

Index

A

Abnormal glycosaminoglycan
(GAG) synthesis, 146, 150
Acetabular protrusion, 97
Acrogeria, 134, 154
Acromicric dysplasia, 85
Activin receptor-like kinase (ALK), 62, 109, 110,
112, 113, 117, 118, 121
Adducted thumb clubfoot syndrome (ATCS), 135, 151
Age-related macular degeneration (ARMD 3), 166
Aggrecan, 22, 23, 50, 52–55, 64, 68, 236, 237
ALK. *See* Activin receptor-like kinase (ALK)
Alopecia, 165, 171, 176, 178, 179
Amblyopia, 97
Aneurysm, 37, 78, 81, 82, 96–100, 102, 112–117,
119, 120, 134, 166, 167, 232, 233
Aneurysm-Osteoarthritis syndrome (AOS), 98, 113,
114, 121
Angiotensin converting enzyme (ACE) inhibitors,
83, 119
Angiotensin receptor blockers (ARBs), 83, 86, 103
Ankles and interphalangeal joints, 188
Antibiotic prophylaxis, 83, 84
Aorta, 34, 36, 37, 52, 54, 68, 69, 78–82, 84, 86, 96,
97, 100, 103, 112, 114, 117, 119, 134, 154,
204, 234, 236
Aortic aneurysms, 36, 69, 85, 87, 95, 96, 98–103, 108,
112, 113, 119, 166
Aortic Aneurysm Thoracic (AAT), 112
Aortic aneurysm with tortuosity, 95
Aortic dissection, 52, 79, 82, 96, 102, 103, 204
Aortic root diameter, 78, 81, 119, 139
AOS. *See* Aneurysm-Osteoarthritis syndrome (AOS)
Apical blebs, 80, 82
Arachnodactyly, 79, 80, 96–100, 109, 113, 115, 122, 167
ARBs. *See* Angiotensin receptor blockers (ARBs)
ARCL1C, 163, 167, 178
ARCL type 2, 163, 164
ARCL type 1A (ARCL1A; MIM 219100), 163
ARCL type 1B (ARCL1B; MIM 614437), 163
ARCL type 2B (ARCL2B; MIM 612940), 163
Arterial tortuosity syndrome (ATS), 100–101, 113, 115,
121, 178
Arteriovenous malformation (AVMs), 113, 116–118, 121
Arthrochalasis or dermatosparaxis type, 130, 137
Arthrogyposis, 151, 170, 187

ATP7A gene, 163, 168
ATP7A protein, 163, 168
AT1r and AT2r pathways, 87
Atrophic scars, 99, 131, 137, 153, 154, 232, 233
Autosomal dominant cutis laxa (ADCL), 162, 166–167,
172–174, 178
Autosomal dominant limb-girdle muscular dystrophy
phenotype, 186, 189–190
Autosomal dominant trait, 84
Autosomal recessive cutis laxa (ARCL), 162–164, 167,
170, 173–174
Autosomal recessive myosclerosis, 186
AVMs. *See* Arteriovenous malformation (AVMs)

B

BCS. *See* Brittle cornea syndrome (BCS)
Beaded filament-forming collagen, 8, 10–13, 24, 202,
212–213
Beighton hypermobility score, 132
Bentall and De Bono procedure, 84
Beta (β)-blockers, 82, 83, 86, 103, 119
Beta-1,4-galactosyltransferase, 136, 149, 150, 152
Bethlem myopathy, 186–191, 195, 196, 206
Bgn⁻⁰ *Fmod*^{+/-} compound mutant mice, 209–211
Bgn⁻⁰ mice, 209
Bifid uvula/cleft palate, 95, 96, 99, 100, 113, 176
Biglycan, 11, 13, 19, 22, 36, 50–53, 111,
136, 209–211
Bioengineering, 69
Blue sclerae, 97, 99, 152
BMP receptor, 112, 117
BMPs. *See* Bone morphogenetic proteins (BMPs)
Bone deformities, fibrillin-1, 204
Bone marrow/peripheral blood-derived
stem cells, 69
Bone morphogenetic proteins (BMPs), 61–63, 68, 85, 87,
88, 111, 112, 122, 215
bp mice, 216
Brachydactyly C, 206, 216
Brachypodism, 216
Brittle cornea syndrome (BCS), 130,
135, 152
Bruising, 97–100, 113, 131, 133, 134, 136, 138, 140,
148, 151, 153, 177
Bullous emphysema, 80

C

Calcium channel blockers, 82, 83
 Cardiac defects, 62, 215
 Cardiomyopathy, 79, 176
 Cartilage associated protein (Crtap), 15, 205, 206
 Cataracts, 80, 164, 170
 Cats, 2, 232
 Cattle, 2, 232, 233
 CDG. *See* Congenital disorders of glycosylation (CDG)
 Cd44-null mice, 221
 Cervical spine malformation, 97
 Cho mouse model, 204
 Chondrodysplasia, 17, 204–206, 216, 224
 chondroitin sulfate (CS) chain, 51, 136, 146, 155–157
 Classic subtype, 139
 COG7-CDG (CDG type IIe), 168–169
COL6A2 and *COL6A3*, 186, 187, 189, 192, 195
COL1A1 and *COL1A2* mutations, 130, 137, 152, 218, 220
COL3A1 gene, 100, 134, 138
Coll1a1^{-/-} mouse model, 207
Col6a1-null mice, 213
 Collagen
 fibrillogenesis, 16, 50, 52, 132, 133, 202, 203, 211, 212
 fibrils, 2, 6–11, 13, 15–21, 40, 41, 51–53, 60, 65, 69, 131, 133, 135–138, 140, 151, 155–157, 174, 202, 204, 206, 209, 211–213, 216, 220, 232–234
 Collagens I-XXVIII, 6, 8
 Collagen VI, 10–13, 52, 185–197, 202, 212, 213
 Collagen VI deficient mice, 193
 Collagen XII, 11, 207, 219
 Collagen XIV, 9, 20, 207
 Congenital disorders of glycosylation (CDG), 168, 169, 172
 Congenital hip dislocation, 97, 133, 163, 169, 186
 Contractures, 2, 11, 85, 96, 97, 99, 113, 115, 133, 135, 136, 151, 152, 164, 165, 186–190, 194, 196
 Copper-transporting ATPase, 163, 168
 Craniofacial deformities, 79
 Craniofacial features, 97, 98, 152
 Craniosynostosis, 96–100, 113, 115, 120
 Crosslinking, 16, 38
 Crtap. *See* Cartilage associated protein (Crtap)
 Cryptorchidism, 99, 115, 148, 154
 CS/DS hybrid chain, 155–157
 Curacao diagnostic criteria, 117
 Cutis laxa, 2, 37, 66, 100–101, 122, 131, 161–179
 Cyclophin D inhibitor, 194
 Cyclosporine A, 194

D

Dcn^{-/-} mice, 209, 210
 De Barsy syndrome, 164, 165, 171, 178
 De Barsy syndrome type A (ARCL3 A; MIM 219150), 164
 Debré-type cutis laxa (ARCL2A; MIM 219200), 163
 Decorin, 11, 13, 19, 23, 41, 50–53, 111, 115, 136, 151, 155–157, 207, 218, 236, 237

Deficiency of urea cycle intermediates, 170
 Degenerative suspensory ligament desmitis (DSLSD), 234–237
 Delayed motor milestones, 187
 Deletions, 17, 20, 84, 96, 130, 132–134, 136, 150, 166, 171, 191, 192, 207, 222
 Dermatan 4-O-sulfotransferase 1 (D4ST1)-deficient EDS, 146–149, 151–157
 Dermatan sulfate (DS) chain, 50, 52, 136, 146, 155, 156, 236
 Dermatan-4-sulfotransferase 1 (D4ST-1), 130, 135, 136
 Dermatosparaxis, 130, 137, 138, 152, 232, 233
 Dilatation of aortic root, 78, 81, 96
 Dogs, 2, 232, 233, 237
 Dolichocephaly, 79, 82, 83, 97, 98
 Dolichostenomelia, 79, 97, 98, 113, 115
 Δ¹-Pyrroline-5-carboxylate synthase (P5CS), 170, 171, 173–175
 Dural ectasia, 79, 80, 82, 83, 96, 98, 99, 113
 Dysregulated TGFβ and BMP signaling, 85, 122
 Dystrophic scars, 98

E

Easy bruising, 97–99, 113, 131, 133, 136, 138
 Ectopia lentis, 80, 82, 83, 98, 99, 113
 EDS. *See* Ehlers-Danlos syndrome (EDS)
 EDS type VI, 135, 151, 197
 EFEMP2 or FBLN4 (MIM 604633), 101, 163, 167
Egr1^{-/-}*Egr2*^{-/-} mice, 218
Egr1^{-/-} mice, 218
Egr2^{-/-} mice, 218
 Ehlers-Danlos, 1, 2, 55, 69, 119, 170, 232, 233, 236
 Ehlers-Danlos syndrome (EDS), 1, 2, 19, 40, 54, 60, 66, 98, 100, 122, 129–141, 145–157, 177, 196–197, 202, 204–206, 224, 232, 233, 237
 Elastin, 31–42, 55, 101, 111, 114, 162, 163, 166, 169, 172–175, 177, 213, 214, 236
 ELN (MIM 130160), 163
 Embolotherapy, 121
 Enalapril, 83
 Endoglin, 109, 110, 113, 114, 117, 118, 121
 Endophthalmos, 80
 Endovascular aortic repair (EVAR), 119
 Enlargement/dissection of aortic root and proximal ascending aorta, 78
 Extracellular matrix, 1, 6, 10, 11, 16, 19, 20, 22, 24, 31–42, 50, 51, 53–55, 61, 62, 65, 78, 103, 109, 130, 146, 150, 156, 157, 162, 166, 169, 173–175, 186, 191, 192, 208, 210, 211, 213, 214, 221, 233, 234
 Extracellular matrix proteins, 33, 51, 53, 163, 169, 195, 213

F

Facilitated Glucose Transporter Member 10 (SLC2A10), 115
 FACIT. *See* Fibril-associated collagens with interrupted triple helices (FACIT)

Failure to thrive, 163, 169, 177, 187
 Familial thoracic aortic aneurysm, 101, 112–115
 Familial thoracic aortic aneurysm and dissection syndrome (FTAAD), 112–115
FBLN5 (MIM 604580), 163
FBLN5 mutations, 166, 167, 172–174
FBLN4 mutations X-linked recessive cutis laxa, 163, 178
Fbn1^{C1039G/+} mice, 86, 87, 102
Fbn1^{mgR/mgR} mice, 85–87
Fbn1^{-/-} mice, 86, 87, 212
 FGFs. *See* Fibroblast growth factors (FGFs)
 Fibril-associated collagens with interrupted triple helices (FACIT), 2, 7–11, 15, 16, 18–20, 24, 202, 207–208, 212, 224
 Fibril-forming collagens, 2, 8–10, 16, 19, 20, 32, 202–205, 207, 209, 224
 Fibrillar collagens, 9, 10, 12, 53, 132, 133, 138, 139
 Fibrillin, 31–42, 53, 54, 84, 202, 213–214, 233
 Fibrillin-1 assemblies, 79, 85
 Fibrinogen, 31–42
 Fibroblast growth factors (FGFs), 61, 64–65
 Fibrodysplasia ossificans progressive (FOP), 112
 Fibromodulin, 19, 20, 50–53, 209–212
 Fibronectin, 11, 16, 19, 31–42, 69, 193
 Fibulins, 31–42, 53, 54, 101, 163, 166, 167
 Flexion contractures of the elbows, 188
Fmod^{-/-}*Lum*^{-/-} mice, 212
Fmod^{+/-} mice, 209–212
 Fragile soft connective tissues, 131

G

Gdf5-null mice, 216
Gdf6-null mice, 216
Gdf7-null mice, 216
Gdf8-null mice, 217
 Geleophysic dysplasia, 85
 Genetic testing, 99, 117, 119–121, 139, 168, 191, 196
 Geroderma Osteodysplastica (GO; MIM 231070), 164, 165, 171–172, 178
 Ghent nosology, 81–83
 Glaucoma, 41, 80, 154, 176
 Golgi, 15, 150, 155, 165, 169, 171, 173–175
 Growth and motor developmental delay, 154

H

Haploinsufficient *Col3a1*^{+/-} and *Col5a1*^{+/-} mice, 204
 Heart development, 55
 HERDA. *See* Hereditary equine regional dermal asthenia (HERDA)
 Hereditary equine regional dermal asthenia (HERDA), 233, 234
 Hereditary hemorrhagic telangiectasia (HHT), 112, 113, 115–118, 120–122
 HHT. *See* Hereditary hemorrhagic telangiectasia (HHT)
 Hierarchical structure of tendon, 7
 Hindfoot valgus, 79
 Horses, 2, 69, 233–236

Hunter-Thompson or Grebe type chondrodysplasias, 206, 216
 Hyperammonemia, 170
 Hyperelastosis cutis, 233
 Hyperextensibility and fragility of skin, 148, 152
 Hypermobility subtype, 130
 Hypertelorism, 95–100, 113, 115, 152
 Hypoprolinaemia, 170
 Hypotonia, 91, 100, 115, 131, 135–137, 140, 149, 163, 169, 170, 177, 178, 186, 187, 189, 196

I

IdoA:GlcA ratio, 157
 IGF-I. *See* Insulin-like growth factor I (IGF-I)
 Improper activation of latent TGF β , 86
 Increased TGF β signalling, 102, 109, 115, 116, 118
 In-frame exon out-splicing, 84
 Insulin-like growth factor I (IGF-I), 60, 61, 65–68

J

Joint hyperlaxity, 171
 Joint hypermobility, 82, 97, 99, 100, 115, 131, 133, 135–139, 148, 196
 Joint laxity, 2, 60, 61, 66, 96, 97, 100, 113, 151, 163, 169, 170, 186, 187, 189, 196, 197, 204, 206, 212, 232

K

Knockout mice, 2, 37, 51–53
 Kyphoscoliosis, 100, 130, 135–137, 151–153, 186, 187, 206
 Kyphoscoliotic type or type VIA, 135
 Kyphosis, 80, 83, 186, 195, 206, 233

L

Laminin, 32–42
 Laxity of distal joints, 186, 187, 189
 LDS. *See* Loey-Dietz syndrome (LDS)
Lepre null mice, 204
 Ligament/tendon laxity, 80
 Loey-Dietz syndrome (LDS), 2, 95–103, 109, 112–118, 121, 122
 Lordosis, 80
 Losartan, 83, 86, 87, 103, 119, 120, 195
LTBP4 (MIM 604710), 163
 Lumican, 19, 50, 51, 53, 209, 212

M

Macrocephaly, 154, 165, 171, 178
 Macrocephaly, alopecia, cutis laxa, and scoliosis (MACS; 613075), 165, 171, 176–178
 Malar hypoplasia, 80, 82, 83
 MAPK. *See* Mitogen-activated protein kinase (MAPK)
 MAP kinase pathway defects, 165

- Marfan syndrome (MFS), 1, 2, 34, 36, 37, 54, 60, 62, 63, 68, 77–88, 96, 101, 102, 108, 112, 113, 122, 166, 195, 206, 213, 214, 224, 233, 237
- Mature tendon fibrils, 16
- Medial degeneration, 68, 78, 84, 101
- Member A1 gene or Delta-1-pyrroline-5-carboxylate synthetase gene (*ALDH18A1* or *P5CS*; MIM 138250), 164
- Menkes disease (MD; MIM 309400), 163, 167, 168, 173
- Mental retardation, 163, 169–170, 176
- Metabolic cutis laxa, 167–172
- Metalloproteinase, 13, 36, 38, 39, 55, 67, 84
- MFS. *See* Marfan syndrome (MFS)
- Mild developmental delay, 188
- Mild intellectual disability, 148, 154
- Minimal connective tissue involvement, 189
- Missense mutations, 14, 37, 101, 132, 134, 138, 155, 170, 189, 191, 192, 234
- Mitogen-activated protein kinase (MAPK), 85, 86, 110, 111, 118, 165, 217
- Mitral valve, 79, 116, 117, 121, 154
- Mitral valve prolapse (MVP), 54, 79, 82, 83, 86, 99, 108, 113, 115, 116, 140, 237
- Mkx*^{-/-} mice, 219, 220
- MMP-mediated elastolysis, 86, 87
- Mouse model for mutated *Coll2a1*, 207
- Moyamoya disease, 114
- MSTN*^{-/-} mice, 217
- Muscle hypotonia, 100, 131, 136, 163, 169, 177
- Musculocontractural type, 146, 151
- Mutation in *ALDH18A1*, 170
- Mutation in pyrroline-5-carboxylate reductase 1 gene (*PYCR1*; MIM 179035), 163, 164, 170–171, 173, 175, 179
- Mutation in the aldehyde dehydrogenase 18 family, 164
- Mutation in the RAS and RAB interactor 2 gene (*RIN2*; MIM 610222), 165
- Mutations in *ACTA2*, 101
- Mutations in *B4GALT7* and *B3GALT6* genes, 136, 150
- Mutations in *CHST14*, 135, 136, 151, 155, 197
- Mutations in collagen VI genes *COL6A1*, 186, 187, 189, 192
- Mutations in gene encoding for the H⁺ transporting α 2 subunit of the vesicular ATPase complex (*ATP6V0A2*; MIM 611716), 163
- Mutations in gene for fibrillin-1 (*FBNI*), 37, 78, 81–85, 88, 101, 109, 115, 119–121, 233
- Mutations in *SKI*, 98
- Mutations in *TGFBR1*, 96, 99–101
- MVP. *See* Mitral valve prolapse (MVP)
- MYH11* and *MYLK*, 101
- Myopia, 80, 83, 97, 99, 115, 135, 163, 169
- Myxomatous valve thickening, 79
- N-terminal propeptide of type I procollagen, 137
- Null mice for *Tgfb1*, 215
- Null mouse for fibrillin-2, 214
- O**
- Occipital Horn Syndrome (OHS; MIM 304150), 163, 168, 173, 178
- OI. *See* Osteogenesis imperfecta (OI)
- Oim* mouse model, 203, 204
- Osteogenesis imperfecta (OI), 15, 122, 130, 202–204, 206
- Osteopenia, 79, 80, 86, 87, 113, 135–137, 149, 153, 164, 170, 171, 204, 206
- Osteoporosis, 97, 164, 171, 206
- Overlap with Marfan and Ehlers-Danlos syndrome, 96
- P**
- PDGF. *See* Platelet-derived growth factor (PDGF)
- Pectus carinatum, 80, 82, 83, 97
- Pectus excavatum, 80, 82, 83, 97, 98, 113, 115, 148
- Peripartur uterine rupture, 98
- Pes planus, 79, 97, 98, 148
- Platelet-derived growth factor (PDGF), 40, 61, 66–67, 215
- Platelet-rich plasma (PRP), 68
- Pneumothorax, 80, 82, 83, 134, 154
- Poor breast development in women, 154
- Ppib*, 206
- Primary pulmonary hypertension, 114
- Procollagen-N-proteinase, 137
- Procollagens, 9, 10, 13–16, 19, 130, 137, 146, 205, 224, 233
- Progeroid EDS, 136, 146
- Progeroid facial appearance, 148, 171
- Progeroid type, 146–151
- Progressive kyphoscoliosis, 135
- Progressive muscle fibrosis, 195
- Propranolol, 82
- Proteoglycans, 2, 6, 9, 11, 13, 16, 19, 22, 32, 33, 36, 40, 50–55, 61, 111, 115, 136, 146–148, 155, 202, 207, 208, 212, 216, 234–236
- Protofibrils, 6, 16–20, 35, 207, 208, 212
- Protusio acetabuli, 79
- Proximal weakness, 188
- Pulmonary artery dilatation, 78, 79
- R**
- RAB6-interacting gene (*GORAB*, MIM 607983), 165
- Retinal detachment, 80, 98, 135, 154
- Retrognathia, 97, 152, 198
- S**
- Scleraxis* transgenic model mice, 217
- Scoliosis, 80, 82, 83, 96–99, 113, 115, 151, 152, 165, 171, 177–179, 186, 194, 197, 206
- Scx*-null (*Scx*^{-/-}) mice, 218
- N**
- Network-forming collagens, 8, 13
- Nevi, 148
- Non-functional *COL5A1* allele, 139
- N-telopeptide of collagen type I, 152

Serum creatine kinase, 187, 189, 196
 SGS. *See* Shprintzen-Goldberg syndrome (SGS)
 Sheep, 232, 233, 236
 Shprintzen-Goldberg syndrome (SGS), 85, 98, 99, 112, 113, 115–116, 120–121
 Signaling pathway, 63, 109–112, 114, 118, 121, 122
 Six subtypes, 130
 Skeletal muscle hypoplasia, 81
 Skin hyperextensibility, 100, 131, 152, 206
 Skin involvement, 163, 176
 SLRPs. *See* Small leucine-rich proteoglycans (SLRPs)
 Smad, 61–63, 69, 85, 110, 111, 113, 114, 117, 118, 120–122, 195, 215, 217
 SMAD3 or TGFB2, 96, 102
 Small leucine-rich proteoglycans (SLRPs), 2, 6, 13, 16, 18–20, 22, 41, 50–53, 136, 202, 208–212, 216, 224
 Solute Carrier Family 2, 115
 Spondylocheirodysplastic form, 136
 Spondylolisthesis, 82, 97
 Spontaneous bowel rupture, 98
 Spontaneous pneumothorax, 80, 82
 Stiff skin syndrome, 85
 Strabismus, 96, 97, 154, 163, 169
 Striae atropicae, 81
 Subcutaneous hematomas, 152–154
 Supramolecular structures of collagens, 8
 Surgical interventions, 2, 84, 102, 140

T

Talipes equinovarus, 97, 152
 Tenascins, 1, 32–42, 53, 55, 63–65
 Tenascin-X, 39, 54, 130, 133
 Tendon-derived progenitor cells, 69
 Tendon disorders, 53
 Tendon repair, 60–62, 64, 69, 215, 217
Tgfb2, 215
Tgfb3, 215, 221
 TGF β -inducible early gene (*Tieg*), 215
TGFBR2, 96, 99
Tgfb2, 215, 222
 TGF- β receptor, 40, 96, 101, 102, 109, 112–119, 121, 122
Tgfb2^{PrrxlCre} mice, 215
 Thoracic and abdominal aortic aneurysm, 112
 Thoracic aortic aneurysm and dissection (TAAD) syndrome, 101
 Thrombospondins, 32–42, 103, 109, 152
 Tissue fragility, 146, 206
Tnmd^{-/-} mice, 220
 Transaldolase (TALDO) deficiency (MIM 606003), 165

Transforming growth factor- β (TGF- β), 96, 107–122, 163, 195, 214, 215
 Transforming growth factor- β (TGF- β) family, 61–64
 Translucent skin, 98, 100, 134
 Transmembrane collagens, 8, 13
 Triple helix, 8, 13–15, 132, 137, 155, 204, 205
 Type I collagen, 1, 33, 40, 41, 50–53, 60, 63, 64, 67–69, 130, 131, 135, 137, 138, 152
 Type III collagen, 8, 41, 52, 54, 55, 60, 67, 99, 100, 130, 134, 138, 152

U

UCMD. *See* Ullrich congenital muscular dystrophy (UCMD)
 UDP-Gal: β Gal β 1,3-galactosyltransferase, 150, 152
 Ullrich congenital muscular dystrophy (UCMD), 186–188, 191–196, 206
 Urban-Rifkin-Davis Syndrome (URDS; MIM 613177), 163, 167

V

Valvulopathy, 62, 79
 Vascular endothelial growth factor (VEGF), 35, 40, 61, 63, 66–68
 Vascular imaging for aortic aneurysm, 119
 Vascular impairment and rupture, 140
 Vascular subtype, 130, 131, 133, 140
 VEGF. *See* Vascular endothelial growth factor (VEGF)
 Verapamil, 83
 Versican, 52–55
 Villefranche classification, 130

W

Walt Disney dwarfism, 171
 Weill-Marchesani syndrome, 37, 85, 233
 Williams syndrome (MIM 194050), 166
 Wrinkly Skin Syndrome (WSS), 164, 169, 171
 Wrists, 22, 80, 82, 83, 97, 163, 165, 186–188, 219
 WSS. *See* Wrinkly Skin Syndrome (WSS)

X

Xylosylprotein beta 1,4-galactosyltransferase, 148–150, 152

Z

Zinc fingers, 135