

# Index

## A

Acute implant failure, 26–28  
Adaptive optics scanning laser  
  ophthalmoscopy (AOSLO), 268  
Adeno-associated virus (AAV), 258  
Adipose-derived stem cells (ADSCs), 156, 230  
Adult retinal pigment epithelial-19  
  (ARPE-19), 263  
Adult stem cells, 229, 230  
Age-related macular degeneration (AMD),  
  250, 252, 255, 257  
Air-liquid interface model, 207  
 $\beta$ -Air oxygenated macroencapsulation  
  device, 34  
Alginate, 127, 130, 152, 153, 155  
Amniotic fluid-derived stem cells (AFSCs), 243  
Angiogenesis, 144–146  
Anionic ring-opening polymerization, 158  
Anterior chamber-associated immune  
  deviation (ACAID), 254  
Anticoagulation therapy, 122  
Antiepileptic drugs (AEDs), 87  
Antiepileptogenic, 90  
Antigen-presenting cells (APCs), 100  
ARPE-19 cells, 284  
Artificial oxygen carriers (AOCs), 35

## B

B7/CD28 family, 102  
Biocompatibility  
  appropriate host response, 124  
  bioartificial organ, 124  
  biopolymers, 127  
  biotolerability, 126  
  cell encapsulation, 127  
  chemical anomalies, 126  
  chemotactic cytokines, 124  
  DAMPs, 126

  definition, 123  
  hydrophilic polymers, 126  
  immune response, 124  
  innate immune system, 126  
  intracapsular modifications, 130, 131  
  LPS, 128  
  microfluids, electrospinning and  
    emulsification approaches, 127  
  NEC-1, 126  
  necrosis and necroptosis, 126  
  PAMPs, 128  
  polyaminoacids, 127  
  PRRs, 125  
Bioluminescence imaging (BLI), 7, 8  
Biomaterial-based systems, 143  
Biomaterials, 40, 152, 153, 155–158, 160–162  
  cell anchorage, 151  
  cellular-based therapies, 150  
  ECM, 151  
  naturally occurring polymers  
    alginate, 152, 153, 155  
    characteristics, 152  
    fibrin, 156, 157  
    gelatin, 157  
  physical immobilization and covalent  
    coupling, 152  
  polymeric materials, 152  
  synthetic polymers  
    PEG, 158, 160  
    PLGA, 160, 161  
    PLLA, 161, 162  
Bioprinting, 230  
Biotolerability  
  factors, 129  
  homeostasis interfering process, 130  
  intracapsular milieu, 130  
  mechanotransduction, 130  
  physicochemical methodologies, 129  
  polymer brushes, 129

- BLI. *See* Bioluminescence imaging (BLI)
- Blood-mediated inflammatory reactions (BMIR), 2
- B16 melanoma model, 109
- Bone, 240
- Bone marrow stem cells (BMSCs), 149, 179
- Brain-derived neurotrophic factor (BDNF), 92
- C**
- Cancer immunotherapy
  - anti-PD-1 and anti-PD-L1 agents, 109
  - CpG oligonucleotides (TLR ligand), 109
  - DCs and antigen loading, 106, 107
  - intratumoral injection, 109
  - in vivo DC targeting, 107–109
  - vaccine, 109–112
- Cancer vaccines, 100
- Cardiac progenitor cells (CPCs)
  - cell-free approaches, 179
  - optimal cell type, cardiac regeneration, 180
- Cardiac regeneration, cell reprogramming, 180, 182–185
  - BMSC, 179
  - cell-free approaches, 179
  - from differentiated iPSC
    - CM enrichment protocols, 182
    - CPC potential, 182, 183
    - embryoid bodies, 180
    - VEGF, use of, 182
  - direct reprogramming
    - adult mouse fibroblasts into iCPC, 185
    - human amniotic fluid-derived cells into EC, 184
    - human fibroblasts into iCM, 183, 184
  - in vivo conversion, cardiac fibroblasts, 185
  - mammalian capacity, 178
  - optimal cell types, 180
  - partial cell reprogramming approach, 183
  - reprogramming strategies, 180
  - xenotransplantation, 179
- Cardiovascular system, 145
- Cartilage, 241–242
- CD133+ stem cells, 304, 310
- Cell-based medicinal product (CBMP), 310
- Cell culture systems
  - advantages, 199
  - 2D cell culture, 199
- Cell encapsulation systems, 23
- Cell-free treatment, 64, 65
- Cell grafting
  - antiepileptogenic, 90
  - BNC- and FC-treated grafts, 89
  - bystander effects, 88
  - cell types, 88
  - GABAergic precursor cells and neurons, 90
  - inhibition strategies, 90
  - MSCs, 89
  - therapeutic effects, 88
- Cell homing, 162
- Cell NewCos, 282, 289
- Cell reprogramming, 174–176, 185, 186
  - application, 177, 178
  - cardiac regeneration (*see* Cardiac regeneration, cell reprogramming)
  - cell fusion experiments, 173
  - iPSCs
    - differentiation potential, 176
    - discovery and derivation, 174, 175
    - partial and direct, 176, 177
    - rare disease modeling (*see* Rare disease modeling)
    - reprogramming strategies, cardiac and vascular cells, 181
    - tumorigenicity, 191
- Cell therapy
  - adult cell therapy, 283, 284
  - applications
    - organ printing, 238
    - post-organ printing, 238, 239
    - pre-organ printing, 234–238
    - regenerative medicine, 227, 228
    - scaffold-based bioprinting, 234–237
    - scaffold-free bioprinting, 235–238
  - assay-based approaches, 3
  - BMIR, 2
  - Cell NewCo, 289
  - cell sample isolation, 291
  - cellular environment, 2
  - drug companies, 281
  - economic considerations, 292
  - immune modification, 3
  - inflammatory and immune responses, 3
  - innovation ecosystem, 282
  - marketing considerations, 292, 293
  - muscular dystrophies, 303, 308
  - pharma, 290
  - regenerative cell therapy, 2, 282–284
  - team considerations, 285–288
  - technology considerations, 285
  - timing considerations, 289
- Cell tracking, 6, 7, 10
- Chemical and manufacturing control (CMC), 291
- Chinese hamster ovary (CHO), 255
- Chip drug screening platforms, 216, 217
- Chronic fibrosis
  - biomaterial, 40

- FACS, 41
  - parathyroidectomy, 40
- PTH, 40
- TMTD, 41
  - zwitterionic coatings, 41
- Ciliary neurotrophic factor (CNTF), 260
- Computer-aided design (CAD), 232
- Cone cells, 251
- Conventional/myeloid DCs (cDCs), 101
- Crypt base columnar (CBC), 204
- Cystic fibrosis, 212
- Cytokine storm, 27
- Cytotoxic T lymphocytes (CTLs), 100
  
- D**
- 2D and 3D culture systems, 198
- Danger-associated molecular patterns (DAMPs), 125
- Dendritic cells (DCs)
  - activating signals, 102, 103
  - antigen, 105 (*see also* Cancer immunotherapy)
  - cancer vaccines, 111
  - cDCs, 101
  - clinical trials, 108, 110
  - co-stimulatory molecules, 102
  - inflammatory, 102
  - inhibitory signals, 103
  - pDCs, 101
  - skin, 102
  - T cells, 104
  - tumors, 105, 106
- 3D Matrigel, 204
- Dopamine, 73, 74, 79
- Droplet-based bioprinting (DBB), 230, 232
- Drug discovery, 218
- Duchenne muscular dystrophy (DMD), 190
  - cell membrane fragility, 301
  - mutations, 301
  - myofibers, 301
  
- E**
- Edmonton protocol, 209
- Ellipsoid zone (EZ), 250, 269
- Embryonic stem cells (ESCs), 63, 228, 302, 307
- Encapsulated cell biodelivery (ECB)
  - advantage, 91
  - BDNF and GDNF, 92, 93
  - galanin, 92
  - NTF, 92–94
- Encapsulated cell technology (ECT), 263
  
- Encapsulation
  - bioartificial organs, 132
  - $\beta$ -cell therapy
    - biomass, 23
    - cell encapsulation, 23, 24
    - endocrine pancreas, 23
    - microencapsulated islets, 24
  - donor tissue, 121
  - hypoxia, 31–33
  - immune rejection, 28–30
  - immune system, 121
  - immunoisolation, 121
  - immunosuppression, 121
  - innate and adaptive immune responses, 131
  - macrodevices, 28
  - metabolites, 122
  - minimal capsule properties, 128
  - organ and cell transplantation, 121
- Endothelial cells (ECs), 146
- Endothelial colony forming cells (ECFCs), 149
- Endothelial dysfunction, 147
- Endothelial progenitor cells (EPCs), 149
- Epilepsy
  - AEDs, 87
  - clinical features, 86
  - definition, 86
  - history, 85, 86
  - SRSs, 87
  - TLE, 86
- Epileptogenesis, 86
- Ex vivo experimental models, 102
- Exosome transplantation therapies, 65
- Expanded polytetrafluoroethylene (ePTFE), 30
- Extracellular matrix (ECM), 131, 144, 234
- Extravascular devices, 123
- Extrusion-based bioprinting (EBB), 232
- Eye, 249–251
  
- F**
- Fetal stem cells, 229
- Fetal tissue, 74, 77
- Fibrin, 156
- Fibrinogen, 156
- Fibro-adipogenic progenitors (FAPs), 306
- Förster resonance energy transfer (FRET), 5
- Fovea, 259
- FVM grafts, 78
  
- G**
- $\alpha$ -Galactoceramide ( $\alpha$ -GalCer), 103
- Galanin, 92
- Gamma-aminobutyric acid (GABA), 90

- Gelatin, 157  
 Generally recognized as safe (GRAS), 157  
 Geographic atrophy, 255, 264, 266–268  
 Glaucoma, 253, 268, 269  
 Glial cell-derived neurotrophic factor (GDNF), 92  
 Glial fibrillary acidic protein (GFAP), 270  
 Good manufacturing practice (GMP), 141  
 Granulocyte-macrophage colony-stimulating factor (GM-CSF), 102
- H**
- Hematopoietic stem cells (HSCs), 148, 283  
 High-throughput screening (HTS), 190  
 Hippocampal sclerosis (HS), 86  
 Human dermal microvascular endothelial cells (HDMECs), 146  
 Hyposalivation, 213  
 Hypoxia, 31, 33
  - AOCs, 35
  - β-cells, 31
  - CP, 36
  - MIN6 cells, 37
  - OCR, 32
  - oxygen partial pressure, 32
  - PFC, 35
  - PFD, 35
  - PLGA-CP scaffolds, 36
  - refillable gas supply, 34, 35
  - SP, 36
- I**
- Iatrogenic hypoglycemia, 19  
 Immature DCs (iDCs), 101  
 Immune modification, 3  
 Immune rejection, 28–31  
 Immunoisolation, 124  
 Immunoprotection, 30, 34, 42  
 In vivo system, 197–199  
 Induced pluripotent stem cells (iPSCs), 63, 77, 210, 211, 229, 261, 307
  - application, 177, 178
  - characteristics, 174
  - CM enrichment protocols, 182
  - differentiation potential, 176
  - disease modelling development, 187
  - DMD, 190
  - embryoid bodies, 180
  - HTS, 190
  - molecular features, 175
  - patient-specific, reprogramming, 187, 188
  - somatic cells, reprogramming, 174, 177
  - VEGF, use of, 182
- Inflammation, 26–28, 40  
 Inflammatory DCs, 102  
 Inner and outer segments (IS/OS), 250, 272  
 Insulin, 131  
 Insulin-producing cells (IPC), 210  
 Interleukin (IL)-4, 102  
 Intestinal stem cells, 199, 204, 206–208  
 Intraocular pressure (IOP), 268  
 Invariant natural killer T cells (iNKTs), 103  
 Ipilimumab, 109  
 Ischemic diseases, 148, 149, 162  
 Ischemic stroke, 53, 54  
 Ischemic vascular diseases, 139  
 Islet encapsulation failure modes
  - acute implant failure, 26–28
  - subacute processing stress, 26
 Islet transplantation, 23–26
  - CIT-07, 21
  - side effects, 21
  - site selection, 22
- K**
- Keyhole limpet hemocyanin (KLH), 106
- L**
- Langerhans cells (LCs), 102  
 Laser-based bioprinting (LBB), 233  
 Lateral temporal lobe epilepsy (ITLE), 86  
 Leber congenital amaurosis (LCA2), 259  
 Lgr5 stem cell, 208  
 Limited efficacy, 311  
 Lipopolysaccharide (LPS), 127  
 Lipoteichoic acids (LTA), 128  
 Liver, 242  
 +4 Label retaining cells (LRCs), 204  
 Lucentis™, 254  
 Lymphangiogenesis (lymphatic vessels), 144–146  
 Lymphatic endothelial cells (LECs), 147  
 Lymphatic endothelial progenitor cells (LEPCs), 148  
 Lymphatic vascular system, 145
- M**
- Macro/microencapsulation, 122, 123  
 Macrodevice, 28, 34, 38, 46  
 Macular telangiectasia (MacTel), 252, 269, 270, 272  
 Magnetic resonance imaging (MRI), 7  
 Major histocompatibility complex (MHC), 101  
 Matrigel, 208, 210, 219

- Mechanotransduction, 130  
Mesenchymal cell therapy, 283  
Mesenchymal stem cells (MSCs), 149, 283  
  bone marrow, 305  
  characterized, 304  
  clinical trials, 308  
  immunosuppressive function, 305  
  inflammation, 306  
  therapeutic applications, 305  
  UCB-MSCs, 306  
Mesial temporal lobe epilepsy (mTLE), 86  
Mesoangioblasts, 303, 304, 310, 311  
MiniMed 670G hybrid closed-loop system, 20  
Molecular imaging, 4, 6  
  BLI, 7  
  MRI, 7, 9, 10  
  optical imaging  
    bright-field mode, 4  
    fluorescent mode, 4, 6  
  PET imaging, 6–7  
  spectroscopy, 9  
MSC spheroids  
  chondrogenic differentiation, cell, 200  
  clinical trials, 200  
  2D system, 202  
  3D system, 200–202  
  ECM, 200  
  ex vivo, 200  
  intracellular and paracrine signaling, 202  
Müller cell, 253, 254, 269  
Muscle contraction process, 298  
Mycobacterium tuberculosis heat shock protein X (HspX), 107  
Myosin heavy chain (MYH) gene expression, 299
- N**  
NEC-1, 126, 131  
Nerve/brain, 242  
Neural grafting, 77  
Neural stem cells (NSC), 76  
Neurodegeneration, 55, 61  
Neuroprotection, 264, 268, 269  
Neurotrophic factors (NTFs), 92, 93  
Neurovascular disease, 56–63  
  cell-free treatment, 64, 65  
  components, 54  
  exosome transplantation therapies, 65  
  stem cells (*see* Stem cell therapy)  
  TBI and stroke, 53  
Niche factors, 207, 209
- O**  
Ophthalmic diseases  
  anti-angiogenic proteins, 272–274  
  ciliary neurotrophic factor, 264–266  
  drugs, 253  
  encapsulated cell-based delivery, 262–264  
  eye, 249–251  
  gene delivery, 260  
  geographic atrophy and retinitis pigmentosa, 266–268  
  glaucoma, 268, 269  
  macular telangiectasia, 269–272  
  ocular immune privilege, 254  
  recombinant proteins, 254–258  
  viral vectors, 258–260  
Optical coherence tomography (OCT), 259, 267, 269, 272  
Optical imaging, 5, 6  
  bright-field mode, 4  
  fluorescent mode  
    EosFP, 6  
    FRET, 5  
  spinal cord injury, 5  
Organ on a chip, 217, 218  
Organoids, 204, 206–209, 212, 213  
  biomaterial-free architectures, 203  
  CNS, 204  
  defined, 203  
  disease models  
    AIAT, 213  
    bacterial and viral infection, 213  
    cancer cells, 212  
    CRISPR/Cas9 and viral transduction, 212  
    cystic fibrosis, 212  
    hyposalivation, 213  
    transcriptional and proteomic analysis, 213  
  3D Matrigel, 204  
  drug screening, 213, 215  
  intestine  
    air-liquid interface model, 207  
    BMP, 207  
    CBC, 204  
    Lgr5+ ISCs, 206  
    LRCs, 204  
    Matrigel, 208  
    niche factors, 207, 209  
    stem cells, 208  
    Wnts, 207, 209  
  iPSC, 211  
  lingual tissue, 212  
  mini-brain development, 203, 204, 206  
  pallium tissues, 204  
  pancreas, 209–211

Organoids (*cont.*)  
 therapeutics and injectable products, 215  
 tumor, 214  
 Outgrowth endothelial cells (OECs), 149  
 Oxygen consumption rate (OCR), 32, 33

## P

Pancreas, 242  
 Pancreatic organoids  
 endocrine functions, 210  
 hydrogels, 210  
 IPC, 210  
 iPS, 211  
 Matrigel, 210  
 neonatal rat endocrine cells, 210  
 T1D, 210  
 Paracrine signaling, 198, 202  
 Parkinson's disease (PD), 75, 76  
 cell transplantation, 79  
 clinical trial outcomes  
 DA neurons, 75  
 NIH trial, 75  
 UPDRS, 75  
 VM allografts, 76  
 FVM grafts, 78  
 L-dopa, 73  
 Lewy bodies transfer, 78  
 SN, 73  
 stem cell grafting, 76–79  
 UPDRS, 75  
 VM grafting, 74, 79  
 Pathogen-associated molecular patterns  
 (PAMPS), 125, 128  
 Pattern recognition receptors (PRRs), 125  
 Perfluorocarbon (PFD), 35  
 Peripheral blood mononuclear cells  
 (PBMCs), 106  
 PET tracer Pittsburgh compound B (PiB), 6  
 Photoreceptors (PRs), 251, 252, 254, 258–262,  
 264, 269, 270  
 Plasmacytoid DCs (pDCs), 101  
 Poly(ethylene glycol) (PEG), 158, 160  
 Poly(lactic-co-glycolic acid) (PLGA), 160, 161  
 Poly(l-lactic acid) (PLLA), 161, 162  
 Polyaminoacids, 127  
 Polydimethylsiloxane (PDMS), 216  
 Polymers of lactic acid and glycolic acid  
 (PLGA), 108  
 Positron-emission tomography  
 (PET), 6, 75  
 Primary open-angle glaucoma (POAG), 269

Prospective Randomized Study of  
 Mesenchymal Stem Cell Therapy in  
 Patients Undergoing Cardiac  
 Surgery (PROMETHEUS), 149  
 Proteoglycans (PG), 128

## R

Rare disease modeling, 186, 187  
 cell reprogramming  
 iPSC disease modelling development,  
 187  
 iPSC generation, 187  
 mouse models, 186  
 definition, 186  
 epidemiology, 186  
 genome editing, 189, 190  
 patient-specific iPSC, reprogramming,  
 187, 188  
 Recombinant adeno-associated virus  
 (rAAV), 76  
 Regenerative medicine, 2, 57, 58  
 Retina  
 AMD, 252  
 glaucoma, 253  
 MacTel, 252  
 pluripotent stem cells, 261  
 stem cells, 261, 262  
 Retinal ganglion cell (RGC), 268  
 Retinal pigment epithelium (RPE), 250, 252,  
 253, 258  
 Retinitis pigmentosa (RP), 249, 257, 261, 264,  
 266–268, 274  
 Revascularization, 148–150  
 angiogenesis and lymphangiogenesis,  
 144–146  
 biology challenges, 141–143  
 biomaterial systems, 140, 151  
 blood and lymphatic vasculatures, 145  
 blood perfusion, 141  
 bolus methods, 141  
 cell-based therapies, 139  
 cell therapy approaches, 142  
 coronary artery disease, 141  
 differentiated cells, 146–148  
 engineering challenges, 143, 144  
 naturally occurring and synthetic polymers,  
 153–155  
 organs, 140  
 progenitors cells  
 adult blood vessel formation and  
 postnatal vasculogenesis, 150

- bone marrow-derived mononuclear cells, 150
  - EPCs, 149
  - HSCs, 148
  - MSCs, 149
  - OECs, 150
  - vascular networks, 148
  - synthetic polymers, 159–160
  - TAC-HFT trial evaluation, 141
  - Risk analysis approach, 310
- S**
- Satellite cells, 302
  - SC-Islets, 43
  - Seahorse extracellular flux technique, 33
  - Sequence-specific nucleases (SSNs), 189, 190
  - Severe combined immunodeficient (SCID), 146
  - Sipuleucel-T, 109
  - Skeletal muscle tissue, 297, 298, 308
    - architecture
      - actin, 298
      - myosin, 297
      - plasma membrane, 297
      - tissue regeneration process, 308
    - fiber organization, 299, 300
    - muscle contraction process, 298
    - sarcomere structure, 298
  - Skin dendritic cells, 102
  - Soluble VEGF receptor (sVEGFR), 273
  - Spheroid. *See* MSC spheroid
  - Spontaneous recurrent seizures (SRSs), 87
  - Squamous cell carcinoma (SCC), 109
  - Stem cell bioprinting
    - bone, 240
    - cardiac, 243
    - cartilage, 241–242
    - liver, 242–243
    - nerve/brain, 242
    - pancreas, 242
    - skin tissue, 243
    - vasculature, 239, 240
  - Stem cell-derived B-cells
    - clinical translation, 44, 45
    - ESC, 42
    - glucoreponsive, 43, 44
  - Stem cell grafting, PD
    - clinical setting, 77
    - DA neurons, 76, 77
    - iPSC, 77
    - NSC, 76
    - rAAV, 76
- Stem cells
- CD133+, 304
  - characteristics, 302
  - combination therapies, 60
  - complication, 62
  - DMD, 309, 310
  - ESCs, 302
  - FAPs, 306
  - intra-arterial transplantation, 311
  - iPSCs, 307
  - mechanisms, 58, 59
  - mesoangioblasts, 303, 304
  - MSCs (*see* Mesenchymal stem cells (MSCs))
  - potential adverse effects, 63
  - satellite cells, 302
  - spleen, 61
  - stroke, 57
  - TBI, 57, 58
  - therapeutic compounds, 60
  - tPA, 56
- Stroke and TBI, 53
- acute pathology, 54–55
  - cell-free treatment, 64, 65
  - chronic pathology, 55, 56
- Substantia nigra (SN), 73
- Superparamagnetic iron oxide (SPIO), 9
- T**
- Temporal lobe epilepsy (TLE), 86
  - Therapeutic angiogenesis, 139
  - Tissue engineering, 139, 158
  - Tissue plasminogen activator (tPA), 56
  - Tissue regeneration processes, 308
  - Transcription activator-like effector nucleases (TALENs), 189
  - Tumor necrosis factor (TNF) family receptors, 102
  - Type 1 diabetes (T1D)
    - insufficient insulin, 19
    - pharmacological challenge, 19
- U**
- Unified Parkinson's Disease Rating Scale (UPDRS), 75
  - Upconversion nanoparticles (UCNPs), 107–108

**V**

Vaccination, 100  
Valley of death, 282  
Vascular endothelial growth factor (VEGF), 254  
Vascularization, 37–40  
Vasculature, 239, 240  
Ventral mesencephalon (VM), 74, 75

**X**

Xenotransplantation, 179

**Z**

Zinc finger nucleases (ZFNs), 189  
Zwitterionic coatings, 41