|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Group / Name of Disorder** | **Inheri-tance** | **Gene(s)** | **OMIM number** | **ORPHANET code** | **Notes** |
| **1. FGFR3 chondrodysplasia group** |  |  |  |  |  |
| Thanatophoric dysplasia type 1 | AD | *FGFR3* | 187600 | 18060 | Includes previous San Diego type |
| Thanatophoric dysplasia type 2 | AD | *FGFR3* | 187601 | 93274 |  |
| Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN) | AD | *FGFR3* | 616482 | 85165 |  |
| Achondroplasia | AD | *FGFR3* | 100800 | 15 |  |
| Hypochondroplasia | AD | *FGFR3* | 146000 | 427 |  |
| Camptodactyly, tall stature and hearing loss syndrome (CATSHL) | AD, AR | *FGFR3* | 610474 | 85164 | Loss-of-function mutations |
| See also group 33 for craniosynostosis syndromes linked to *FGFR3* mutations, as well as LADD syndrome in group 41 for another *FGFR3-*related phenotype |  |  |  |  |  |
| **2. Type 2 collagen group** |  |  |  |  |  |
| Achondrogenesis type 2 (Langer-Saldino) | AD | *COL2A1* | 200610 | 93296 | Achondrogenesis type 2 and hypochondrogenesis form one phenotypic continuum |
| Hypochondrogenesis | AD | *COL2A1* | 200610 | 93297 | Achondrogenesis type 2 and hypochondrogenesis form one phenotypic continuum |
| Platyspondylic dysplasia, Torrance type | AD | *COL2A1* | 151210 | 85166 | see also severe spondylodysplastic dysplasias (group 14) |
| Spondyloepiphyseal dysplasia congenita (SEDC) | AD, AR\* | *COL2A1* | 183900  616583  604864 | 94068 | Includes mild SED with premature onset arthrosis and SED Stanescu type.  Mild SED cases may resemble MED (see note).  AR\*: A few cases with bi-allelic COL2A1 mutations have been reported |
| Spondyloepiphyseal dysplasia with marked metaphyseal changes (SEMD) | AD | *COL2A1* | 184250  184253  184255 | 93346  93316  93315  85198 | Includes SEMD Strudwick type, SMD Algerian type, dysspondyloenchondromatosis and some cases of SMD corner fracture type |
| Kniest dysplasia | AD | *COL2A1* | 156550 | 485 |  |
| Spondyloperipheral dysplasia | AD | *COL2A1* | 271700 | 1856 |  |
| SED with metatarsal shortening (formerly Czech dysplasia) | AD | *COL2A1* | 609162 | 137678 | Often associated with the p.R275C mutation |
| Stickler syndrome type 1 | AD | *COL2A1* | 108300 | 828  90653 | See also COL11A1, COL11A2, COL9A1, COL9A2, COL9A3 |
| Dysplasia of the proximal femoral epiphyses | AD | *COL2A1* | 608805  150600 | 2380 | Heterogeneous condition, not all cases are due to COL2A1 mutations (usually p.G393S; p.G717S; p.G1170S) |
| See also group 10 (multiple epiphyseal dysplasia) for overlapping phenotypes with normal stature and premature onset arthrosis |  |  |  |  |  |
| **3. Type 11 collagen group** |  |  |  |  |  |
| Stickler syndrome type 2 | AD | *COL11A1* | 604841 | 90654 | Can also result from somatic mosaicism for a COL11A1 mutation |
| Marshall syndrome | AD | *COL11A1* | 154780 | 560 | One report with homozygous p.Gly901Glu mutation in two affected sibs (PMID 22499343) |
| Stickler syndrome type 3 (non-ocular) | AD | *COL11A2* | 184840 | 166100 |  |
| Fibrochondrogenesis | AR, AD  AR, AD | *COL11A1*  *COL11A2* | 228520  614524 | 2021 |  |
| Otospondylomegaepiphyseal dysplasia (OSMED), recessive type | AR | *COL11A2* | 215150 | 1427 |  |
| Otospondylomegaepiphyseal dysplasia (OSMED), dominant type (Weissenbacher-Zweymüller syndrome, Stickler syndrome type 3) | AD | *COL11A2* | 184840 | 3450 |  |
| See also Stickler syndrome type 1 in group 2 |  |  |  |  |  |
| **4. Sulphation disorders group** |  |  |  |  |  |
| Achondrogenesis type 1B (ACG1B) | AR | *SLC26A2* | 600972 | 93298 | formerly known as achondrogenesis, Fraccaro type |
| Atelosteogenesis type 2 (AO2) | AR | *SLC26A2* | 256050 | 56304 | Includes de la Chapelle dysplasia, McAlister dysplasia, and neonatal osseous dysplasia |
| Diastrophic dysplasia (DTD) | AR | *SLC26A2* | 222600 | 628 |  |
| MED, autosomal recessive type | AR | *SLC26A2* | 226900 | 93307 | Classified in OMIM as EDM4; See also multiple epiphyseal dysplasia and pseudoachondroplasia group (group 10) and EDM7 in group 20 |
| SEMD, PAPSS2 type | AR | *PAPSS2* | 612847 | 93282 | Formerly “Pakistani type”. See also SEMD group (group 13) |
| Brachyolmia, recessive type | AR | *PAPSS2* | 612847 | 448242 | Probably includes Toledo and Hobaek types of brachyolmia |
| Chondrodysplasia gPAPP type (includes Catel-Manzke-like syndrome) | AR | *IMPAD1* | 614078 | 280586 |  |
| Chondrodysplasia with congenital joint dislocations, CHST3 type (recessive Larsen syndrome) | AR | *CHST3* | 143095 | 263463 | includes recessive Larsen syndrome, humero-spinal dysostosis, and SED Omani type |
| Ehlers-Danlos syndrome, musculocontractural type | AR  AR | *CHST14*  *DSE* | 601776  615539 | 2953 | includes adducted thumb-clubfoot syndrome |
| See also group 7 and group 20 for other conditions with multiple dislocations. |  |  |  |  |  |
| **5. Perlecan group** |  |  |  |  |  |
| Dyssegmental dysplasia, Silverman-Handmaker and Rolland-Desbuquois types | AR | *HSPG2* | 224410  224400 | 1865  156731 |  |
| Schwartz-Jampel syndrome (myotonic chondrodystrophy) | AR | *HSPG2* | 255800 | 800 | Mild and severe forms; includes previous Burton dysplasia |
| Note: *HSPG2* encodes perlecan, hence the group name |  |  |  |  |  |
| **6. Aggrecan group** |  |  |  |  |  |
| SED, Kimberley type | AD | *ACAN* | 608361 | 253 |  |
| SEMD, Aggrecan type | AR | *ACAN* | 612813 | 171866 |  |
| Short stature and advanced bone age | AD | *ACAN* | 165800 | 364817 | Sometimes with osteochondritis dissecans |
|  |  |  |  |  |  |
| **7. Filamin group and related disorders** |  |  |  |  |  |
| Frontometaphyseal dysplasia | XL  AD  AD | *FLNA*  *MAP3K7*  *TAB2* | 305620  617137 | 1826 |  |
| Cardiospondylocarpofacial syndrome | AD | *MAP3K7* | 157800 | 3238 |  |
| Melnick-Needles syndrome | XL | *FLNA* | 309350 | 2484 | Includes osteodysplasty |
| Otopalatodigital syndrome type 1 (OPD1) | XL | *FLNA* | 311300 | 90650 |  |
| Otopalatodigital syndrome type 2 (OPD2) | XL | *FLNA* | 304120 | 90650 |  |
| Terminal osseous dysplasia (TOD) | XL | *FLNA* | 300244 | 88630 | Includes digitocutaneous dysplasia |
| Atelosteogenesis type 1 (AO1) | AD | *FLNB* | 108720  112310 | 1190  1263 | Includes Boomerang dysplasia, Piepkorn dysplasia, and spondylohumerofemoral (giant cell) dysplasia |
| Atelosteogenesis type 3 (AO3) | AD | *FLNB* | 108721 | 56305 |  |
| Larsen syndrome (dominant) | AD | *FLNB* | 150250 | 503 |  |
| Spondylocarpotarsal synostosis syndrome | AR  AD, AR | *FLNB*  *MYH3* | 272460 | 3275 |  |
| Frank-ter Haar syndrome | AR | *SH3PXD2B* | 249420 | 137834 | Includes Borrone dermatocardioskeletal syndrome |
| See also group 4 for recessive Larsen syndrome and group 20 for conditions with multiple dislocations |  |  |  |  |  |
| **8. TRPV4 group** |  |  |  |  |  |
| Metatropic dysplasia | AD | *TRPV4* | 156530 | 2635 | Includes “hyperplastic”, lethal and non-lethal forms. Can also result from somatic mosaicism for a TRPV4 mutation |
| Spondyloepimetaphyseal dysplasia, Maroteaux type (Pseudo-Morquio syndrome type 2) | AD | *TRPV4* | 184095 | 263482 | Includes parastremmatic dwarfism (OMIM 168400) |
| Spondylometaphyseal dysplasia, Kozlowski type | AD | *TRPV4* | 184252 | 93314 |  |
| Brachyolmia, autosomal dominant type | AD | *TRPV4* | 113500 | 93304 |  |
| Familial digital arthropathy with brachydactyly | AD | *TRPV4* | 606835 | 85169 |  |
| See also groups 4 and 13 for other forms of brachyolmia |  |  |  |  |  |
| **9. Ciliopathies with major skeletal involvement** |  |  |  |  |  |
| Chondroectodermal dysplasia (Ellis-van Creveld) | AR  AR  AR  AR | *EVC1*  *EVC2*  *WDR35*  *DYNC2LI1* | 225500 | 289 | See also Weyers acrofacial (acrodental) dysostosis in group 34 |
| Short rib–polydactyly syndrome (SRPS) type 1/3 (Saldino-Noonan/Verma-Naumoff) | AR  AR  AR  AR  AR | *DYNC2H1*  *IFT80*  *WDR34*  *WDR60*  *DYNC2LI1* | 613091 | 93270  93271 | There is significant clinical and radiological overlap between SRP1/3 and ATD. Some forms of both remain unlinked to the known genes. |
| Asphyxiating thoracic dysplasia (ATD; Jeune) | AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR | *DYNC2H1*  *DYNC2LI1*  *WDR34*  *TCTEX1D2*  *WDR60*  *WDR19*  *IFT140*  *TTC21B*  *IFT80*  *IFT172*  *IFT81*  *IFT52*  *TRAF3IP1*  *CFAP410*  *CEP120*  *KIAA0586*  *KIAA0753* | 613091 | 474 | Dynein motor  Retrograde transport (IFT-A)  Anterograde transport (IFT-B)  Basal body  Centrosome |
| SRPS type 2 (Majewski) | AR  AR  AR  AR | *DYNC2H1*  *NEK1*  *IFT81*  *TRAF3IP1* | 263520 | 93269 |  |
| SRPS type 4 (Beemer) | AR  AR | *IFT122*  *IFT80* | 269860 | 93268 |  |
| SRPS type 5 | AR | *WDR35* | 614091 | 1505 |  |
| SRPS unclassified | AR  AR  AR  AR  AR | *ICK*  *INTU*  *FUZ*  *IFT43*  *WDR35* |  |  |  |
| Orofaciodigital syndrome type 4 (Mohr-Majewski) | AR | *TCTN3* | 258860 | 2753 |  |
| Orofaciodigital syndrome type 2 (Mohr syndrome) | AR | *NEK1* | 252100 | 2751 | There are also overlapping OFD phenotypes due to mutations in *INTU, CEP120* and *C2CD3* |
| Cranioectodermal dysplasia (Levin-Sensenbrenner) type 1, 2 | AR  AR  AR  AR  AR | *IFT122 WDR35*  *WDR19*  *IFT43*  *IFT52* | 218330 | 1515 |  |
| Mainzer-Saldino syndrome | AR  AR | *IFT140*  *IFT172* | 266920 | 140969 |  |
| Axial spondylometaphyseal dysplasia | AR  AR | *CFAP410*  *NEK1* | 602271 | 168549 |  |
| Thoracolaryngopelvic dysplasia (Barnes) | AD |  | 187760 | 3317 |  |
| See also paternal UPD14 and cerebrocostomandibular syndrome (group 35) |  |  |  |  |  |
| **10. Multiple epiphyseal dysplasia and pseudoachondroplasia group** |  |  |  |  |  |
| Pseudoachondroplasia (PSACH) | AD | *COMP* | 177170 | 750 |  |
| Multiple epiphyseal dysplasia (MED) | AD  AD  AD  AD  AD | *COMP*  *COL9A2*  *COL9A3*  *MATN3*  *COL9A1* | 132400  600204  600969  607078  614135 | 93308  166002  166002  93311  166002 | Not all MED (-like) cases seem to have mutations in these genes |
| Stickler syndrome, recessive type | AR  AR  AR | *COL9A1*  *COL9A2*  *COL9A3* | 614134  614284  120270 | 250984 | See also groups 2 and 3 |
| See also multiple epiphyseal dysplasia, recessive type in groups 4 and 20 as well as ASPED in group 15 |  |  |  |  |  |
| **11. Metaphyseal dysplasias** |  |  |  |  |  |
| Metaphyseal dysplasia, Schmid type (MCS) | AD | *COL10A1* | 156500 | 174 |  |
| Cartilage-hair hypoplasia (CHH; metaphyseal dysplasia, McKusick type) | AR | *RMRP* | 250250 | 175 | Includes anauxetic dysplasia |
| Metaphyseal dysplasia, POP1 type | AR | *POP1* | 617396 | 93347 | Includes anauxetic dysplasia |
| Metaphyseal dysplasia, Jansen type | AD | *PTHR1* | 156400 | 33067 | activating mutations - see also Blomstrand dysplasia (group 23) |
| Eiken dysplasia | AR | *PTHR1* | 600002 | 79106 | activating mutations - see also Blomstrand dysplasia (group 23) |
| Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachman-Bodian-Diamond syndrome, SBDS) | AR  AR  AR  AD | *SBDS*  *EFL1*  *DNAJC21*  *SRP54* | 260400  617941 | 811 |  |
| Metaphyseal anadysplasia type 1 | AD, AR | *MMP13* | 602111 | 1040 | Includes SEMD Missouri type. |
| Metaphyseal anadysplasia type 2 | AR | *MMP9* | 613073 | 1040 |  |
| Metaphyseal dysplasia, Spahr type | AR | *MMP13* | 250400 | 2501 |  |
| Metaphyseal dysplasia with maxillary hypoplasia | AD | *RUNX2* | 156510 | 2504 | May cause multiple vertebral fractures due to osteoporosis |
|  |  |  |  |  |  |
| **12. Spondylometaphyseal dysplasias (SMD)** |  |  |  |  |  |
| Spondyloenchondrodysplasia (SPENCD) | AR | *ACP5* | 271550 | 1855 | Includes combined immunodeficiency with autoimmunity and spondylometaphyseal dysplasia (OMIM 607944) |
| Odontochondrodysplasia (ODCD) | AR | *TRIP11* | 184260 | 166272 | See also achondrogenesis type IA in group 14; may represent a phenotypic spectrum |
| SMD, Sutcliffe type or corner fractures type | AD | *FN1* | 184255 | 93315 | Some cases are linked to COL2A1 but not the original family |
| SMD with cone-rod dystrophy | AR | *PCYT1A* | 608940 | 85167 |  |
| SMD with corneal dystrophy | AR | *PLCB3* |  |  |  |
| See also SMD Kozlowski type (group 8), SMD Sedaghatian type (group 14) and axial SMD (group 9); there are many individual reports of SMD variants. |  |  |  |  |  |
| **13. Spondylo-epi-(meta)-physeal dysplasias (SE(M)D)** |  |  |  |  |  |
| Dyggve-Melchior-Clausen dysplasia (DMC) | AR  AR | *DYM*  *RAB33B* | 223800  615222 | 239 | Includes Smith-McCort dysplasia (OMIM 607326) |
| Immuno-osseous dysplasia (Schimke) | AR | *SMARCAL1* | 242900 | 1830 |  |
| SED with diabetes mellitus, Wolcott-Rallison type | AR | *EIF2AK3* | 226980 | 1667 |  |
| SEMD, Matrilin type | AR | *MATN3* | 608728 | 156728 | See also matrilin-related MED in group 10 |
| SEMD, Shohat type | AR | *DDRGK1* | 602557 | 93352 |  |
| SEMD with leukodystrophy, AIFM1 type | XL | *AIFM1* | 300232 | 168484 |  |
| SEMD, biglycan type | XL | *BGN* | 300106 | 93349 | Previously known as SEMD, Camera type |
| SEMD with immune deficiency, EXTL3 type | AR | *EXTL3* | 617425 | 508533 | Also known as Immunoskeletal dysplasia with neurodevelopmental abnormalities; see also immuno-osseous dysplasia (Schimke) |
| SEMD with intellectual disability, NANS type | AR | *NANS* | 610442 | 168454 | Also known as SEMD, Genevieve type |
| SEMD with intellectual disability, RSPRY1 type | AR | *RSPRY1* | 616723 | 457395 | Also known as SEMD, Faden-Alkuraya type |
| SEMD, TMEM165 type | AR | *TMEM165* | 614727 | 314667 | Congenital disorder of glycosylation type IIk |
| SEMD, PISD type | AR | *PISD* |  |  | Phenotypically variable; see also case reported by Liberfarb RM et al. (PMID: 3561949) |
| SEMD, UFSP2 type | AD | *UFSP2* | 617974  142669 | 2114 | Includes Familial hip dysplasia (Beukes) |
| SEMD, short limb–abnormal calcification type | AR | *DDR2* | 271665 | 93358 | See also other dysplasias with stippling in group 21 |
| SED tarda, X-linked (SED-XL) | XL | *TRAPPC2* | 313400 | 93284 |  |
| Ehlers-Danlos syndrome, spondylodysplastic type | AR | *SLC39A13* | 612350 | 157965 |  |
| SPONASTRIME dysplasia | AR | *TONSL* | 271510 | 93357 |  |
| Platyspondyly (brachyolmia) with amelogenesis imperfecta | AR | *LTBP3* | 601216 | 2899 |  |
| CODAS syndrome | AR | *LONP1* | 600373 | 1458 |  |
| EVEN-PLUS syndrome | AR | *HSPA9* | 616854 | 496751 |  |
| CAGSSS syndrome | AR | *IARS2* | 616007 | 436174 |  |
| Steel syndrome | AR | *COL27A1* | 615155 | 438117 |  |
| See also: opsismodysplasia (group 14), mucopolysaccharidosis type 4 (Morquio syndrome) and other conditions in group 27, as well as PPRD (SED with progressive arthropathy) in group 31 |  |  |  |  |  |
| **14. Severe spondylodysplastic dysplasias** |  |  |  |  |  |
| Achondrogenesis type 1A (ACG1A) | AR | *TRIP11* | 200600 | 93299 |  |
| Schneckenbecken dysplasia | AR | *SLC35D1* | 269250 | 3144 |  |
| Spondylometaphyseal dysplasia, Sedaghatian type | AR | *GPX4* | 250220 | 93317 |  |
| Severe spondylometaphyseal dysplasia (SMD Sedaghatian-like) | AR | *SBDS* |  |  |  |
| Opsismodysplasia | AR | *INPPL1* | 258480 | 2746 | Includes lethal and milder cases |
| MAGMAS related skeletal dysplasia | AR | *PAM16* | 613320 | 401979 |  |
| See also: thanatophoric dysplasia, types 1 and 2 (group 1); achondrogenesis type 2 and Torrance dysplasia (group 2); fibrochondrogenesis (group 3); achondrogenesis type 1B (group 4); and metatropic dysplasia (group 8) |  |  |  |  |  |
| **15. Acromelic dysplasias** |  |  |  |  |  |
| Trichorhinophalangeal dysplasia types 1/3 | AD | *TRPS1* | 190350  190351 | 77258 |  |
| Trichorhinophalangeal dysplasia type 2 (Langer-Giedion) | AD | *TRPS1 and EXT1* | 150230 | 502 | Microdeletion syndrome; see also multiple cartilaginous exostoses in group 29 |
| Acrocapitofemoral dysplasia | AR | *IHH* | 607778 | 63446 |  |
| Geleophysic dysplasia | AR  AD  AD | *ADAMTSL2*  *FBN1*  *LTBP3* | 231050  614185  617809 | 2623 | Some forms unlinked to either gene |
| Acromicric dysplasia | AD  AD | *FBN1*  *LTBP3* | 102370 | 969 | Includes acrolaryngeal dysplasia, previously known as Fantasy Island dysplasia or Tattoo dysplasia, and Moore-Federman syndrome |
| Weill-Marchesani syndrome | AD  AR  AR  AR | *FBN1 ADAMTS10*  *ADAMTS17*  *LTBP2* | 608328  277600  613195  614819 | 3449 |  |
| Myhre dysplasia | AD | *SMAD4* | 139210 | 2588 |  |
| Acrodysostosis | AD  AD | *PDE4D*  *PRKAR1A* | 614613  101800 | 950 | Includes acroscyphodysplasia (PMID 30006632) |
| Angel-shaped phalango-epiphyseal dysplasia (ASPED) | AD |  | 105835 | 63442 | Possibly related or allelic to brachydactyly type C |
| Leri Pleonosteosis | AD | 8q22.1 | 151200 | 2900 | Duplication at 8q22.1 encompassing GDF6 and SDC2 |
| SED, MIR140 type | AD | MIR140 |  |  | Brachydactyly with cone-shaped epiphyses |
| See also brachydactyly group (groups 37 and 38) |  |  |  |  |  |
| **16. Acromesomelic dysplasias** |  |  |  |  |  |
| Acromesomelic dysplasia type Maroteaux (AMDM) | AR | *NPR2* | 602875 | 40 |  |
| Grebe dysplasia | AR  AR | *GDF5*  *BMPR1B* | 200700  609441 | 2098 | Includes acromesomelic dysplasia Hunter-Thompson type and acromesomelic dysplasia with genital anomalies; see also brachydactylies (group 37) |
| Fibular hypoplasia and complex brachydactyly (Du Pan) | AR  AR | *GDF5*  *BMPR1B* | 228900 | 2639 | See also Brachydactylies (group 37) |
| Acromesomelic dysplasia, Osebold-Remondini type | AD |  | 112910 | 93437 |  |
|  |  |  |  |  |  |
| **17. Mesomelic and rhizo-mesomelic dysplasias** |  |  |  |  |  |
| Dyschondrosteosis (Leri- Weill) | Pseudo-AD | *SHOX* | 127300 | 240 | Includes Reinhardt-Pfeiffer dysplasia (OMIM 191400) |
| Mesomelic dysplasia, Langer type | Pseudo-AR | *SHOX* | 249700 | 2632 |  |
| Omodysplasia, recessive type | AR | *GPC6* | 258315 | 93329 |  |
| Omodysplasia, dominant type | AD | *FZD2* | 164745 | 93328 | See also Robinow syndrome, dominant type |
| Robinow syndrome, recessive type | AR  AR | *ROR2*  *NXN* | 268310 | 1507 | Includes previous COVESDEM (costo-vertebral segmentation defect with mesomelia); see also brachydactyly type B |
| Robinow syndrome, dominant type | AD  AD  AD  AD | *WNT5A*  *DVL1*  *DVL3*  *FZD2* | 180700  616331  616894 | 3107 |  |
| Mesomelic dysplasia, Kantaputra type | AD | *HOXD* | 156232 | 1836 | Duplications at HOXD gene cluster locus; includes mesomelic dysplasia, Korean type |
| Mesomelic dysplasia, Nievergelt type | AD |  | 163400 | 2633 |  |
| Mesomelic dysplasia, Kozlowski-Reardon type | AR |  | 249710 | 2631 |  |
| Mesomelic dysplasia with acral synostoses (Verloes-David-Pfeiffer type) | AD | *SULF1 and SLCO5A1* | 600383 | 2496 | Microdeletion syndrome involving two adjacent genes |
| Mesomelic dysplasia, Savarirayan type (Triangular Tibia-Fibular Aplasia) | AD | *ID4* | 605274 | 85170 | Microdeletions on 6p22.3; Microdeletion on 2q11.2 encompassing LAF4 can cause a phenotype with overlapping skeletal features (PMID 18616733) |
| See also Werner syndrome (group 39); also consider: mesomelic dysplasia, Camera type (OMIM 611886) and mesomelic dysplasia, Fryns type (PMID 3342548) |  |  |  |  |  |
| **18. Bent bone dysplasia group** |  |  |  |  |  |
| Campomelic dysplasia (CD) | AD | *SOX9* | 114290 | 140 | Includes acampomelic campomelic dysplasia (ACD), mild campomelic dysplasia (OMIM 602196) and isolated Pierre-Robin sequence |
| Stüve-Wiedemann dysplasia | AR | *LIFR* | 601559 | 3206 | Includes former neonatal Schwartz-Jampel syndrome or SJS type 2 |
| Kyphomelic dysplasia, several forms |  |  | 211350 | 1801 | Probably heterogeneous |
| Bent bone dysplasia | AD | *FGFR2* | 614592 | 313855 |  |
| Bent bones can also been observed in conditions with osseous fragility (group 25) |  |  |  |  |  |
| **19. Primordial dwarfism and slender bones group** |  |  |  |  |  |
| 3-M syndrome | AR  AR  AR | *CUL7*  *OBSL1*  *CCDC8* | 273750  612921  614205 | 2616 | Includes dolichospondylic dysplasia and Yakut short stature syndrome |
| Sanjad-Sakati syndrome | AR | *TBCE* | 241410 | 93324 | Referred to in OMIM as Kenny-Caffey type 1 but does not correspond to the disorder described by Kenny and Caffey which is the dominant form |
| Kenny-Caffey syndrome | AD | *FAM111A* | 127000 | 93325 |  |
| Osteocraniostenosis | AD | *FAM111A* | 602361 | 2763 |  |
| Microcephalic osteodysplastic primordial dwarfism type 1/3 (MOPD1) | AR | *RNU4ATAC* | 210710 | 2636 | Usually homozygous mutations;  includes Taybi-Linder cephaloskeletal dysplasia |
| Roifman syndrome | AR | *RNU4ATAC* | 616651 | 353298 |  |
| Multiple epiphyseal dysplasia with microcephaly and nystagmus (Lowry-Wood syndrome) | AR | *RNU4ATAC* | 226960 | 1824 | See also group 10 because of multiple epiphyseal dysplasia |
| Microcephalic osteodysplastic primordial dwarfism type 2 (MOPD2; Majewski type) | AR | *PCNT2* | 210720 | 2637 |  |
| Microcephalic osteodysplastic primordial dwarfism (other types) | AR  AR  AR  AR  AR  AR  AR  AR  AR | *ATR*  *RBBP8*  *CEP152*  *DNA2*  *TRAIP*  *NSMCE2*  *CENPE*  *CRIPT*  *XRCC4* | 210600  606744  613823  615807  616777  617253  616051  615789  616541 |  | Seckel syndrome 1  Seckel syndrome 2  Seckel syndrome 5  Seckel syndrome 8  Seckel syndrome 9  Seckel syndrome 10  overlaps with primary microcephaly syndromes |
| IMAGE syndrome (intrauterine growth retardation, metaphyseal dysplasia, adrenal hypoplasia, and genital anomalies) | AD  AR | *CDKN1C*  *POLE* | 614732  618336 | 85173 | with immunodeficiency |
| Hallermann-Streiff syndrome | AR |  | 234100 | 2108 |  |
| Saul-Wilson syndrome | AD | *COG4* | 618150 | 85172 |  |
|  |  |  |  |  |  |
| **20. Dysplasias with multiple joint dislocations** |  |  |  |  |  |
| Desbuquois dysplasia type 1 (with accessory ossification center in index finger) | AR | *CANT1* | 251450 | 1425 | there are also cases with or without accessory ossification centers unlinked to CANT1 |
| Desbuquois dysplasia with short metacarpals and elongated phalanges (Kim type) | AR | *CANT1* | 251450 | 1425 |  |
| Desbuquois dysplasia type 2 (Baratela-Scott syndrome) | AR | *XYLT1* | 615777 | 1425 |  |
| Multiple epiphyseal dysplasia, recessive type | AR | *CANT1* | 617719 |  | Classified in OMIM as EDM7; Very rare form of MED |
| SEMD with joint laxity (SEMD-JL), leptodactylic or Hall type | AD | *KIF22* | 603546 | 93360 |  |
| SEMD with joint laxity (SEMD-JL), Beighton type | AR | *B3GALT6* | 271640 | 93359 |  |
| SEMD with joint laxity (SEMD-JL), EXOC6B type | AR | *EXOC6B* | 618395 | 93359 | Phenotype resembles SEMD-JL leptodactylic or Hall type |
| Pseudodiastrophic dysplasia | AR |  | 264180 | 85174 |  |
| CSGALNACT1 deficiency (joint dislocations and mild skeletal dysplasia | AR | *CSGALNACT1* | 616615 |  |  |
| B3GAT3 deficiency | AR | *B3GAT3* | 245600 | 284139 | Multisystem linkeropathy including osteopenia with fractures (osteogenesis imperfecta-like) and dislocations (Larsen-like) and developmental delay |
| Short stature with joint laxity and myopia | AR | *GZF1* | 617662 | 527450 | Phenotype resembles Larsen syndrome |
| Multiple joint dislocations with amelogenesis imperfecta | AR | *SLC10A7* | 618363 |  |  |
| Severe (lethal) neonatal short limb dysplasia with multiple dislocations | AR | *FAM20B* |  |  | Phenotype resembles Desbuquois dysplasia |
| Ehlers-Danlos syndrome, kyphoscoliotic type 1 | AR | *PLOD1* | 225400 | 1900 |  |
| Ehlers-Danlos syndrome, kyphoscoliotic type 2 | AR | *FKBP14* | 614557 | 300179 |  |
| See also: SED with congenital dislocations, CHST3 type (group 4); atelosteogenesis type 3 and Larsen syndrome (group 7); B4GALT7 deficiency in group 25 |  |  |  |  |  |
| **21. Chondrodysplasia punctata (CDP) group** |  |  |  |  |  |
| CDP, X-linked dominant, Conradi-Hünermann type (CDPX2) | XL | *EBP* | 302960 | 35173 |  |
| CDP, X-linked recessive, brachytelephalangic type (CDPX1) | XL | *ARSE* | 302950 | 79345 |  |
| CHILD (congenital hemidysplasia, ichthyosis, limb defects) | XL | *NSDHL* | 308050 | 139 |  |
| Keutel syndrome | AR | *MGP* | 245150 | 85202 |  |
| Greenberg dysplasia | AR | *LBR* | 215140 | 1426 | Includes hydrops-ectopic calcification-moth-eaten appearance dysplasia (HEM) and dappled diaphyseal dysplasia |
| Rhizomelic CDP | AR  AR  AR  AR  AR | *PEX7*  *DHPAT*  *AGPS*  *FAR1*  *PEX5* | 215100  222765  600121  616154  616716 | 177 |  |
| CDP tibial-metacarpal type | AD, AR |  | 118651 | 79346 |  |
| Astley-Kendall dysplasia | AR? |  |  | 85175 | relationship to OI and to Greenberg dysplasia unclear |
| Note that stippling can occur in maternal auto-immune disease and several syndromes such as Zellweger, Smith-Lemli-Opitz and others. See also SEMD short limb-abnormal calcification type in group 13. |  |  |  |  |  |
| **22. Neonatal osteosclerotic dysplasias** |  |  |  |  |  |
| Blomstrand dysplasia | AR | *PTHR1* | 215045 | 50945 | Caused by recessive inactivating mutations; see also Eiken dysplasia and Jansen dysplasia |
| Desmosterolosis | AR | *DHCR24* | 602398 | 35107 | See also other sterol-metabolism related conditions |
| Caffey disease (including prenatal, infantile and attenuated forms) | AD | *COL1A1* | 114000 | 1310 | See also osteogenesis imperfecta related to collagen 1 genes (group 25) |
| Caffey dysplasia (severe variants with prenatal onset) | AR |  | 114000 | 1310 |  |
| Raine dysplasia (lethal and non-lethal forms) | AR | *FAM20C* | 259775 | 1832 | Includes lethal and non-lethal cases (milder cases with hypophosphatemic rickets) |
| Dysplastic cortical hyperostosis, Kozlowski-Tsuruta type | AR? |  |  | 2204 | Two cases reported (see PMID 12401992) |
| Dysplastic cortical hyperostosis, Al-Gazali type | AR? |  | 601356 |  |  |
| See also Astley-Kendall dysplasia and CDPs in group 21 |  |  |  |  |  |
| **23. Osteopetrosis and related disorders** |  |  |  |  |  |
| Osteopetrosis, severe neonatal or infantile forms | AR  AR  AR | *TCIRG1*  *CLCN7*  *SNX10* | 259700  611490  615085 | 667 |  |
| Osteopetrosis, infantile form, with nervous system involvement (OPTB5) | AR | *OSTM1* | 259720 | 85179 | Includes former osteopetrosis with infantile neuraxonal dysplasia (OMIM 600329) |
| Osteopetrosis, infantile form, osteoclast-poor with immunoglobulin deficiency (OPTB7) | AR | *TNFRSF11A* | 612301 | 178389 | *See also* familial expansile osteolysis in osteolysis group (group 28) |
| Osteopetrosis, intermediate form | AR  AR  AR | *TNFSF11*  *PLEKHM1*  *CLCN7* | 259710  611497  259710 | 667  210110 |  |
| Osteopetrosis with renal tubular acidosis (OPTB3) | AR | *CA2* | 259730 | 2785 |  |
| Osteopetrosis, late-onset form type 2 (OPTA2) | AD | *CLCN7* | 166600 | 53 |  |
| Osteopetrosis with ectodermal dysplasia and immune defect (OLEDAID) | XL | *IKBKG* | 300301 | 69088 |  |
| Osteopetrosis, moderate form with defective leucocyte adhesion (LAD3) | AR | *FERMT3* | 612840 | 99844 | Also mutations in RASGRP2 have been reported (PMID 18709451) |
| Osteosclerotic metaphyseal dysplasia | AR | *LRRK1* | 615198 | 500548 | heterogeneous condition |
| Pycnodysostosis | AR | *CTSK* | 265800 | 763 |  |
| Dysosteosclerosis | AR  AR  AR | *SLC29A3*  *TNFRSF11A*  *CSF1R* | 224300  224300 | 1782 | Bi-allelic mutations in *CSF1R* cause a dysosteosclerosis-like phenotype |
| This group is characterized by an impaired bone resorption as common mechanism (osteoclast related) and therefore OPTA1 is not included in this group (see group 24);  Note: osteomesopyknosis may represent a form of osteopetrosis |  |  |  |  |  |
| **24. Other sclerosing bone disorders** |  |  |  |  |  |
| Osteopoikilosis | AD | *LEMD3* | 166700 | 166119  1306 | Includes Buschke-Ollendorff syndrome |
| Melorheostosis with osteopoikilosis | AD | *LEMD3* | 166700 | 1879 | Includes mixed sclerosing bone dysplasia |
| Melorheostosis | SP | *MAP2K1* | 155950 | 2485 | Probably locus heterogeneity |
| Osteopathia striata with cranial sclerosis (OSCS) | XL | *AMER1* | 300373 | 2780 |  |
| Craniometaphyseal dysplasia | AD  AR | *ANKH*  *GJA1* | 123000  218400 | 1522 |  |
| Diaphyseal dysplasia Camurati-Engelmann | AD | *TGFB1* | 131300 | 1328 | Probably locus heterogeneity |
| Hyperostosis-Hyperphosphatemia syndrome | AR  AR  AR | *GALNT3*  *FGF23*  *KL* | 211900  617993  617994 | 306661 |  |
| Cerebellar hypoplasia-endosteal sclerosis | AR | *POLR3B* | 213002 | 85186 |  |
| Hematodiaphyseal dysplasia Ghosal | AR | *TBXAS1* | 231095 | 1802 |  |
| Hypertrophic osteoarthropathy | AR  AR | *HPGD*  *SLCO2A1* | 259100  614441 | 248095 | Includes cranio-osteoarthropathy and cases of recessive pachydermoperiostosis |
| Pachydermoperiostosis (hypertrophic osteoarthropathy, primary, autosomal dominant) | AD |  | 167100 | 2796 | Relationship to recessive form (OMIM 259100, HPGD deficiency) unclear |
| Oculodentoosseous dysplasia (ODOD) mild type | AD | *GJA1* | 164200 | 2710 |  |
| Oculodentoosseous dysplasia (ODOD) severe type | AR | *GJA1* | 257850 | 2710 | Possibly homozygous form of mild ODOD |
| Osteoectasia with hyperphosphatasia (juvenile Paget disease) | AR | *TNFRSF11B* | 239000 | 2801 |  |
| Osteosclerosis | AD | *LRP5* | 144750 | 2790  2783  3416 | Includes AD osteopetrosis type 1 (OPTA1) (MIM 607634) and endosteal hyperostosis, Worth type; see note for group 23 |
| Sclerosteosis | AR  AR | *SOST*  *LRP4* | 269500  614305 | 3152 |  |
| Endosteal hyperostosis, van Buchem type | AR | *SOST* | 239100 | 3416 | Specific 52 kb deletion downstream of *SOST* |
| Trichodentoosseous dysplasia | AD | *DLX3* | 190320 | 3352 |  |
| Diaphyseal medullary stenosis with malignant fibrous histiocytoma | AD | *MTAP* | 112250 | 85182 | Also known as Hardcastle syndrome |
| Craniodiaphyseal dysplasia | AD | *SOST* | 122860 | 1513 | Dominant negative |
| Craniometadiaphyseal dysplasia, Wormian bone type | AR |  | 269300 | 85184 |  |
| Lenz-Majewski hyperostotic dysplasia | AD | *PTDSS1* | 151050 | 2658 |  |
| Metaphyseal dysplasia, Braun-Tinschert type | AD |  | 605946 | 85188 |  |
| Pyle disease | AR | *SFRP4* | 265900 | 3005 |  |
| In this group many disorders have an increased bone formation as common mechanism (osteoblast related).  Consider also: mesomelic dysplasia Robinow type (DVL1) (group 17) and trichothiodystrophy with central osteosclerosis (PMID 15148554) |  |  |  |  |  |
| **25. Osteogenesis Imperfecta and decreased bone density group** |  |  |  |  |  |
| Osteogenesis imperfecta, non-deforming with persistently blue sclerae (OI type 1) | AD | *COL1A1*  *COL1A2* | 166200 | 216796 | OMIM OI type I |
| Osteogenesis imperfecta, perinatal lethal form (OI type 2) | AD  AD  AR  AR  AR | *COL1A1*  *COL1A2*  *CRTAP*  *LEPRE1*  *PPIB* | 166210  166210  610854  610915  259440 | 216804  216804  216804  216804  216804 | OMIM OI type II  OMIM OI type II  OMIM OI type VII  OMIM OI type VIII  OMIM OI type IX |
| Osteogenesis imperfecta, progressively deforming type (OI type 3) | AD  AD  AD  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR  AR | *COL1A1 COL1A2*  *IFITM5*  *SERPINF1*  *CRTAP*  *LEPRE1*  *PPIB*  *SERPINH1*  *FKBP10*  *TMEM38B*  *BMP1*  *WNT1*  *CREB3L1*  *SPARC*  *TENT5A* | 259420  259420  610967  613982  610682  610915  259440  613848  610968  615066  112264  615220  616229  616507  617952 | 216812  216812  216812  216812  216812  216812  216812  216812  216812  216812  216812  216812  216812  216812  216812 | OMIM OI type III  OMIM OI type III  OMIM OI type V  OMIM OI type VI  OMIM OI type VII  OMIM OI type VIII  OMIM OI type IX  OMIM OI type X  OMIM OI type XI  OMIM OI type XIII  OMIM OI type XIV  OMIM OI type XV  OMIM OI type XVI  OMIM OI type XVII  OMIM OI type XVIII |
| Osteogenesis imperfecta, moderate form (OI type 4)  (Note: in adults always normal sclerae) | AD  AD  AD  AD  AR  AR  AR  AR | *COL1A1 COL1A2 WNT1*  *IFITM5*  *CRTAP*  *PPIB*  *FKBP10*  *SP7* | 166220  166220  615220  610967  610682  259440  610968  613849 | 216820  216820  216820  216820  216820  216820  216820  216820 | OMIM OI type IV  OMIM OI type IV  OMIM OI type XV  OMIM OI type V  OMIM OI type VII  OMIM OI type IX  OMIM OI type XI  OMIM OI type XII |
| Osteogenesis imperfecta with calcification of the interosseous membranes and/or hypertrophic callus (OI type 5) | AD | *IFITM5* | 610967 | 216828 |  |
| Osteoporosis – X-linked form | XL  XL | *PLS3*  *MBTPS2* | 300910  301014 | 391330 | -  OMIM OI type XIX |
| Osteoporosis – AD form | AD  AD | *WNT1*  *LRP5* | 615220  166710 | 216820  85193 | OMIM OI type XV  - |
| Bruck syndrome type 1 (BS1) | AR | *FKBP10* | 259450 | 2771 | See autosomal recessive OI, above; intrafamilial variability between OI type 3, arthrogryposis and BS1 documented |
| Bruck syndrome type 2 (BS2) | AR | *PLOD2* | 609220 | 2771 |  |
| Osteoporosis-pseudoglioma syndrome | AR | *LRP5* | 259770 | 2788 | May mimic OI types 3 and 4 without eye involvement |
| Calvarial doughnut lesions with bone fragility | AD | *SGMS2* | 126550 | 85192 | Overlap with SMD phenotype |
| Cole-Carpenter dysplasia (bone fragility with craniosynostosis) | AD | *P4HB* | 112240 | 2050 |  |
| Cole-Carpenter like dysplasia | AR | *SEC24D* | 616294 |  | Cole-Carpenter syndrome 2 |
| Spondylo-ocular dysplasia | AR | *XYLT2* | 605822 | 85194 |  |
| Gnathodiaphyseal dysplasia | AD | *ANO5* | 166260 | 53697 |  |
| Ehlers-Danlos syndrome, spondylodysplastic type | AR | *B4GALT7* | 130070 | 75497 | Formerly known as “EDS, progeroid form”; also known as “Larsen syndrome, la Réunion variant”; see also B3GALT6 deficiency in group 20 |
| Geroderma osteodysplasticum | AR | *GORAB* | 231070 | 2078 |  |
| Cutis laxa, autosomal recessive form, type 2B (ARCL2B) | AR | *PYCR1* | 612940 | 90350 | Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum |
| Cutis laxa, autosomal recessive form, type 2A (ARCL2A)  (Wrinkly skin syndrome) | AR | *ATP6VOA2* | 278250  219200 | 90350 | Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum |
| Wiedemann-Rautenstrauch syndrome | AR | *POLR3A* | 264090 | 3455 |  |
| Singleton-Merten dysplasia type 1 | AD | IFIH1 | 182250 | 85191 |  |
| Singleton-Merten dysplasia type 2 | AR | DDX58 | 616298 | 85191 |  |
| Short stature, optic nerve atrophy and Pelger-Huet anomaly  (SOPH syndrome) | AR | NBAS | 614800 | 391677 |  |
| See also metaphyseal dysplasia with maxillary hypoplasia in group 11 |  |  |  |  |  |
| **26. Abnormal mineralization group** |  |  |  |  |  |
| Hypophosphatasia, perinatal lethal, infantile and juvenile forms | AR | *ALPL* | 241500 | 436 |  |
| Hypophosphatasia, juvenile and adult forms | AD | *ALPL* | 146300 | 247676 | Includes odontohypophosphatasia |
| Hypophosphatemic rickets, X-linked | XL | *PHEX* | 307800 | 89936 |  |
| Hypophosphatemic rickets, autosomal dominant | AD | *FGF23* | 193100 | 89937 |  |
| Hypophosphatemic rickets, autosomal recessive, type 1 (ARHR1) | AR | *DMP1* | 241520 | 289176 |  |
| Hypophosphatemic rickets, autosomal recessive, type 2 (ARHR2) | AR | *ENPP1* | 613312 | 289176 |  |
| Hypophosphatemic rickets with hypercalciuria, X-linked | XL | *CLCN5* | 300554 | 1652 | Part of Dent’s disease complex |
| Hypophosphatemic rickets with hypercalciuria, autosomal recessive (HHRH) | AR | *SLC34A3* | 241530 | 157215 |  |
| Vitamin D-dependent rickets, type 1A | AR | *CYP27B1* | 264700 | 289157 |  |
| Vitamin D-dependent rickets, type 1B | AR | *CYP2R1* | 600081 | 289157 |  |
| Vitamin D-dependent rickets, type 2A | AR | *VDR* | 277440 | 93160 |  |
| Vitamin D-dependent rickets, type 2B | AR? |  | 600785 | 93160 |  |
| Familial hyperparathyroidism, types 1-4 | AD  AD  AD  AD | *CDC73*  *CDC73*  *-*  *GCM2* | 145000  145001  610071  617343 | 99879  99880  99879  99879 | Genetic hyperparathyroidism due to parathyroid adenoma occurs in a number of tumor-associated syndromes such as MEN |
| Neonatal hyperparathyroidism, severe form | AR, AD | *CASR* | 239200 | 417 |  |
| Neonatal hyperparathyroidism, transient form | AR | *TRPV6* | 618188 | 417 |  |
| Familial hypocalciuric hypercalcemia with transient neonatal hyperparathyroidism | AD | *CASR* | 145980 | 405 | Other forms of familial hypocalciuric hypercalcemia do not show significant skeletal phenotypes |
| Calcium pyrophosphate deposition disease (familial chondrocalcinosis) type 2 | AD | *ANKH* | 118600 | 1416 | Loss-of-function mutations (see craniometaphyseal dysplasia in group 24) |
| Cutaneous skeletal hypophosphatemia syndrome | SP  SP | *HRAS*  *NRAS* |  |  |  |
| See also Jansen dysplasia and Eiken dysplasia (group 11) and Cole-Carpenter syndrome (group 25); see also group 22 for *FAM20C* related cases of hypophosphatemic rickets |  |  |  |  |  |
| **27. Lysosomal Storage Diseases with Skeletal Involvement (Dysostosis Multiplex group)** |  |  |  |  |  |
| Mucopolysaccharidosis type 1H-1S | AR | *IDUA* | 607014  607015  607016 | 579 |  |
| Mucopolysaccharidosis type 2 | XL | *IDS* | 309900 | 580 |  |
| Mucopolysaccharidosis type 3A | AR | *SGSH* | 252900 | 79269 |  |
| Mucopolysaccharidosis type 3B | AR | *NAGLU* | 252920 | 79270 |  |
| Mucopolysaccharidosis type 3C | AR | *HSGNAT* | 252930 | 79271 |  |
| Mucopolysaccharidosis type 3D | AR | *GNS* | 252940 | 79272 |  |
| Mucopolysaccharidosis type 4A | AR | *GALNS* | 253000 | 309297 |  |
| Mucopolysaccharidosis type 4B | AR | *GLB1* | 253010 | 309310 |  |
| Mucopolysaccharidosis type 6 | AR | *ARSB* | 253200 | 583 |  |
| Mucopolysaccharidosis type 7 | AR | *GUSB* | 253220 | 584 |  |
| Mucopolysaccharidosis-plus syndrome (VPS33A deficiency) | AR | *VPS33A* | 617303 | 505248 |  |
| Fucosidosis | AR | *FUCA* | 230000 | 349 |  |
| alpha-Mannosidosis | AR | *MAN2B1* | 248500 | 61 |  |
| beta-Mannosidosis | AR | *MANBA* | 248510 | 118 |  |
| Aspartylglucosaminuria | AR | *AGA* | 208400 | 93 |  |
| GM1 Gangliosidosis, several forms | AR | *GLB1* | 230500 | 354 |  |
| Sialidosis, several forms | AR | *NEU1* | 256550 | 812  93399  93400 |  |
| Sialic acid storage disease (SIASD) | AR | *SLC17A5* | 269920 | 834 |  |
| Galactosialidosis, several forms | AR | *PPGB* | 256540 | 351 |  |
| Multiple sulfatase deficiency | AR | *SUMF1* | 272200 | 585 |  |
| Mucolipidosis II (I-cell disease), alpha/beta type | AR | *GNPTAB* | 252500 | 576 |  |
| Mucolipidosis III (Pseudo-Hurler polydystrophy), alpha/beta type | AR | *GNPTAB* | 252600 | 423461 |  |
| Mucolipidosis III (Pseudo-Hurler polydystrophy), gamma type | AR | *GNPTG* | 252605 | 423470 |  |
| Other conditions resembling storage diseases: congenital disorders of glycosylation and geleophysic dysplasia (group 15) |  |  |  |  |  |
| **28. Osteolysis group** |  |  |  |  |  |
| Familial expansile osteolysis | AD | *TNFRSF11A* | 174810  602080 | 85195 | includes early-onset familial Paget disease of bone.  See also osteopetrosis and dysosteosclerosis (group 23) |
| Mandibuloacral dysplasia | AR  AR | *LMNA*  *ZMPSTE24* | 248370  608612 | 2457 |  |
| Progeria, Hutchinson-Gilford type | AD | *LMNA* | 176670 | 740 |  |
| Multicentric osteolysis, nodulosis and arthropathy (MONA) | AR  AR | *MMP2*  *MMP14* | 259600  277950 | 371428 | Includes Winchester-Torg syndrome and nodulosis-arthropathy-osteolysis syndrome |
| Hajdu-Cheney syndrome | AD | *NOTCH2* | 102500 | 955 | Includes serpentine fibula-polycystic kidney syndrome |
| Multicentric carpal-tarsal osteolysis with and without nephropathy | AD | *MAFB* | 166300 | 2774 |  |
| See also pycnodysostosis, cleidocranial dysplasia, Keutel syndrome, Farber disease and Singleton-Merten syndrome.  Note: several neurologic conditions may cause acro-osteolysis |  |  |  |  |  |
| **29. Disorganized development of skeletal components group** |  |  |  |  |  |
| Multiple cartilaginous exostoses (osteochondromas) | AD  AD | *EXT1*  *EXT2* | 133700  133700 | 321  321 |  |
| Cherubism | AD | *SH3BP2* | 118400 | 184 |  |
| Fibrous dysplasia, polyostotic form (McCune-Albright) | SP | *GNAS* | 174800 | 562 | Somatic mosaicism and imprinting phenomena |
| Metachondromatosis | AD | *PTPN11* | 156250 | 2499 |  |
| Osteoglophonic dysplasia | AD | *FGFR1* | 166250 | 2645 | Craniosynostosis is also an important feature (group 33) |
| Fibrodysplasia ossificans progressiva (FOP) | AD | *ACVR1* | 135100 | 337 |  |
| Neurofibromatosis type 1 (NF1) | AD | *NF1* | 162200 | 363700 |  |
| Cherubism with gingival fibromatosis (Ramon syndrome) | AR |  | 266270 | 3019 |  |
| Dysplasia epiphysealis hemimelica (Trevor) | SP |  | 127800 | 1822 |  |
| Lipomembraneous osteodystrophy with leukoencephalopathy (presenile dementia with bone cysts; Nasu-Hakola) | AR | *TREM2, TYROBP* | 221770 | 2770 |  |
| Enchondromatosis (Ollier) and Enchondromatosis with hemangiomata (Maffucci) | SP | *IDH1, IDH2* | 166000 | 296  163634 |  |
| Metaphyseal chondromatosis with D-2-hydroxyglutaric aciduria | SP | *IDH1* | 614875 | 99646 |  |
| Genochondromatosis | AD |  | 137360 | 85197  93398 | Probably includes Vaandrager-Peña syndrome |
| Gorham-Stout Disease | SP |  | 123880 | 73 | See also familial diffuse cystic angiomatosis of bone (PMID 2910603) |
| Osteofibrous Dysplasia | AD, SP | *MET* | 607278 | 488265 |  |
| See also: Proteus syndrome in group 30; spondyloenchondrodysplasia in group 12; dysspondyloenchondromatosis in group 2; cutaneous skeletal hypophosphatemia syndrome in group 26 |  |  |  |  |  |
| **30. Overgrowth (tall stature) syndromes with skeletal involvement** |  |  |  |  |  |
| Weaver syndrome | AD | *EZH2* | 277590 | 3447 | Some cases reported with NSD1, EED and SUZ12 mutations |
| Sotos syndrome | AD  AD  AR | *NSD1*  *NFIX*  *APC2* | 117550  614753  617169 | 821  420179 | Includes Malan syndrome |
| Luscan-Lumish syndrome | AD | *SETD2* | 616831 |  |  |
| Tatton-Brown-Rahman syndrome | AD | *DNMT3A* | 615879 | 404443 |  |
| Marshall-Smith syndrome | AD | *NFIX* | 602535 | 561 |  |
| Proteus syndrome | SP | *AKT1* | 176920 | 744 |  |
| CLOVES | SP | *PIK3CA* | 612918 | 140944 |  |
| Marfan syndrome | AD | *FBN1* | 154700 | 558 |  |
| Congenital contractural arachnodactyly | AD | *FBN2* | 121050 | 115 |  |
| Loeys-Dietz syndrome (types 1-6) | AD  AD  AD  AD  AD  AD | *TGFBR1*  *TGFBR2,*  *SMAD3*  *TGFB2*  *TGFB3*  *SMAD2* | 609192 610168  613795  614816  615582  601366 | 60030 |  |
| Meester-Loeys syndrome | XL | *BGN* | 300989 |  | See also SEMD, biglycan type (group 13) |
| Overgrowth syndrome with 2q37 translocations | SP | *NPPC* |  | 498488 | Overgrowth probably caused by overexpression of *NPPC* |
| Tall stature with long halluces, NPR2 type | AD | *NPR2* | 615923 | 329191 | Includes epiphyseal chondrodysplasia, Miura type; Gain-of-function mutations |
| Tall stature with long halluces, NPR3 type | AR | *NPR3* |  |  | Loss-of-function mutations |
| Moreno-Nishimura-Schmidt syndrome | SP |  | 608811 | 498485 |  |
| *See also:* Shprintzen-Goldberg syndrome in Craniosynostosis group 33 |  |  |  |  |  |
| **31. Genetic inflammatory/rheumatoid-like osteoarthropathies** |  |  |  |  |  |
| Progressive pseudorheumatoid dysplasia (PPRD; SED with progressive arthropathy) | AR | *WISP3* | 208230 | 1159 |  |
| Chronic infantile neurologic cutaneous articular syndrome (CINCA) / neonatal onset multisystem inflammatory disease (NOMID) | AD | *CIAS1* | 607115 | 1451 |  |
| Sterile multifocal osteomyelitis, periostitis, and pustulosis (CINCA/NOMID-like) | AR | *IL1RN* | 147679 | 210115 |  |
| Chronic recurrent multifocal osteomyelitis with congenital dyserythropoietic anemia (CRMO with CDA; Majeed syndrome) | AR | *LPIN2* | 609628 | 77297 |  |
| Hyaline Fibromatosis Syndrome | AR | *ANTXR2* | 236490 | 2176 | Previously known as infantile systemic hyalinosis, juvenile hyaline fibromatosis (OMIM 228600 ) and puretic syndrome |
|  |  |  |  |  |  |
| **32. Cleidocranial dysplasia and related disorders** |  |  |  |  |  |
| Cleidocranial dysplasia | AD | *RUNX2* | 119600 | 1452 | See also metaphyseal dysplasia with maxillary hypoplasia (group 11) |
| CDAGS syndrome (craniosynostosis, delayed fontanel closure, parietal foramina, imperforate anus, genital anomalies, skin eruption) | AR |  | 603116 | 85199 |  |
| Yunis-Varon dysplasia | AR  AR | *FIG4*  *VAC14* | 216340 | 3472 |  |
| Parietal foramina (isolated) | AD  AD | *ALX4*  *MSX2* | 609597  168500 | 60015 | See also frontonasal dysplasia type 1 (group 34) |
| Parietal foramina with cleidocranial dysplasia | AD | *MSX2* | 168550 | 251290 | MSX2 mutations also cause craniosynostosis Boston type (group 33) |
| See also: pycnodysostosis (group 23), wrinkly skin syndrome, mandibuloacral dysplasia, progeria and Hajdu-Cheney syndrome (group 28) for similar clavicular defects. |  |  |  |  |  |
| **33. Craniosynostosis syndromes** |  |  |  |  |  |
| Pfeiffer syndrome | AD  AD | *FGFR1*  *FGFR2* | 101600  101600 | 93258  710 | Most have *FGFR1* p.P252R mutation; Includes Jackson-Weiss syndrome (OMIM 123150) |
| Apert syndrome | AD | *FGFR2* | 101200 | 87 |  |
| Craniosynostosis with cutis gyrata (Beare-Stevenson) | AD | *FGFR2* | 123790 | 1555 |  |
| Crouzon syndrome | AD | *FGFR2* | 123500 | 207 |  |
| Crouzon-like craniosynostosis with acanthosis nigricans (Crouzonodermoskeletal syndrome) | AD | *FGFR3* | 612247 | 93262 | Defined by specific *FGFR3* p.A391E mutation |
| Craniosynostosis, Muenke type | AD | *FGFR3* | 602849 | 53271 | Defined by specific *FGFR3* p.P250R mutation |
| Antley-Bixler syndrome | AR | *POR* | 201750 | 83  63269 |  |
| Craniosynostosis Boston type | AD | *MSX2* | 604757 | 1541 | Heterozygous p.P148H mutation in two families |
| Saethre-Chotzen syndrome | AD | *TWIST1* | 101400 | 794 | Mutations in FGFR3, FGFR2 and TCF12 have been reported to cause phenotypes resembling Saethre-Chotzen syndrome |
| Shprintzen-Goldberg syndrome | AD | *SKI* | 182212 | 2462 |  |
| Baller-Gerold syndrome | AR | *RECQL4* | 218600 | 1225 |  |
| Carpenter syndrome | AR  AR | *RAB23*  *MEGF8* | 201000  614976 | 65759 |  |
| Coronal craniosynostosis | AD | *TCF12* | 615314 | 35099 |  |
| Complex craniosynostosis | AD | *ERF* | 600775 |  | Mutations in ERF also cause Chitayat hyperphalangism syndrome |
| See also cranioectodermal dysplasia (group 9), SEMD type RSPRY1 (group 13), osteocraniostenosis (group 19), Cole-Carpenter syndrome (group 25), CDAGS syndrome (group 32), and craniofrontonasal syndrome (group 34), Philadelphia type craniosynostosis (IHH duplication) (group 41) and multiple synostosis syndrome FGF9 type (group 42). Craniosynostosis can also be present in Loeys-Dietz syndrome (group 30) |  |  |  |  |  |
| **34. Dysostoses with predominant craniofacial involvement** |  |  |  |  |  |
| Mandibulofacial dysostosis (Treacher Collins, Franceschetti-Klein) | AD  AR  AD, AR | *TCOF1 POLR1C POLR1D* | 154500  248390  613717 | 861 |  |
| Mandibulofacial dysostosis with microcephaly | AD | *EFTUD2* | 610536 | 79113 |  |
| Mandibulofacial dysostosis with alopecia | AD | *EDNRA* | 616367 | 443995 |  |
| Miller syndrome (postaxial acrofacial dysostosis) | AR | *DHODH* | 263750 | 246 |  |
| Acrofacial dysostosis, Nager type | AD, AR | *SF3B4* | 154400 | 245 |  |
| Acrofacial dysostosis, Rodriguez type | AR | *SF3B4* | 201170 | 1788 |  |
| Acrofacial dysostosis, Cincinnati type | AD | *POLR1A* | 616462 | 1200 |  |
| Frontonasal dysplasia, type 1 | AR | *ALX3* | 136760 | 391474 |  |
| Frontonasal dysplasia, type 2 | AR | *ALX4* | 613451 | 228390 |  |
| Frontonasal dysplasia, type 3 | AR | *ALX1* | 613456 | 306542 |  |
| Craniofrontonasal syndrome | XL | *EFNB1* | 304110 | 1520 |  |
| Acromelic frontonasal dysostosis | AD | *ZSWIM6* | 603671 | 1827 |  |
| Hemifacial microsomia | SP, AD |  | 164210 | 374 | Includes Goldenhar syndrome and oculo-auriculo-vertebral spectrum; genetically heterogeneous; in some cases a microduplication on 14q23.1 |
| Richieri-Costa-Pereira syndrome | AR | *EIF4A3* | 268305 | 3102 |  |
| Auriculocondylar syndrome, type 1 | AD | *GNAI3* | 602483 | 137888 |  |
| Auriculocondylar syndrome, type 2 | AR, AD | *PLCB4* | 614669 | 137888 |  |
| Auriculocondylar syndrome, type 3 | AR | *EDN1* | 615706 | 137888 |  |
| Orofaciodigital syndrome type I (OFD1) | XL | *OFD1* | 311200 | 2750 |  |
| Weyers acrofacial (acrodental) dysostosis | AD  AD | *EVC1*  *EVC2* | 193530 | 952 | See also ciliopathy group 9- |
| See also Orofaciodigital syndrome type IV in the Ciliopathies (group 9) |  |  |  |  |  |
| **35. Dysostoses with predominant vertebral with and without costal involvement** |  |  |  |  |  |
| Currarino syndrome | AD | *MNX1* | 176450 | 1552 | Overlap with caudal regression syndrome (see OMIM 600145; heterozygous mutations in *VANGL1*) |
| Spondylocostal dysostosis | AR  AR  AR  AR  AR, AD  AR | *DLL3*  *MESP2*  *LFNG*  *HES7*  *TBX6*  *RIPPLY2* | 277300  608681  609813  613686  122600  616566 | 2311  2311  2311  2311  122600  2311 |  |
| NAD deficiency syndrome | AR  AR | *HAAO*  *KYNU* | 617660  617661 | 521438 | With associated cardiac, limb and renal defects |
| Vertebral segmentation defect (congenital scoliosis) with variable penetrance | AD  AD | *MESP2*  *HES7* | 608681  613686 | 2311  2311 |  |
| Klippel-Feil syndrome | AD  AR  AD  AR | *GDF6*  *MEOX1*  *GDF3*  *MYO18B* | 118100  214300  613702  616549 | 2345  2345  2345  447974 | role of *GDF6* mutations in AD spondylothoracic dysostosis remains unclear |
| Cerebrocostomandibular syndrome (rib gap syndrome) | AD | *SNRPB* | 117650 | 1393 | Mutations in COG1 are found in a cerebrocostomandibular-like syndrome (CDG type IIg) |
| Diaphanospondylodysostosis | AR | *BMPER* | 608022 | 66637 | includes ischiospinal dysostosis |
| Spondylo-megaepiphyseal-metaphyseal dysplasia (SMMD) | AR | *NKX3-2* | 613330 | 228387 |  |
| See also Spondylocarpotarsal synostosis syndrome in group 7 |  |  |  |  |  |
| **36. Patellar dysostoses** |  |  |  |  |  |
| Ischiopatellar dysplasia (small patella syndrome) | AD | *TBX4* | 147891 | 1509 |  |
| Nail-patella syndrome | AD | *LMX1B* | 161200 | 2614 |  |
| Genitopatellar syndrome | AD | *KAT6B* | 606170 | 85201 |  |
| Ear-patella-short stature syndrome (Meier-Gorlin) | AR  AR  AR  AR  AR  AD  AR | *ORC1*  *ORC4 ORC6*  *CDT1 CDC6*  *GMNN*  *CDC45L* | 224690  613800  613803  613804  613805  616835  617063 | 2554  2554  2554  2554  2554  2554  2554 |  |
| See also MED group (group 10) for conditions with patellar changes as well as ischio-pubic-patellar dysplasia as mild expression of campomelic dysplasia (group 18) and RAPADILINO syndrome (group 39); patellar hypoplasia is variable present in PITX1 related clubfoot (group 39) |  |  |  |  |  |
| **37. Brachydactylies (without extraskeletal manifestations)** |  |  |  |  |  |
| Brachydactyly type A1 | AD | *IHH* | 112500 | 93388 |  |
| Brachydactyly type A2 | AD  AD  AD | *BMPR1B*  *BMP2*  *GDF5* | 112600  112600  112600 | 93396 | Duplication of BMP2 enhancer |
| Brachydactyly type B | AD | *ROR2* | 113000 | 93383 | see also Robinow syndrome/COVESDEM |
| Brachydactyly type B2 | AD | *NOG* | 611377 | 140908 |  |
| Brachydactyly type C | AD, AR | *GDF5* | 113100 | 93384 | See also ASPED (group 15) and other *GDF5* disorders |
| Brachydactyly type D | AD | *HOXD13* | 113200 |  | Brachydactyly type D is often a component of Brachydactyly type E |
| Brachydactyly type E | AD  AD | *PTHLH*  *HOXD13* | 613382  113300 | 93387 |  |
| Brachydactyly with anonychia (Cooks syndrome) | AD | *KCNJ2* | 106995 | 1487 | Duplications of SOX9/KCNJ2 regulatory region |
| Preaxial brachydactyly, PAX3 type | AD | *PAX3* |  |  | See PMID 25959774 |
|  |  |  |  |  |  |
| **38.Brachydactylies (with extraskeletal manifestations)** |  |  |  |  |  |
| Brachydactyly - mental retardation syndrome | AD | *HDAC4* | 600430 | 1001 | some patients have microdeletions involving contiguous genes (2q37 deletion syndrome) |
| Hyperphosphatasia with mental retardation, brachytelephalangy, and distinct face | AR | *PIGV* | 239300 | 247262 |  |
| Brachydactyly-hypertension syndrome (Bilginturan) | AD | *PDE3A* | 112410 | 1276 |  |
| Microcephaly-oculo-digito-esophageal-duodenal syndrome (Feingold syndrome) | AD | *MYCN* | 164280 | 1305 |  |
| Hand-foot-genital syndrome | AD | *HOXA13* | 140000 | 2438 |  |
| Rubinstein-Taybi syndrome | AD  AD | *CREBBP*  *EP300* | 180849  613684 | 783  353284 |  |
| Brachydactyly, Temtamy type | AR | *CHSY1* | 605282 | 363417 |  |
| Coffin-Siris syndrome1 | AD  AD  AD  AD | *ARID1B*  *SMARCB1*  *SMARCA4*  *SMARCE1* | 135900  614608  614609  616938 | 1465 | Mutations in various components of the SWI/SNF complex have been reported in patients with a diagnosis of Coffin-Siris syndrome |
| Catel-Manzke syndrome | AR | *TGDS* | 616145 | 1388 |  |
| Pseudohypoparathyroidism type IA | AD | *GNAS* | 103580 | 79443 | Caused by loss-of-function mutations on the maternal allele; formerly known as Albright hereditary osteodystrophy |
| See also group 15 for other conditions with brachydactyly as well as brachytelephalangic CDP (group 21). |  |  |  |  |  |
| **39. Limb hypoplasia – reduction defects group** |  |  |  |  |  |
| Ulnar-mammary syndrome | AD | *TBX3* | 181450 | 3138 |  |
| de Lange syndrome | AD  XL  AD  AD  XL | *NIPBL*  *SMC1A*  *SMC3*  *RAD21*  *HDAC8* | 122470  300590  610759  614701  300882 | 199 |  |
| Fanconi anemia *(see note below)* | AR | *several* | 227650 | 84 | Several complementation groups and genes |
| Thrombocytopenia-absent radius (TAR) | AR | *RBM8A* | 274000 | 3320 | Deletion and common SNP on other allele that has regulatory function |
| Thrombocythemia with distal limb defects | AD | *THPO* | 187950 | 329319 | Distal limb defects postulated as consequence of vascular occlusions |
| Holt-Oram syndrome | AD | *TBX5* | 142900 | 392 |  |
| Okihiro syndrome (Duane – radial ray anomaly) | AD | *SALL4* | 607323 | 93293 |  |
| Cousin syndrome | AR | *TBX15* | 260660 | 93333 |  |
| Roberts syndrome | AR | *ESCO2* | 268300 | 3103 |  |
| Split-hand-foot malformation with long bone deficiency (SHFLD) | AD | *BHLHA9* | 612576 | 3329 | Duplication which is less than 50% penetrant and shows markedly variable expression |
| Tibial hemimelia | AR |  | 275220 | 93322 |  |
| Tibial hemimelia-polysyndactyly-triphalangeal thumb (Werner syndrome) | AD | *SHH* | 188740 | 988 | Mutations in ZRS (limb enhancer of SHH) |
| Acheiropodia | AR | *SHH* | 200500 | 931 | Deletion in LMBR1 that affects ZRS (limb enhancer of SHH) |
| Tetra-amelia | AR  AR | *WNT3*  *RSPO2* | 273395  618021 | 3301 |  |
| Gollop-Wolfgang syndrome | AD | *BHLHA9* | 228250 | 1986 | Duplications or triplications of genomic region including BHLHA9 |
| Al-Awadi Raas-Rothschild limb-pelvis hypoplasia-aplasia | AR | *WNT7A* | 276820 | 2879 |  |
| Fuhrmann syndrome | AR | *WNT7A* | 228930 | 2854 |  |
| RAPADILINO syndrome | AR | *RECQL4* | 266280 | 3021 |  |
| Adams-Oliver syndrome | AD  AR  AD  AR  AD  AD | *ARHGAP31 DOCK6*  *RBPJ EOGT*  *NOTCH1*  *DLL4* | 100300  614219  614814  615297  616028  616589 | 974 |  |
| Poland syndrome | SP, AD |  | 173800 | 2911 |  |
| Femoral hypoplasia-unusual face syndrome (FHUFS) | SP |  | 134780 | 1988 | Some phenotypic overlap with FFU syndrome (below) |
| Fibular Aplasia, Tibial Campomelia, and Oligosyndactyly syndrome (FATCO) | SP, AD? |  | 246570 | 2492 |  |
| Femur-fibula-ulna syndrome (FFU) | SP |  | 228200 | 2019 |  |
| Hanhart syndrome (Hypoglossia-hypodactylia) | AD |  | 103300 | 989 |  |
| Scapulo-iliac dysplasia (Kosenow) | AD |  | 169550 | 2839 |  |
| Clubfoot with or without deficiency of long bones and/or mirrorimage polydactyly | AD | *PITX1* | 119800 | 199315 | In some patients bilateral patellar hypoplasia (see group 36) |
| Sirenomelia | SP |  |  | 3169 | Probably heterogeneous |
| Terminal transverse defects | SP |  | 102650 | 973 |  |
| *Note:* the particularly complex genetic basis of Fanconi anemia and its complementation groups is acknowledged but not further listed in this Nosology. The reader is referred to OMIM or to specialized reviews. - *See also* CHILD in group 21 and the mesomelic and acromesomelic dysplasias. |  |  |  |  |  |
| **40.Ectrodactyly with and without other manifestations** |  |  |  |  |  |
| Ankyloblepharon-ectodermal dysplasia-cleft palate (AEC) | AD | *TP63* | 106260 | 1071 |  |
| Ectrodactyly-ectodermal dysplasia cleft-palate syndrome Type 3 (EEC3) | AD | *TP63* | 604292 | 1896 |  |
| Ectrodactyly-ectodermal dysplasia-macular dystrophy syndrome (EEM) | AR | *CDH3* | 225280 | 1897 |  |
| Limb-mammary syndrome (including ADULT syndrome) | AD | *TP63* | 603543 | 69085 |  |
| Split hand-foot malformation, isolated form, type 4 (SHFM4) | AD | *TP63* | 605289 | 2440 |  |
| Split hand-foot malformation, isolated form, type 1 (SHFM1) | AD  AD | *DLX5*  *DLX6* | 220600  183600 | 2440 | Structural variations at locus; also regulatory mutations affecting exons of DYNC1I1 that regulate DLX5 |
| Split hand-foot malformation, isolated form, type 3 (SHFM3) | AD | *10q24* | 246560 | 2440 | Duplications at 10q24 encompassing LBX1, BTRC, POLL, DPCD and FBXW4 |
| Split hand-foot malformation, isolated form, type 6 (SHFM6) | AR | *WNT10B* | 225300 | 2440 |  |
| Split-foot malformation with mesoaxial polydactyly (SFMMP) | AR | *ZAK* | 616890 | 488232 |  |
| Hartsfield syndrome | AD | *FGFR1* | 615465 | 2117 |  |
|  |  |  |  |  |  |
| **41. Polydactyly-Syndactyly-Triphalangism group** |  |  |  |  |  |
| Preaxial polydactyly type 1 (PPD1) | AD | *SHH* | 174400 | 93339 | regulatory mutation or duplication of ZRS (limb enhancer of SHH) |
| Preaxial polydactyly type 2 (PPD2)/ Triphalangeal thumb (TPT) | AD | *SHH* | 174500 | 93336 | regulatory mutation or duplication of ZRS (limb enhancer of SHH) |
| Preaxial polydactyly type 3 (PPD3) | AD |  | 174600 | 93337 |  |
| Preaxial polydactyly type 4 (PPD4) | AD | *GLI3* | 174700 | 93338 |  |
| Greig cephalopolysyndactyly syndrome | AD | *GLI3* | 175700 | 380 |  |
| Pallister-Hall syndrome | AD | *GLI3* | 146510 | 672 |  |
| Synpolydactyly (complex, fibulin1 - associated) | AD | *FBLN1* | 608180 | 93403 |  |
| Synpolydactyly | AD | *HOXD13* | 186000 | 295195 |  |
| Townes-Brocks syndrome (Renal-Ear-Anal-Radial syndrome) | AD | *SALL1* | 107480 | 857 |  |
| Lacrimo-auriculo-dento-digital syndrome (LADD) | AD  AD  AD | *FGFR2*  *FGFR3*  *FGF10* | 149730 | 2363 |  |
| Acrocallosal syndrome | AR | *KIF7* | 200990 | 36 |  |
| Acro-pectoral syndrome | AD |  | 605967 | 85203 |  |
| Acro-pectoro-vertebral dysplasia (F-syndrome) | AD | *WNT6* | 102510 | 957 | Structural variations of locus resulting in ectopic activation of WNT6 |
| Mirror-image polydactyly of hands and feet (Laurin-Sandrow syndrome) | AD | *SHH* | 135750 | 2378 | Duplication of ZRS (limb enhancer of SHH) |
| Cenani-Lenz syndactyly | AR | *LRP4* | 212780 | 3258 |  |
| Cenani-Lenz like syndactyly | SP, AD? | *GREM1, FMN1* |  |  | Monoallelic duplication of both loci (observed in one case only so far) |
| Oligosyndactyly, radio-ulnar synostosis, hearing loss and renal defects syndrome | SP, AR? | *FMN1* |  |  | Deletion |
| Syndactyly, Malik-Percin type | AD | *BHLHA9* | 609432 | 157801 |  |
| STAR syndrome (syndactyly of toes, telecanthus, ano- and renal malformations) | XL | *FAM58A* | 300707 | 140952 |  |
| Syndactyly type 1 (III-IV) | AD |  | 185900 | 93402 |  |
| Syndactyly type 3 (IV-V) | AD | *GJA1* | 186100 | 93404 |  |
| Syndactyly type 4 (I-V) Haas type | AD | *SHH* | 186200 | 93405 | Duplication of ZRS (limb enhancer of SHH) |
| Syndactyly Lueken type | AD | *IHH* |  | 295189 | Duplication of IHH and regulatory region |
| Syndactyly type 5 (syndactyly with metacarpal and metatarsal fusion) | AD | *HOXD13* | 186300 | 93406 |  |
| Syndactyly with craniosynostosis (Philadelphia type) | AD | *IHH* | 185900 | 1527 | Duplication of IHH regulatory region |
| Syndactyly with microcephaly and mental retardation (Filippi syndrome) | AR | *CKAP2L* | 272440 | 3255 |  |
| Meckel syndrome type 1,2,3,4,5,6 | AR  AR  AR  AR  AR  AR | *MKS1*  *TMEM216*  *TMEM67*  *CEP290*  *RPGRIP1L*  *CC2D2A* | 249000  603194  607361  611134  611561  612284 | 564 |  |
| Note: Smith-Lemli-Opitz syndrome can present with polydactyly and/or syndactyly. See also the Ciliopathy group 9. |  |  |  |  |  |
| **42. Defects in joint formation and synostoses** |  |  |  |  |  |
| Multiple synostoses syndrome | AD  AD  AD  AD | *NOG*  *GDF5*  *FGF9*  *GDF6* | 186500  610017  612961  617898 | 3237 |  |
| Radio-ulnar synostosis with amegakaryocytic thrombocytopenia | AD  AD | *HOXA11*  *MECOM* | 605432  616738 | 71289 |  |
| Liebenberg syndrome | AD | *PITX1* | 186550 | 1275 | Deletion of H2AFY gene resulting in ectopic activation of PITX1 in the upper limb |
| SAMS syndrome | AR | *GSC* | 602471 | 397623 |  |
| See also spondylocarpotarsal synostosis syndrome (group 7); mesomelic dysplasia with acral synostoses (group 17) and others. |  |  |  |  |  |