

# Index

## A

- Adaptive immune system, 103
- Adeno-associated viral (AAV), 10
- Adult-onset vitelliform macular dystrophy (AVMD), 7
- Age-related macular degeneration (AMD), 2–4, 38, 58, 59, 142, 172
- Alcon Constellation®, 158
- Alcon NGENUITY® 3D Visualization System, 158
- Allogeneic transplantation, 108
- Anesthesia
  - animal positioning, 153
  - eye-specific preparations, 153
  - macaques/non-human primates, 152
  - pig, 152
  - rabbit
    - eye-specific preparations, 151, 152
    - head positioning, 151
    - pain management, 151
    - premedication, 151
    - rectal thermometer, 151
  - small rodents (mice and rats), 150
- Angiotensin-1 (ANG-1), 173
- Anterior Chamber-Associated Immune Deviation (ACAID), 82
- Apolipoprotein E (*APOE*), 8
- Assay systems, 183
- Autosomal dominant radial drusen (ARD), 13
- Autosomal dominant
  - vitreoretinohoroidopathy (ADVIRC), 7
- Autosomal recessive bestrophinopathy (ARB), 7

## B

- Balance salt solution (BSS), 155
- Basic fibroblast growth factor (bFGF), 66
- Basiliximab, 109
- Best disease (BD), 7, 38
- Best vitelliform macular dystrophy (BVMD), 16
- Bioink, 174, 175
- Bioprinting, 174
- Bipolar cells, 124
- Bleb retinal detachment (bRD), 157, 162, 163
- Blindness, 57
- Blood–brain barrier (BBB), 100
- Bone marrow mesenchymal stem cells (MSCs), 67, 68
- Bone morphogenic protein (BMP), 178
- Brain-derived neurotrophic factor (BDNF), 65

## C

- Calcium- and magnesium-containing Hank's balanced salt solution (CM-HBSS), 156
- Cell rejection
  - allogenic cells, 107, 108
  - circumvent, 108, 109
  - prevention, 108
- Cell replacement, 100, 106, 107, 132
- CellTiterGlo, 185
- Cell transplantation, 63, 64, 99, 100
- Cellular replacement strategies, 123
- Cellular retinaldehyde-binding protein (*CRALBP*), 8
- Cellular systems, 172
- Cell viability assay, 185

- Central nervous system (CNS), 100, 125  
 Chemical biology studies, 184  
 Chetomin, 70  
 Chondroitin sulfate proteoglycan (CSPG), 105  
 Choriocapillaris, 175, 177  
 Choroid, 174  
 Choroidal neovascularization (CNV), 4, 63, 174  
 Choroideremia, 38  
 Ciliary neurotrophic factor (CNTF), 66  
 Complement system, 103, 104  
 Connective tissue growth factor (CTGF), 41  
 CRISPR/Cas technology, 143  
 CRXp-GFP reporter, 184  
 Cyclosporine, 107, 146  
 Cyclosporine A, 62  
 Cynomolgus (*Macaca fascicularis*), 146
- D**  
 Dendritic cells (DC), 107  
 3,3'-Diaminobenzidine (DAB), 181  
 Differentiated RPE cells  
   functionality, 76  
   purity, 75  
   safety, 73–75  
 Disk diameter (DD), 162  
 Dominant optic atrophy (DOA), 129  
 Doxycycline, 148  
 Doyne's honeycomb retinal dystrophy/  
   Malattia Leventinese (DHRD/ML), 4–6  
 Drug development, 123  
 Drusen, 4, 9  
 Dual leucine zipper kinase (DLK)  
   pathway, 130
- E**  
 EGF-containing fibulin extracellular matrix  
   protein 1 (EFEMP1), 3  
 Electric cell-substrate impedance sensing (ECIS), 13  
 Electroretinogram (ERG), 61  
 Embryoid body (EB), 70  
 Embryonic development, 122  
 Embryonic stem cells (ESCs), 34, 178  
 Endoplasmic reticulum (ER), 7  
 Epidermal growth factor (EGF), 41  
 Epithelial–mesenchymal transition (EMT), 40,  
   41, 43  
 Extracellular matrix (ECM), 3, 39, 132
- F**  
 Fenestrated endothelial cell linked protein  
   (FELS), 177  
 Fenestration marker, 177  
 Fibroblast growth factor (FGF), 178  
 Fibroblasts, 173  
 Fluid–air exchange (FAX), 157  
 Fluorescence imaging-based assays, 187  
 Fluorescence reporter, 184  
 4-hydroxytamoxifen (4-OHT), 185
- G**  
 Genetic disease models, 130  
 Genetic engineering, 143  
 Glasgow Minimum Essential Medium  
   (GMEM), 72  
 Glial-derived neurotrophic factor (GDNF), 66  
 Global Haplotype Cell Banking Initiative,  
   84, 85  
 Glucocorticoids, 109  
 Green fluorescent protein (GFP), 67  
 Gyrate atrophy, 16, 17
- H**  
 Hematoxylin and eosin (H&E), 181  
 Hepatocyte growth factor (HGF), 41  
 High content screening (HCS), 184  
 High-performance liquid chromatography  
   (HPLC), 37  
 High-throughput drug screening (HTS), 34,  
   183–185  
 hiPSC-based disease modeling, 18–22  
 Human amniotic membrane (hAM), 77  
 Human central nervous system stem cells  
   (HuCNS-SCs), 67  
 Human cortical progenitor cells, 66  
 Human embryonic stem cells (hESCs), 69  
 Human hematopoietic stem cells (HSCs), 173  
 Human-induced pluripotent stem cells  
   (hiPSCs), 69  
   AMD, 12, 14  
   CNV, 12  
   ECM, 13  
   L-ORD, 13  
   PGC-1 $\alpha$ , 15  
   ROS, 13  
   RP, 15, 16  
   RPE characteristics, 12  
   RPE-related disorders, 16–18  
   sources, 12  
   tissue-on-chip approach, 13

Human pluripotent stem cell (hPSC), *see*  
Retinal ganglion cells (RGCs)

Human umbilical tissue-derived cells  
(hUTCs), 68

**I**

Immune modulation  
factors, 110  
synthetic, 110, 111

Immune privilege of eye, 82–84

Immune system development  
adaptive, 103  
BBB, 100  
BRB, 100  
complement system, 103, 104  
innate, 101, 103  
protein-based complement system, 100  
TGF- $\beta$ , 100

Immunosuppression  
monkey, 150  
mouse, 146  
pig, 148, 149  
rabbit, 148  
rat, 146

Immunosuppressive treatment, 84, 85

InCyte Zoom, 186

Induced pluripotent stem cells (iPSCs), 69,  
107, 173

Innate immune system, 101, 103

Inner limiting membrane (ILM), 156

Insulin-like growth factor 1 (IGF-1), 110

Interferon beta (IFN- $\beta$ ), 111

Intraocular pressure (IOP), 155, 161

Intraoperative optical coherence tomography  
(iOCT), 158, 163

Investigational new drug (IND), 172

In vitro models  
anti-inflammatory agents, 39  
 $\beta$ -catenin signaling, 42  
blood–ocular barriers, 39  
cellular signaling mechanisms, 41  
drug screening, 38  
EMT, 40  
injury, 38  
iPS-RPE, 42  
myofibroblasts, 41  
PDGF, 41  
post-traumatic intraocular fibrotic  
conditions, 38  
PVR, 39, 40, 42–44  
retinal detachment, 40  
TGF $\beta$ , 41  
wound healing, 38

iPSC-derived cells, 173

Iris pigment epithelium (IPE), 65, 66

**K**

Knockout serum replacement (KSR), 64, 72

**L**

Late-onset macular degeneration (L-ORMD), 6

Late-onset retinal degeneration (L-ORD), 4,  
6, 7

LCHAD deficiency, 38

Leber congenital amaurosis (LCA), 2, 16, 17,  
58, 186

Lecithin retinol acyltransferase (LRAT), 8, 57

Leucine zipper kinase (LZK) pathway, 130

Liquid chromatography-mass spectrometry  
(LC-MS), 187

Low-density lipoprotein (LDL), 8

Lymphocytes, 103

**M**

Macrophages, 101, 110

Macula, 143

Matrix-assisted laser desorption/ionization-  
mass spectrometry (MALDI-MS)  
technologies, 187

Matrix-metalloproteases (MMPs), 5

Mechanical traction, 156

Mechanism interrogation plate (MIPE), 184

Membrane attack complex (MAC), 9, 106

Membrane-type frizzled-related protein  
(MFRP), 8

Mendelian retinal disorders, 2

Mer tyrosine kinase receptor (MERTK), 8

Mesencephalic astrocyte-derived neurotrophic  
factor (MANF), 110

Methyl thiazol tetrazolium (MTT) assay, 185

MicroDose™ injection kit, 159

Microglia, 101, 102

Microglia/macrophage activation  
anti-inflammatory cytokines, 105  
CD40, 106  
CSPG, 105  
gliosis, 106  
IL-33, 106  
inflammasome, 106  
intracellular miRNA-155 expression, 104  
MAC, 106  
M2 transition process, 105  
neurotrophic factors, 105  
oligodendrogenesis, 105

- Microglia/macrophage activation (*cont.*)  
 proinflammatory and cytotoxic factors, 105  
 remyelination, 105  
 retinal disorders, 102  
 retinal inflammation process, 104  
 VEGF, 105
- Microphthalmia-associated transcription factor (MITF), 178
- MicroRNAs (miRNAs), 43
- Microvitreal (MVR), 155
- Minimal-invasive procedure, 164
- Minocycline, 110, 148
- Monkey, 150
- Monkey surgery  
 implantation, 162, 163  
 instrument and machine preparations, 160  
 preparing implantation instrumentation, 162  
 vitrectomy, 160, 161  
 wound closure, 163
- Monocyte chemoattractant protein 1 (MCP1), 9
- Mouse, 146
- Mouse embryonic fibroblast (MEF), 72
- Müller glia, 103, 106, 124
- Multipotent stem cells, 34
- N**
- Nanostring technology, 187
- Nerve fiber layer, 124
- Neural retina leucine zipper (NRL), 179
- Neurodegeneration, 123
- Neuronal cell types, 125
- Neuroprotective strategies, 130
- Neurosensory retina, 174
- Neurotransmitter, 124
- Neurotrophins, 69
- Neutrophils, 101
- Non-human primate, 162
- Nonsense mediated decay (NMD), 17
- Normal tension glaucoma (NTG), 128
- O**
- Ocular tissue models  
 ESC/iPSC-derived cells, 185  
 HTS, 183–185
- Ophthalmology, 174
- Optic atrophy, 129
- Optic nerve, 124
- Optic neuropathies, 122, 123, 132
- Optineurin (OPTN), 128
- Optokinetic paradigm, 66
- Outer blood–retina barrier, *see* 3D engineering
- P**
- Patient-specific cells, 130
- Perfluorocarbon liquids (PFC), 157
- Pericytes, 173
- Peripheral layers, 124
- Pharmacological approaches, 123
- Photodynamic therapy, 60
- Photoreceptor outer segments (POS),  
 3, 7, 16
- Photoreceptors (PR), 123, 124, 142,  
 174, 175
- Photoreceptor transplantation  
 graft preparation, 164  
 transplant delivery strategies, 164
- Phototransduction, 56
- Pig surgery  
 bleb retinal detachment, 160  
 implantation, 158  
 instrument and equipment preparation, 157  
 nasal sclerotomy, 160  
 retinal detachment, 158  
 retinotomy, 160
- Pigment epithelium-derived factor (PEDF), 3, 174
- Pigs, 149, 152  
 domestic, 145  
 mini-pigs, 145  
 Yucatan, 146
- Platelet-derived growth factor (PDGF), 41
- Pluripotent stem cell (PSC), 34
- Porous polyester terephthalate (PET), 154
- Posterior vitreous detachment (PVD),  
 155, 161
- Post-traumatic ocular fibrosis, 44
- Preclinical study, 143, 164
- Proliferative vitreoretinopathy (PVR)  
 advantages, 43  
 categories, 39  
 cellular basis, 40  
 compounds, 42  
 ECM, 39  
 epiretinal/subretinal membranes, 41  
 etiology, 40  
 iPSC-RPE model, 44  
 medical treatments, 39  
 ocular trauma, 39  
 pathogenesis, 39–42  
 pathology, 42  
 progression, 39  
 retinal detachments, 40  
 surgical techniques, 39  
 vitreoretinal surgery, 39
- Punctate inner choroidopathy, 39

**Q**

QuantiGene Plex Gene Expression Assay, 187

**R**

Rabbit surgery

- implantation, 156, 157
- instrument preparation, 155
- loading implantation instrument, 156
- vitrectomy, 155, 156
- wound closure, 157

Rabbits, 144, 145, 147, 148

Rapamicin, 149

Rat, 146

Reactive oxygen species (ROS), 13, 14, 185

Reprogramming techniques, 35

Resight®, 158

Retinal cell types, 123

Retinal degenerative diseases (RDDs)

- AMD, 2–4, 8
- BD, 7, 10
- cell types, 2
- complement system, 9
- DHRD/ML, 5, 6
- electron lucent particles, 8
- genetic diseases, 8
- knock-in mice model, 10
- light absorption, 2
- L-ORD, 6, 7, 10
- MERTK, 11
- non-human primates, 11
- oxidative stress, 8, 9
- POS, 3
- retinoids, 3
- RP, 7, 8
- RPE functions, 2
- SFD, 5
- Y204H mutation, 9

Retinal development, 122

Retinal ganglion cells (RGCs)

- applications, 122, 123
- BRN3 expression, 127
- cell types, 124
- degeneration and pathogenesis, 122
- future applications
  - apoptotic and autophagy pathways, 133
  - cell replacement strategies, 132
  - CRISPR engineering, 133
  - development and disease pathologies, 130
  - early disease progression, 132
  - peripheral layers, 131
  - retinal organoids, 131
  - spatial lamination, 131

subtypes, 132

temporal development, 131

genetic markers, 125–127

human-derived cells, 127

molecular signatures, 127

optic neuropathies, 122

translational applications

- animal models, 128
- BDNF and GDNF, 129
- CRISPR gene editing, 130
- disease-causing mutations, 128
- human degenerative diseases, 128
- neural and retinal cells, 128
- optic neuropathies, 128, 129
- OPTN, 129
- TBK1, 128

Retinal neurospheres (RNS), 68

Retinal organoids, 124, 131

Retinal pigment epithelium (RPE), 174

adult and fetal, 78

adult eye, 63, 64

animal preparation, 154

bone marrow MSCs, 67, 68

cell sheet implantation, 155

cell sheet preparation, 154

cell suspension injection, 155

cell suspension preparation, 154

dystrophies, 57

fetal brain-derived neural progenitors, 66, 67

fetal-derived cells, 61, 62

hiPSCs/hESCs, 78–80

injection strategy, 76–78

IPE, 65, 66

logistic and management advice, 144

non-human primates, 146

photoreceptors, 56

pigs, 145

pluripotent stem cells

clinical translation, 71

continuous adherent culture method, 69

culture medium, 72

EBs, 70, 72

embryoid body method, 69

exogenous molecules, 71

in vitro fertilization, 69

neuroectodermal differentiation, 70

neuroepithelium structure, 71

pigmented regions, 70

RC-09, 72

TGF- $\beta$  pathway, 70

transcription factors, 69

types, 69

WNT pathway, 70

Retinal pigment epithelium (RPE) (*cont.*)  
 quality controls (*see* Differentiated RPE cells)  
 rabbits, 144, 145  
 retinopathies (*see* Retinopathies)  
 RNS, 68  
 Schwann cells, 66  
 small rodents, 144  
 stem cell trials, 80  
 umbilical-cord stem cells, 68  
 Retinal pigment epithelium derived from induced pluripotent stem cells (iPS-RPE), 35, 36, 38  
 Retinitis pigmentosa (RP), 2, 7, 8, 57, 58, 186  
 Retinitis pigmentosa 50 (RP50), 7  
 Retinoid X receptor (RXR) gamma, 179  
 Retinol, 3  
 Retinopathies  
 AMD, 58, 59  
 global burden evolution and treatments, 59, 60  
 interconnected neurons, 56  
 photoreceptors, 56  
 RP, 57, 58  
 SRS, 56  
 Retinotomy edges, 163  
 Retrobulbar injections, 153  
 Retroviral gene delivery systems, 35  
 Reverse transcriptase polymerase chain reaction (RT-PCR), 66  
 Rhesus monkeys (*Macaca mulatta*), 146  
 RNA-binding protein with multiple splicing (RBMP5), 127  
 Royal College of Surgeons (RCS), 144  
 RPE stem cells (RPESCs), 63, 64

## S

Scaffolding device, 132  
 Schwann cells, 66  
 Silent information regulator T1 (SIRT1), 15  
 Sirolimus, 148  
 Sorsby's fundus dystrophy (SFD), 4, 5  
 Specific pathogen-free (SPF), 146  
 Spontaneous mutations, 142  
 Stargardt's disease, 2, 38  
 Stargardt's macular dystrophy (SMD), 38, 78  
 Stem cell sources, 34  
 Subretinal space (SRS), 56  
 Subretinal transplantation, 164  
 Sunitinib, 130  
 Superoxide dismutase 1 (SOD1), 8

## T

Tacrolimus, 149  
 TANK Binding Kinase 1 (TBK1), 128  
 Teratogenicity assays, 142  
 Teratomas, 74  
 3D automated reporter quantification (3D-ARQ) assay, 186  
 3D engineering  
 animal model systems, 172  
 bioprinting, 174  
 cellular systems, 172  
 diencephalon, 177  
 disease cellular and molecular mechanisms, 172  
 engineered systems, 175  
 eye and neurosensory retina, 177  
 eye-field transcription factors, 178  
 fibroblasts and pericytes, 173  
 fluidic channel, 173  
 HTS readouts and validation, 186, 187  
 human iPSC-derived retinal cup, 185, 186  
 in vitro cell assays, 172  
 in vivo mouse models, 172  
 machine learning, 187  
 microfluidics, 173  
 ophthalmology, 174  
 pharmaceutical and biotechnology industries, 172  
 physiological differences, 173  
 pluripotent stem cell-derived optic cup, 178–180  
 segmentation and quantification, 182  
 stem cell technology, 177  
 tissue clearing, 181, 182  
 traditional histology, 180, 181  
 validation, 176  
 vascular channel, 173  
 vascular endothelial cells, 173  
 TIMP metalloproteinase inhibitor 3 (TIMP3), 3  
 Transcriptomics analysis, 184  
 Transepithelial electrical resistance (TEER), 175  
 Transforming growth factor  $\alpha$  (TGF $\alpha$ ), 41  
 Transforming growth factor beta (TGF- $\beta$ ), 41, 100  
 Translational read-through-inducing drugs (TRIDs), 16  
 Transmission electrical microscopy (TEM), 175  
 Transscleral injection, 164  
 Transvitreal injection, 164  
 Traumatic maculopathy, 39  
 Tumorigenicity, 74  
 Tumor spheroids, 187

**U**

Unfolded protein response (UPR), 6  
US food and drug administration (FDA), 144

**V**

Vascular endothelial cells, 173  
Vascular endothelial growth factor (VEGF), 3,  
41, 105

Very low-density lipoprotein (VLDL), 8

Visual impairment, 58

Vitrectomy, 155

**W**

Wnt pathways, 178

World Precision Instruments, 154

Wound healing, 34, 38, 42–44