i> .....	259
<i>Intra-uterine repair of congenital defects using amniotic fluid MSCs</i> .....	259
Cell-based tissue engineering in genitourinary system .....	260
<i>Urinary incontinence</i> .....	260
<i>Tissue engineering of urinary bladder</i> .....	261
<i>Label retaining urothelial cells for bladder repair</i> .....	262
<i>Repair of the pelvic floor with stem cells from the uterus</i> .....	262
<i>Reconstruction of vagina from stem cells</i> .....	262
Facial skin regeneration by stem cells as an alternative to face transplant.....	262
<b>Cell therapy for rejuvenation .....</b>	<b>263</b>
<b>Cell therapy for performance enhancement in sports .....</b>	<b>263</b>
<b>Application of stem cells in veterinary medicine.....</b>	<b>263</b>
Use of stem cells to repair tendon injuries.....	263
Stem cells for spinal cord injury in dogs.....	264

<b>5. Cell Therapy for Cardiovascular Disorders .....</b>	<b>265</b>
<b>Introduction to cardiovascular disorders .....</b>	<b>265</b>
<b>Limitations of current therapies for myocardial ischemic disease.....</b>	<b>265</b>
<b>Types of cell therapy for cardiovascular disorders.....</b>	<b>265</b>
Cell-mediated immune modulation for chronic heart disease .....	266
Human cardiovascular progenitor cells.....	267
Inducing the proliferation of cardiomyocytes .....	267
Role of the SDF-1-CXCR4 axis in stem cell therapies for myocardial ischemia .....	268
Role of splenic myocytes in repair of the injured heart.....	268
Small molecules to enhance myocardial repair by stem cells .....	268
<b>Cell therapy for atherosclerotic coronary artery disease.....</b>	<b>268</b>
MyoCell™ (Bioheart).....	269
Cardiac stem cells .....	269
Cardiomyocytes derived from epicardium.....	270
<b>Methods of delivery of cells to the heart.....</b>	<b>271</b>
Cellular cardiomyoplasty .....	271
IGF-1 delivery by nanofibers to improve cell therapy for MI.....	271
Non-invasive delivery of cells to the heart by Morph@guide catheter .....	271
<b>Cell therapy for cardiac revascularization .....</b>	<b>272</b>
Transplantation of cardiac progenitor cells for revascularization of myocardium .....	272
Stem cells to prevent restenosis after coronary angioplasty.....	272
<b>Role of cells in cardiac tissue repair.....</b>	<b>273</b>
Transplantation of myoblasts for myocardial infarction.....	273
Patching myocardial infarction with fibroblast culture .....	274
Cardiac repair with myoendothelial cells from skeletal muscle .....	274
Myocardial tissue engineering.....	274
<b>Role of stem cells in repair of the heart .....</b>	<b>275</b>
Role of stem cells in cardiac regeneration following injury .....	275
Cardiomyocytes derived from ESCs .....	276
Studies to identify subsets of progenitor cells suitable for cardiac repair .....	277
Technologies for preparation of stem cells for cardiovascular therapy .....	278
<i>Pravastatin for expansion of endogenous progenitor and stem cells</i> .....	278
<i>Cytokine preconditioning of human fetal liver CD133+ SCs</i> .....	278
<i>Expansion of adult cardiac stem cells for transplantation</i> .....	279
Role of ESCs in repair of the heart .....	279
<i>ESC transplantation for tumor-free repair of the heart</i> .....	280
Transplantation of stem cells for acute myocardial infarction .....	280
<i>Autologous bone marrow-derived stem cell therapeutics</i> .....	280
<i>Autologous bone marrow-derived mesenchymal precursor stem cells</i> .....	281

<i>Transplantation of cord blood stem cells</i> .....	281
<i>Transplantation of hESCs</i> .....	281
<i>Transplantation of HSCs</i> .....	282
<i>Transplantation of autologous angiogenic cell precursors</i> .....	283
<i>Transplantation of adipose-derived stem cells</i> .....	283
<i>Intracoronary infusion of bone marrow-derived cells for AMI</i> .....	284
<i>Intracoronary infusion of mobilized peripheral blood stem cells</i> .....	284
<i>Transplantation of endothelial cells</i> .....	285
<i>Transplantation of cardiomyocytes differentiated from hESCs</i> .....	285
Stem cell therapy for cardiac regeneration .....	285
<i>Regeneration of the chronic myocardial infarcts by HSC therapy</i> .....	285
<i>Human mesenchymal stem cells for cardiac regeneration</i> .....	286
<i>In vivo tracking of MSCs transplanted in the heart</i> .....	287
<i>MSCs for hibernating myocardium</i> .....	287
<i>Simultaneous transplantation of MSCs and skeletal myoblasts</i> .....	288
<b>Transplantation of genetically modified cells</b> .....	<b>288</b>
Transplantation of genetically modified MSCs .....	288
Transplantation of cells secreting vascular endothelial growth factor .....	288
Transplantation of genetically modified bone marrow stem cells.....	288
<b>Cell transplantation for congestive heart failure</b> .....	<b>289</b>
Myoblasts for treatment of congestive heart failure .....	289
Injection of adult stem cells for congestive heart failure.....	289
AngioCell gene therapy for congestive heart failure .....	290
Stem cell therapy for dilated cardiac myopathy.....	291
<b>Role of cell therapy in cardiac arrhythmias</b> .....	<b>291</b>
Atrioventricular conduction block .....	291
<i>Genetically engineered cells as biological pacemakers</i> .....	292
Ventricular tachycardia .....	293
Prevention of myoblast-induced arrhythmias by genetic engineering .....	293
<b>ESCs for correction of congenital heart defects</b> .....	<b>293</b>
<b>Cardiac progenitors cells for treatment of heart disease</b> .....	<b>294</b>
<b>Autologous stem cells for chronic myocardial ischemia</b> .....	<b>294</b>
<b>Role of cells in cardiovascular tissue engineering</b> .....	<b>295</b>
Construction of blood vessels with cells .....	295
Targeted delivery of endothelial progenitor cells labeled with nanoparticles .....	296
Fetal cardiomyocytes seeding in tissue-engineered cardiac grafts.....	296
UCB progenitor cells for engineering heart valves.....	296
<b>Cell therapy for peripheral vascular disease</b> .....	<b>296</b>
ALD-301 .....	297
Cell/gene therapy for PVD .....	297
Colony stimulating factors for enhancing peripheral blood stem cells .....	297
Intramuscular autologous bone marrow cells .....	298
Vascular Repair Cell .....	298
<b>Clinical trials of cell therapy in cardiovascular disease</b> .....	<b>298</b>
<b>Mechanism of the benefit of cell therapy for heart disease</b> .....	<b>301</b>
<b>A critical evaluation of cell therapy for heart disease</b> .....	<b>301</b>
Publications of clinical trials of cell therapy for CVD .....	301
Current status of cell therapy for cardiovascular disease .....	302
<b>Future directions for cell therapy of CVD</b> .....	<b>302</b>
Prospects of adult stem cell therapy for repair of heart .....	302
Regeneration of cardiomyocytes without use of cardiac stem cells.....	303
<b>6. Cell Therapy for Cancer</b> .....	<b>305</b>
<b>Introduction</b> .....	<b>305</b>
<b>Cell therapy technologies for cancer</b> .....	<b>305</b>
<b>Cellular immunotherapy for cancer</b> .....	<b>306</b>
Treatments for cancer by ex vivo mobilization of immune cells .....	306
Granulocytes as anticancer agents .....	307
Neutrophil granulocytes in antibody-based immunotherapy of cancer .....	307
<b>Cancer vaccines</b> .....	<b>308</b>
Autologous tumor cell vaccines .....	308
<i>BIOVAXID</i> .....	308
<i>OncoVAX</i> .....	308
<i>Tumor cells treated with dinitrophenyl</i> .....	309
Vaccines that simultaneously target different cancer antigens .....	309
Gene modified cancer cells vaccines .....	309
<i>GVAX cancer vaccines</i> .....	309
<i>K562/GM-CSF</i> .....	310
Active immunotherapy based on antigen specific to the tumor .....	310
The use of dendritic cells for cancer vaccination.....	311
<i>Autologous dendritic cells loaded ex vivo with telomerase mRNA</i> .....	311

<i>Dendritic/tumor cell fusion</i> .....	311
<i>Genetically modified dendritic cells</i> .....	312
<i>In vivo manipulation of dendritic cells</i> .....	312
<i>Preclinical and clinical studies with DC vaccines</i> .....	312
<i>Vaccines based on dendritic cell-derived exosomes</i> .....	313
<i>Limitations of DC vaccines for cancer</i> .....	313
<i>Future developments to enhance clinical efficacy of DC vaccines</i> .....	313
Lymphocyte-based cancer therapies .....	315
<i>Adoptive immunotherapy</i> .....	315
<i>Rescue of CD8+ T cells for use in tumor immunotherapy</i> .....	316
<i>Expansion of antigen-specific cytotoxic T lymphocytes</i> .....	316
<i>Genetically targeted T cells for treating B cell malignancies</i> .....	317
<i>Tumor infiltrating lymphocytes</i> .....	317
<i>Genetic engineering of tumor cells</i> .....	318
Hybrid cell vaccination .....	318
<b>Stem cell-based anticancer therapies</b> .....	<b>319</b>
Stem cell transplantation in cancer .....	319
<i>Peripheral blood stem cell transplantation</i> .....	319
<i>Stem cell transplantation for hematological malignancies</i> .....	321
<i>Complications of stem cell transplants in cancer</i> .....	322
<i>Long-term results of HSC transplantation</i> .....	323
<i>Prediction of T-cell reconstitution after HSC transplantation</i> .....	324
<i>HSC transplantation followed by GM-CSF-secreting cell vaccines</i> .....	324
Role of MSCs in cancer .....	325
Nonmyeloablative allogeneic hematopoietic stem cell transplantation .....	325
Umbilical cord blood transplant for leukemia .....	326
hESC-derived NK cells for treatment of cancer .....	326
ESC vaccine for prevention of lung cancer .....	327
Genetic modification of stem cells for cancer therapy .....	327
<i>Genetic modification of hematopoietic stem cells</i> .....	327
<i>Use of hematopoietic stem cells to deliver suicide genes to tumors</i> .....	327
<i>Delivery of anticancer agents by genetically engineered MSCs</i> .....	328
<i>Mesenchymal progenitor cells for delivery of oncolytic adenoviruses</i> .....	328
<i>Genetically modified NSCs for treatment of neuroblastoma</i> .....	329
<b>Innovations in cell-based therapy of cancer</b> .....	<b>329</b>
Use of immortalized cells .....	329
Cancer therapy based on natural killer cells .....	329
Mesothelin as a target for cancer immunotherapy .....	330
Nanomagnets for targeted cell-based cancer gene therapy .....	330
Implantation of genetically modified encapsulated cells for anticancer therapy .....	331
<i>Antiangiogenesis therapy by implantation of microencapsulated cells</i> .....	331
<i>Recombinant tumor cells secreting fusion protein</i> .....	331
<i>NovaCaps® for pancreatic cancer</i> .....	331
A device for filtering cancer and stem cells in the blood .....	331
Cancer stem cells .....	332
<i>Role of integrative nuclear signaling in stem cell development</i> .....	332
<i>Cancer stem cell markers</i> .....	332
<i>Breast cancer stem cells</i> .....	333
<i>Role of intestinal stem cells in intestinal polyposis</i> .....	333
<i>Role of endothelial progenitor cells in tumor angiogenesis</i> .....	334
<i>Role of cancer stem cells in metastases</i> .....	334
<i>Therapeutic implications of cancer stem cells</i> .....	334
<i>Targeting cancer stem cells in leukemia</i> .....	335
<i>Targeting stem cells in ovarian cancer</i> .....	336
<i>Targeting cancer stem cells to screen anticancer drugs</i> .....	336
Cell-based therapies for malignant brain tumors .....	336
<i>Role of cancer stem cells in resistance to radiotherapy</i> .....	336
<i>Targeting stem cells in brain tumors</i> .....	337
<i>Neural stem cells for drug/gene delivery to brain tumors</i> .....	337
<i>Mesenchymal stem cells for the treatment of gliomas</i> .....	338
<i>Bone morphogenetic protein for inhibition of glioblastoma multiforme</i> .....	339
<i>Dendritic cell therapy for brain tumors</i> .....	339
<i>Encapsulated cells for brain tumors</i> .....	340
<b>Companies involved in cell-based cancer therapy</b> .....	<b>341</b>
<b>American Association for Cancer Research and ESCs</b> .....	<b>342</b>
<b>Future of cell-based immunotherapy for cancer</b> .....	<b>343</b>
<b>7. Cell Therapy for Neurological Disorders</b> .....	<b>345</b>
<b>Introduction</b> .....	<b>345</b>
<b>Regeneration of the nervous system by endogenous stem cells</b> .....	<b>345</b>
Molecular mechanism of neurogenesis .....	345

Generation of neurons from astroglia .....	346
In vivo cell replacement therapy by locally induced neural progenitor cells.....	346
<b>Types of cells used for treatment of neurological disorders.....</b>	<b>347</b>
Activated T lymphocytes .....	347
Differentiation of placenta-derived multipotent cells into neurons.....	347
Mesenchymal stem cells induced to secrete neurotrophic factors.....	348
Neural stem cells .....	348
<i>Development of human CNS stem cells.....</i>	<i>348</i>
<i>Distinction between NSCs and intermediate neural progenitors.....</i>	<i>349</i>
<i>Embryonic stem cell-derived neurogenesis.....</i>	<i>349</i>
<i>Mechanism of migration of neural stem cells to sites of CNS injury.....</i>	<i>351</i>
<i>Monitoring of implanted NSCs labeled with nanoparticles .....</i>	<i>351</i>
<i>Neural progenitor cells.....</i>	<i>351</i>
<i>Neural stem cells as therapeutic delivery vehicles .....</i>	<i>353</i>
<i>Neural stem cells in the subventricular zone of the brain.....</i>	<i>354</i>
<i>Oligodendrocyte progenitor cells .....</i>	<i>354</i>
<i>Proteomics of neural stem cells.....</i>	<i>354</i>
<i>Regulation of neural stem cells in the brain .....</i>	<i>355</i>
<i>Study of neural differentiation of hESCs by NeuroStem Chip.....</i>	<i>356</i>
<i>Transformation of neural stem cells into other cell types.....</i>	<i>356</i>
<i>Use of epidermal neural crest stem cells for neurological disorders.....</i>	<i>356</i>
Olfactory epithelium stem cells for transplantation in the CNS .....	356
Development of CNS cells from extraneural stem cells.....	357
<i>Hair-follicle stem cells for neural repair.....</i>	<i>358</i>
<i>Stem cells from human umbilical cord blood for CNS disorders .....</i>	<i>358</i>
Immortalized cells for CNS disorders .....	358
Fetal tissue transplants.....	359
Choroid plexus cells .....	360
Laboratory mice with human brain cells .....	360
Expansion of adult human neural progenitors .....	360
Neurospheres .....	361
Dental pulp cells for neuroprotection .....	361
Ideal cells for transplantation into the nervous system .....	361
<b>Cell therapy techniques for neurological applications.....</b>	<b>362</b>
Carbon nanotubes to aid stem cell therapy of neurological disorders .....	362
Cells used for gene therapy of neurological disorders.....	362
<i>Fibroblasts .....</i>	<i>362</i>
<i>Stem cells.....</i>	<i>363</i>
<i>Neuronal cells.....</i>	<i>363</i>
<i>Immortalized neural progenitor cells .....</i>	<i>363</i>
<i>Astrocytes.....</i>	<i>364</i>
<i>Cerebral endothelial cells .....</i>	<i>364</i>
<i>Human retinal pigmented epithelial cells .....</i>	<i>365</i>
Enhancement of growth of stem cells in the brain by drugs .....	365
<i>C3-induced differentiation and migration of NPC for repair of the brain .....</i>	<i>365</i>
hESCs for CNS repair.....	366
Methods of delivery of cells to the CNS .....	366
Neuronal differentiation of stem cells.....	367
Stem cells preparations for CNS disorders.....	368
Tracking of stem cells in the CNS by nanoparticles and MRI .....	368
Use of neural stem cells to construct the blood brain barrier.....	369
<i>Encapsulated cells.....</i>	<i>369</i>
<i>CNS neotissue implant.....</i>	<i>370</i>
<i>Intrathecal delivery of stem cells .....</i>	<i>370</i>
<i>CNS delivery of cells by catheters .....</i>	<i>371</i>
<i>Intravascular administration.....</i>	<i>371</i>
<b>Neurological disorders amenable to cell therapy .....</b>	<b>371</b>
Neuroprotection by cell therapy .....	372
<i>Cells secreting neuroprotective substances.....</i>	<i>372</i>
<i>Stem cells for neuroprotection.....</i>	<i>372</i>
<i>Neuroprotection by intravenous administration of HSCs.....</i>	<i>372</i>
<i>Human UCB-derived stem cells for the aging brain .....</i>	<i>373</i>
<i>hESC transplantation to prevent cognitive impairment from radiation .....</i>	<i>373</i>
Neurodegenerative disorders.....	373
<i>Role of stem cells in neurodegenerative disorders .....</i>	<i>374</i>
<i>MSCs for therapy of neurodegenerative disorders .....</i>	<i>374</i>
<i>Role of NSCs in disorders associated with aging brain.....</i>	<i>375</i>
<i>NSCs for improving memory.....</i>	<i>376</i>
Parkinson's disease .....	376
<i>Origin and fate of dopamine neurons.....</i>	<i>377</i>
<i>Human dopaminergic neurons for PD.....</i>	<i>378</i>

<i>Graft survival-enhancing drugs</i> .....	378
<i>Xenografting porcine fetal neurons</i> .....	379
<i>Encapsulated cells for PD</i> .....	379
<i>Stem cells for PD</i> .....	379
<i>Stem cells for production of glial derived neurotrophic factor</i> .....	382
<i>Potential of regeneration of endogenous stem cells in PD</i> .....	382
<i>Human retinal pigment epithelium cells for PD</i> .....	382
<i>Coaxing hESCs to produce dopamine</i> .....	383
<i>Tumorigenic potential of transplanted dopaminergic hESCs</i> .....	383
<i>Delivery of cells for PD</i> .....	384
<i>MSCs for multiple system atrophy</i> .....	384
Cell therapy for Huntington's disease.....	384
<i>Fetal striatal cell transplantation</i> .....	384
<i>Transplantation of encapsulated porcine choroids plexus cells</i> .....	385
Cell therapy for Alzheimer's disease.....	385
<i>Neural stem cell implantation for Alzheimer's disease</i> .....	385
<i>Implantation of genetically engineered cells producing NGF</i> .....	386
Cell therapy for amyotrophic lateral sclerosis.....	386
<i>Cell nuclear replacement technique for study of ALS</i> .....	387
<i>Use of stem cells for ALS</i> .....	387
<i>Transplantation of glial restricted precursors in ALS</i> .....	388
<i>Stem cell-based drug discovery for ALS</i> .....	388
Cell therapy for lysosomal storage disorders.....	389
<i>Cell therapy for Batten disease</i> .....	389
<i>Cell/gene therapy for Farber's disease</i> .....	390
<i>Genetically modified HSCs for metachromatic leukodystrophy</i> .....	390
Cell therapy for demyelinating disorders.....	390
<i>Hematopoietic stem cell transplantation for multiple sclerosis</i> .....	391
<i>Embryonic stem cells for remyelination</i> .....	392
<i>Neural precursor cells for neuroprotection in multiple sclerosis</i> .....	392
<i>Stem cells for chronic inflammatory demyelinating polyneuropathy</i> .....	392
<i>Fusokine method of personalized cell therapy of multiple sclerosis</i> .....	393
<i>X-linked adrenoleukodystrophy</i> .....	393
Cell therapy of stroke.....	393
<i>Transplantation of encapsulated porcine choroids plexus</i> .....	394
<i>Transplantation of fetal porcine cells</i> .....	394
<i>Adult stem cell therapy in stroke</i> .....	395
<i>Implantation of genetically programmed ESCs</i> .....	395
<i>Intravenous infusion of marrow stromal cells</i> .....	395
<i>Intravenous infusion of UCB stem cells</i> .....	396
<i>Intracerebral administration of human adipose tissue stromal cells</i> .....	397
<i>Intracerebral administration of multipotent adult progenitor cells</i> .....	397
<i>Neural stem cell therapy for stroke</i> .....	397
<i>Future of cell therapy for stroke</i> .....	398
Cell therapy of traumatic brain injury.....	399
<i>Cell/gene therapy for TBI</i> .....	399
<i>Clinical trials of autologous HSC therapy for TBI</i> .....	400
<i>Limitations of stem cell therapy for acute TBI</i> .....	400
<i>Improving the microenvironments of transplanted cells in TBI</i> .....	400
Cell therapy for spinal cord injury.....	401
<i>Fetal neural grafts for SCI</i> .....	401
<i>Olfactory-ensheathing cells for SCI</i> .....	402
<i>Oligodendrocyte precursor cells for treatment of SCI</i> .....	402
<i>Schwann cell transplants for SCI</i> .....	402
<i>Transplantation of glial cells for SCI</i> .....	403
Stem cells for SCI.....	403
<i>Bone marrow stem cells for SCI</i> .....	403
<i>Embryonic stem cells for SCI</i> .....	403
<i>Transplantation of MSCs for SCI</i> .....	404
<i>Transplantation of NSCs for SCI</i> .....	405
<i>Transdifferentiation of BM stem cells into cholinergic neurons for SCI</i> .....	405
Spinal stem cells for treatment of ischemic injury of spinal cord.....	405
Combined approaches for regeneration in SCI.....	406
<i>Combined cell/gene therapy for SCI</i> .....	406
Delivery of cells in SCI.....	407
<i>Intrathecal injection of cells labeled with magnetic nanoparticles</i> .....	407
<i>Intravenous injection of stem cells for spinal cord repair</i> .....	407
Clinical applications of stem cells for SCI.....	407
<i>Autologous bone marrow cell transplantation for SCI</i> .....	408
<i>Cell therapy of syringomyelia</i> .....	408
Cell therapy for neurogenetic disorders.....	408

<i>UCB stem cells for Krabbe's disease</i> .....	408
<i>Combination of cell and gene therapy for Krabbe's disease</i> .....	409
<i>Stem cell therapy for Hurler's syndrome</i> .....	409
<i>UCB stem cells for Sanfilippo syndrome type B</i> .....	410
Cell therapy of epilepsy .....	410
<i>Cell therapy of posttraumatic epilepsy</i> .....	410
<i>Cell therapy for temporal lobe epilepsy</i> .....	411
<i>Cell therapy for pharmaco-resistant epilepsies</i> .....	411
Cell therapy for developmental neurological disorders .....	411
Cell therapy for cerebral palsy .....	412
Cell therapy for muscular dystrophy .....	412
<i>Combination of cell and pharmacotherapy for DMD</i> .....	413
<i>Myoblast transplant for Duchenne muscular dystrophy</i> .....	413
<i>Myoblast-based gene transfer</i> .....	413
<i>Myoblasts lacking the MyoD gene</i> .....	414
<i>Myoblast injection for treatment of other muscular dystrophies</i> .....	414
<i>Stem cells for DMD</i> .....	415
Cell therapy for Autism .....	416
Management of chronic intractable pain by cell therapy .....	416
<i>Implantation of chromaffin cells</i> .....	417
<i>Role of stem cells in management of pain</i> .....	417
<i>Implantation of astrocytes secreting enkephalin</i> .....	418
<i>Cells for delivery of antinociceptive molecules</i> .....	418
<i>Implantation of genetically engineered cells</i> .....	418
<i>Cell therapy for low back pain</i> .....	418
Cell therapy for retinal degenerative disorders.....	419
<i>Genetically engineered retinal pigmented epithelial cell lines</i> .....	420
<i>Delivery of CNTF by encapsulated cell intraocular implants</i> .....	420
<i>Stem cell transplantation in the retina</i> .....	420
<i>Isolation of RPE cells from hESCs using transcriptomics</i> .....	421
<i>ESCs for retinal degenerative disorders</i> .....	421
<i>Neuroprotective effect of neural progenitor cell transplantation</i> .....	422
<i>Human retinal stem cells</i> .....	422
<i>Combining cell and gene therapies for retinal disorders</i> .....	422
Stem cell therapy for hearing loss.....	422
Cell therapy for peripheral nerve lesions.....	423
<i>Cell transplants for peripheral nerve injuries</i> .....	423
<i>Treatment of diabetic neuropathy with endothelial progenitor cells</i> .....	424
<b>Clinical trials of cell therapy in neurological disorders</b> .....	<b>424</b>
<b>Future prospects for cell therapy of CNS disorders</b> .....	<b>425</b>
<b>8. Ethical, Regulatory, and Safety Aspects of Cell Therapy .....</b>	<b>427</b>
<b>Introduction</b> .....	<b>427</b>
<b>Safety issues of cell therapy</b> .....	<b>427</b>
Immune-mediated reactions to transplanted stem cells .....	427
Human virus infections associated with stem cell transplantation .....	428
<i>Herpes simplex virus type 1</i> .....	428
<i>Cytomegalovirus</i> .....	428
Opportunistic infections among hematopoietic stem cell transplant recipients .....	428
Carcinogenic potential of stem cells and its prevention .....	429
FDA safety regulations for cell and tissue products.....	429
FDA Guidance on license applications for umbilical cord blood products.....	429
<b>Political and ethical aspects of hESC research in the US</b> .....	<b>430</b>
Ethical issues concerning fetal tissues.....	430
<i>Morality and hESC research</i> .....	431
Opponents of hESC research in the US .....	431
<i>Use of hESCs in NIH-supported research</i> .....	432
<i>Public opinion in the US about hESC research</i> .....	434
<i>Human stem cell cloning in the US</i> .....	435
<i>Stem cell guidelines of various US institutions</i> .....	435
Ethics of transplanting human NSCs into the brains of nonhuman primates .....	437
<b>Stem cell lines available worldwide</b> .....	<b>437</b>
<b>Stem cell policies around the world</b> .....	<b>438</b>
Countries with no defined policies on hESC research .....	439
Australia .....	439
Canada.....	440
China .....	440
Denmark .....	441
France.....	441
Germany .....	442
India .....	443

Ireland .....	444
Israel .....	444
Italy .....	445
Japan .....	445
The Netherlands .....	446
Saudi Arabia.....	446
Singapore .....	446
South Africa .....	447
South Korea .....	447
Spain .....	447
Sweden .....	448
Switzerland .....	448
United Kingdom.....	449
<i>ESC bank</i> .....	449
European Union .....	450
<i>EU guidelines for stem cell research</i> .....	450
<i>EMBO's recommendations for stem cell research</i> .....	452
United Nations, cloning and nuclear transfer.....	453
The Embryo Project for information on ESC research .....	453
Concluding remarks about ethics of ESC research .....	453
<b>Ethical issues concerning umbilical cord blood .....</b>	<b>454</b>
<b>Cell therapy tourism .....</b>	<b>454</b>
<b>Regulatory issues .....</b>	<b>455</b>
Regulation of cord blood banks in the US .....	455
Regulatory issues for biotechnology-derived drugs.....	455
Regulation of cell selection devices for production of PBSCs at point of care .....	455
FDA rules for human cells and tissues.....	456
FDA regulation of fetal cellular or tissue products.....	457
FDA and clinical trials using hESCs .....	457
Cell and gene therapy INDs placed on hold by the FDA .....	458
Regulatory issues for genetically engineered cell transplants .....	459
FDA guidelines for human tissue transplantation .....	459
Xenotransplantation .....	459
<i>Clinical Protocol Review and Oversight</i> .....	459
<i>Informed consent and patient education</i> .....	460
<i>Xenotransplantation product sources</i> .....	460
<i>FDA guidelines for xenografts</i> .....	461
Regulations relevant to cell therapy in the European Union .....	462
<i>Regulations about use of stem cells</i> .....	463
<i>EMA regulation of cell/gene therapy</i> .....	463
<i>Guidelines for cell therapy in the UK</i> .....	464
<b>NIH and stem cells.....</b>	<b>464</b>
ESC lines approved under the new NIH guidelines.....	465
<b>Clinical trials in cell therapy.....</b>	<b>465</b>
<b>Stem cell patents .....</b>	<b>465</b>
Stem cell patents in the United States .....	465
<i>Current status of Thomson patents at WARF</i> .....	466
Stem cell patents in the European Union.....	467
<b>9. References.....</b>	<b>469</b>

## Tables

Table 1-1: Landmarks in the history of cell therapy .....	25
Table 1-2: Examples of cells involved in various diseases .....	30
Table 2-1: Types of human cells used in cell therapy.....	33
Table 2-2: A selection of companies providing cell culture media .....	37
Table 2-3: A sampling of companies supplying cell sorters .....	40
Table 2-4: Companies involved in cell-based drug discovery .....	46
Table 2-5: Methods of delivery of cells for therapeutic purposes .....	48
Table 2-6: Therapeutic applications of encapsulated cells.....	52
Table 2-7: Companies working on encapsulated cell technology.....	55
Table 2-8: Molecular imaging methods for tracking cells in vivo.....	60
Table 3-1: Companies involved in cord blood banking as a source of stem cells .....	94
Table 3-2: Sources of adult human stem cells .....	101
Table 3-3: Enhancing engraftment, mobilization and expansion of stem cells .....	123
Table 3-4: Applications of stem cells .....	141
Table 3-5: Advantages and limitations of methods for optimizing MSCs .....	150
Table 3-6: Growth factors with positive effects on stem cells and applications .....	161
Table 3-7: Examples of drugs that induce granulocytopenia at stem cell level .....	163
Table 3-8: Academic institutes involved in stem cell research.....	174
Table 3-9: Companies involved in stem cell technologies .....	176
Table 4-1: Therapeutic applications of regulatory T cells (T-regs) .....	192
Table 4-2: Various tissue/cell therapy approaches to the treatment of type 1 diabetes .....	197
Table 4-3: Companies involved in cell therapy for insulin-dependent diabetes .....	212
Table 4-4: Major pulmonary disorders potentially treatable by stem cell manipulation .....	226
Table 4-5: Cell-based repair of knee cartilage damage .....	241
Table 5-1: Classification of various types of cell therapy for cardiovascular disorders .....	265
Table 5-2: Clinical trials of cell therapy in cardiovascular disease.....	298
Table 6-1: Cell therapy technologies used for cancer.....	305
Table 6-2: Companies involved in developing cell-based therapies for cancer.....	341
Table 7-1: Experimental use of immortalized cells for CNS disorders .....	358
Table 7-2: Methods for delivering cell therapies in CNS disorders.....	367
Table 7-3: Neurological disorders amenable to cell therapy.....	371
Table 7-4: Types of cell used for investigative treatment of Parkinson's disease .....	376
Table 7-5: Status of cell therapies for Parkinson's disease .....	377
Table 7-6: Clinical trials with cell-based therapies in neurological disorders.....	424
Table 8-1: Possible adverse reactions and safety issues of cell therapy.....	427
Table 8-2: Listed numbers of stem cell lines around the world as of end of 2008 .....	438
Table 8-3: Stem cell policies around the world .....	438

## Figures

Figure 1-1: Interrelationships of cell therapy to other technologies .....	27
Figure 1-2: Interrelationships of gene, cell and protein therapies.....	29
Figure 3-1: A simplified biological scheme of embryonic stem Cells .....	66
Figure 3-2: Steps of iPS cell production .....	97
Figure 3-3: Flow chart of development of stem cells with potential bottlenecks.....	181
Figure 5-1: hESC-derived cardiomyocytes from laboratory to bedside .....	277
Figure 6-1: A scheme of generation and administration of tumor antigen-pulsed dendritic cells .....	314
Figure 6-2: Stem cell transplantation techniques .....	320
Figure 7-1: Stem cells that can give rise to neurons.....	353
Figure 7-2: Approaches to stem cell therapy in stroke .....	395