Index

A

Activin, 118, 217 AD, see Alzheimer's disease Age-related macular degeneration (AMD), 59-60, 62 - 64, 74Aging alveolar epithelial stem cells, 169 DNA damage and mutations, 152-153 Airway epithelia, see also Alveolar epithelial stem cells archetype cells and evolution, 110 cells distribution of epithelial functions by cell type, 106-108 ionocytes, 103, 105 lineage relationships, 108-110 multiciliated cells, 103 neuroendocrine cells, 106 tuft cells, 105-106 overview, 101-104 ALS, see Amyotrophic lateral sclerosis Alveolar epithelial stem cells activation by injury, 167 anatomical compartments and microenvironments, 164-167 AT2 cell aging and disease, 169 fibroblast association, 167-168 functional overview, 163-164, 167 growth factors, 168-169 lung cancer studies, 173 proliferation restraint, 168 repair signaling, 169-171 prospects for study, 174 Alzheimer's disease (AD), induced pluripotent stem cell-derived neuron models, 6-7 AMD, see Age-related macular degeneration Amyotrophic lateral sclerosis (ALS), induced pluripotent stem cell-derived neuron models, 6-7 Angiomotin, 207 ARX, 118 ASD, see Autism spectrum disorder ASLX1, 150, 152 Autism spectrum disorder (ASD), induced pluripotent stem cell-derived neuron models, 7-9

В

BDNF, 238 Bestrophin, 60 β Cell, see Diabetes; Pancreas **Biomaterials** cell fate manipulation biochemical factors controlled release from biomaterials, 91-92 immobilization on biomaterials, 91 reversible immobilization of biochemical clues, 92-93 biochemically defined static biomaterials, 90-91 reversible stiffening biomaterials, 89 softening biomaterials, 87-88 stiffening biomaterials, 88-89 tunable mechanics of biomaterials, 86 tunable stress-relaxation biomaterials, 90 stem cell behavior detection, 93-94 culture advances, 84-86 Bipolar disorder, induced pluripotent stem cell-derived neuron models, 7-9 BMP4, 171 BMP6, 20 BMP7, 21 $BMPR1\alpha$, 172 Brain organoid assembled organoids, 26-27 cell diversity and architecture, 23-26 cell survival and maturation, 26 circuit formation, 24-25 historical perspective extracellular matrix gels, 19-20 three-dimensional brain protocols, 19 neuronal activity and maturation, 24 overview, 16-17 patterning heterogeneity-uniformity tradeoff, 22-23 self-patterning, 20-21 small molecules in organoid patterning, 21-22 prospects for study, 28 signaling center assembly, 27-28

С

CACNA1C, 9 Cancer

Index

Cancer (Continued) alveolar epithelial stem cells in lung cancer, 173 initiation and somatic mutations, 151-152 lineage-tracing research, 190-192 stem cell imaging maintenance by cancer stem cells, 261-263 progression, 260 tumor initiation, 259-261 CARM1, 210 CCL2, 170 CD45, 184 CD73, 73 CDKL5,9 CDX2, 205 Cell fate, see Biomaterials; Preimplantation embryo; Multimodal single-cell analysis CFTR, 105 CGD, see Chronic granulomatous disease Chronic granulomatous disease (CGD), gene therapy, 35-36 COL7A1, 42-44, 47 COL17A1, 149 CRISPR/Cas9 multimodal single-cell analysis, 240 progenitor cell discovery, 192-194 skin disease gene editing epidermolysis bullosa dominant, 47 recessive, 47 epidermolytic ichthyosis, 48 limitations, 48 overview, 46-47 CTLA-4, 120 CXCL12, 282

D

Diabetes regenerative therapies hepatocyte reprogramming to β cells, 134–136 overview, 132 prospects, 136-138 reprogramming somatic cells to β cells, 132 - 134type 1 β-cell development, 116-117 historical perspective, 116 overview, 115-116 stem cell therapy, 117-120 DIS2, 8 DISC1,8 DKK-1, 68 DNA damage model systems for spontaneous mutation in tissues, 154-156 mutation

aging, 152-153 cancer initiation and somatic mutations, 151-152 clonal expansion in blood and solid tissues, 150 diversity in somatic genomes, 149-150 mechanisms, 144-145 stem cell persistent damage and decline, 153-154 protection competition between cells and lineages, 147 - 149DNA damage response and repair, 145-147 quiescence, 147 DNMT3A, 150, 152 DNMT3A/B, 212

Ε

EB, see Embryoid body; Epidermolysis bullosa EC, see Endothelial cell ECM, see Extracellular matrix EGFR, 168-169, 173 Embryogenesis, see Preimplantation embryo Embryoid body (EB), history of study, 17 Embryonic stem cell (ESC) artificial embryo derivation, 216-217 history of study, 17 neural fate promotion, 17-19 properties human, 217-218 mouse, 213-216 EMT, see Epithelial-to-mesenchymal transition Endothelial cell (EC) imaging of generation, 251 progenitor discovery blood vessels, 184, 186 lymphatic vessels, 186-187 Enterocyte, 103 EOMES, 216 Epidermolysis bullosa (EB) gene editing dominant, 47 recessive, 47 gene therapy, 34-35, 37, 40-46 Epidermolytic ichthyosis, gene editing, 48 Epigenetics, preimplantation embryo, 210-213 Epithelia, see Airway epithelia; Intestinal epithelia Epithelial-to-mesenchymal transition (EMT), 238 - 239ESC, see Embryonic stem cell ESRRB, 214, 216 ETS2, 216 Extracellular matrix (ECM) decellularized matrix for culture, 84-85 stem cell niche, 84-85

Index

F

FGF, see Fibroblast growth factor FGFR2, 171 Fibroblast growth factor (FGF), 278 FGF2, 21 FGF8, 21 FGF10, 171 FGF19, 21–22 Fli1, 235 FOXA2, 117 FOXI1, 105 FUS, 7

G

Gata1, 235 GATA3, 205, 216 GATA6, 216 GBX2, 214 GCG, 118 Gdf9, 239 GDNF, 271, 273, 278 Gene editing, see CRISPR/Cas9 Gene therapy, skin diseases, see also specific diseases epidermal stem cell targeting, 38-40 overview, 34 prospects, 49 vectors herpes simplex virus, 37-38 lentivirus, 36-37 retrovirus, 35-36 Germ line stem cell (GSC), Drosophila, 280-281 GESTALT, 192 GFRα1, 271, 277–278 GSK3B, 6

Н

Hair follicle, stem cells, 145-149, 187-188, 254, 259, 277-278, 281-282 Hematopoietic stem cell (HSC) imaging generation, 251 regenerative processes, 257 multimodal single-cell analysis, 237-238 niche, 282 progenitor discovery, 184-185 quantitative modeling, 301-302 Hepatocyte growth factor (HGF), 169 Herpes simplex virus (HSV), gene therapy vector for skin, 37-38 HGF, see Hepatocyte growth factor Hippo, 207-208 HLA-G, 120 HNF4a, 117 HPX, 23

HSC, *see* Hematopoietic stem cell HSV, *see* Herpes simplex virus Hydrogel, stem cell culture, 85

I

Idiopathic pulmonary fibrosis (IPF), 169 IGFR, 169 Induced pluripotent stem cell (iPSC) brain disorder modeling with derived neurons neurodegenerative disorders, 6-7 neuropsychiatric disorders, 7-9 overview, 1-3 prospects for study, 9-10 validity of model system, 3-6 epidermal repair, 40 Inner cell mass, see Preimplantation embryo Insulin, 21 Interfollicular epidermis (IFE), 276, 282, 299-301 Intestinal epithelia archetype cells and evolution, 110 cells distribution of epithelial functions by cell type, 106-108 enterocytes, 103 enteroendocrine cells, 106 lineage relationships, 108-110 tuft cells, 105-106 crypt stem cells, 281, 295-299 overview, 101-104 stem cells in regeneration, 188 Intravital microscopy (IVM) organogenesis, 251-253 overview, 249-251 stem cell imaging cancer maintenance by cancer stem cells, 261-263 progression, 260 tumor initiation, 259-261 plasticity during tissue homeostasis, 253-257 prospects, 264 regenerative processes, 257-259 IPF, see Idiopathic pulmonary fibrosis IPF1, 117 iPSC, see Induced pluripotent stem cell IVM, see Intravital microscopy

K

KCC2, 24 Klf1, 235 KLF2, 214 KLF4, 214–215 KRAS, 263 *KRT1*, 48 *KRT10*, 48

Index

L

LAMA3, 41 LAMB3, 41-42 LAMC2, 41 LATS1/2, 207 LCA, see Leber congenital amaurosis Leber congenital amaurosis (LCA), 70 LEKTI, 46 LincGET, 210-211, 213 LINE1, 149, 212-213 Lineage tracing, see also Multimodal single-cell analysis cancer research, 190-192 historical perspective, 178-180 progenitor cell discovery endothelial cell progenitors blood vessels, 184, 186 lymphatic vessels, 186-187 hematopoietic stem cell progenitors, 184-185 overview, 177-178 vascular smooth muscle cell progenitors, 187 prospects, 192-195 site-specific recombination systems, 180-182 Liver developmental relationship with pancreas, 127-132 hepatocyte reprogramming to β cells, 134-136 structure and function, 126-127 LOH, see Loss of heterozygosity Loss of heterozygosity (LOH), 145, 149-150 LRAT, 60 Lung, see Alveolar epithelial stem cells

Μ

MAFA, 117 Mammary stem cell, 302-303 MCM4, 153 MCM6, 153 MECP2, 9 MERTK, 60 Mettl7a1, 238 Microglia, brain organoids, 26 MMP14, 168 Multimodal single-cell analysis molecular mechanism inference, 234-236 molecular time inference, 239-241 overview of techniques, 228-232 prospects, 241-242 pseudotime concept, 236-239 single-cell map charting, 233-234 single-cell state defining, 229, 233 Mutation, see DNA damage MYC, 215-216

Ν

NANOG, 210 Neat1, 210–211 NEB, *see* Neuroepithelial body NESTIN, 23 Netherton syndrome (NS), gene therapy, 46 Neuroepithelial body (NEB), 106 NF2, 207 NGN3, 117 NHEJ, *see* Nonhomologous end-joining NKCC1, 24 NKX6.1, 117–118 Noggin, 68 Nonhomologous end-joining (NHEJ), 144, 146 *NOTCH1*, 150, 152 NS, *see* Netherton syndrome NTRK2, 238

0

Obox6, 239 OCT4, 205, 215 OKT, *see* Optokinetic head tracking Oligodendrocyte precursor cell (OPC), brain organoids, 25 OPC, *see* Oligodendrocyte precursor cell Optokinetic head tracking (OKT), 72 Organoid, *see* Brain organoid

Р

p53, 149, 151 Pancreas, see also Diabetes developmental relationship with pancreas, 127-132 hepatocyte reprogramming to β cells, 134–136 structure and function, 126-127 Parkinson's disease (PD), induced pluripotent stem cell-derived neuron models, 6-7 PAX4, 117 PAX6, 23 PD, see Parkinson's disease PD-L1, 120 PDX1, 117-118 Photoreceptor cell transplantation, see Retinal degeneration PNEC, see Pulmonary neuroendocrine cell PPM1D, 152 PRDM14, 210 Preimplantation embryo cell difference origins epigenetic modifications and transcription factor binding, 210-211 partitioning errors, 208, 210 timing, 208 cell fate commitment timing, 208-209 embryonic stem cell properties in mice, 213-216 first lineage decision, 205-208 overview, 203, 205 pluripotency regulation

Index

chromatin remodeling, 211 DNA methylation, 212 histone modifications, 211–212 retrotransposon activation, 212–213 timeline in mouse, 204 Proliferative vitreoretinopathy (PVR), 60 PTPRZ1, 23 Pulmonary neuroendocrine cell (PNEC), 106 PVR, *see* Proliferative vitreoretinopathy

R

RA, see Retinoic acid Reaggregation, history of study, 16-17 Retinal degeneration overview, 59-61 photoreceptor cell transplantation clinical application, 72-74 donor-derived cell suspensions, 64-66 human PSC-derived neuroretinal cell suspensions, 67-69 mouse PSC-derived retinal cell suspensions, 66 - 67rescuing end-stage degeneration, 69-71 retinal pigment epithelial transplantation animal models, 60, 62 clinical studies of stem cell transplantation, 62 - 64structure, 60 retinal sheet transplantation, 71-72 Retinoic acid (RA), 117, 271, 273, 290-291 RPE65, 60

S

Schizophrenia, induced pluripotent stem cell-derived neuron models, 7-9 SCID, see Severe combined immunodeficiency SCNT, see Somatic cell nuclear transfer Severe combined immunodeficiency (SCID), gene therapy, 35 SHH, 21, 27-28 Single-cell analysis, see Multimodal single-cell analysis **SMAD**, 21 SOD1, 7 Somatic cell nuclear transfer (SCNT), 211, 215, 217 SOX2, 23, 205, 210, 215 Spermatogenesis, mouse advantages as model system, 273, 275 overview, 269 spermatogenic stem cells

context dependence of function, 277 differential competence to extracellular signals, 278 dynamic heterogeneity, 277 identity and regulation, 271–273, 292 ligand competition, 278 motion, 277–278, 282–283 neural competition and clonal drift, 276–277 niche system unity and diversity, 279–280 open niche microenvironment, 273–274 population asymmetry, 275–276 prospects for study, 283 quantitative modeling, 291–293 Spi1, 235 *SPINK5*, 46

Т

TARDP, 7 TBX3, 214 TDP-43, 7 TEAD4, 207 TEB, *see* Terminal end bud Terminal end bud (TEB), 303 *TET2*, 150, 152 TET3, 212 TFAP2C, 216 TFCP2L1, 214 TGIF2, 136 Transit-amplifying cell, 108 Trophectoderm, *see* Preimplantation embryo

V

Vascular smooth muscle cell (VSMC), progenitor discovery, 187 VSMC, *see* Vascular smooth muscle cell

W

WAS, *see* Wiscott–Aldrich syndrome Wiscott–Aldrich syndrome (WAS), gene therapy, 35 WNT, 169–171

Y

YAP1, 170, 207

Z Zfp42, 239