

# International Nosology and Classification of Constitutional Disorders of Bone

## Osteochondrodysplasias

	Mode of Inheritance	OMIM Syndrome	Comments	Chromosome Locus	Gene	Gene Product
<b>1. Achondroplasia group</b>						
Thanatophoric dysplasia, Type I (includes San Diego Type)	AD	187600 270230		4p16.3	FGFR3	FGFR3
Thanatophoric dysplasia, Type II	AD	187601		4p16.3	FGFR3	FGFR3
Achondroplasia	AD	100800		4p16.3	FGFR3	FGFR3
Hypochondroplasia	AD	146000		4p16.3	FGFR3	FGFR3
Hypochondroplasia	AD	146000		other		
SADDAN (severe achondroplasia, developmental delay, acanthosis nigricans)	AD			4p16.3	FGFR3	FGFR3
<b>2. Severe Spondylodysplastic dysplasias</b>						
Lethal platyspondylic skeletal dysplasias (Torrance type, Luton type)	SP	151210				
Achondrogenesis type IA	AR	200600				
Opsismodysplasia	AR	258480				
SMD Sedaghatian Type	AR	250220				
			see also: Thanatophoric dysplasia Types I/II Achondrogenesis Types IB/II and Group 3.			
<b>3. Metatropic dysplasia group</b>						
Fibrochondrogenesis	AR	228520				
Schneckenbecken dysplasia	AR	269250				
Metatropic dysplasia (various forms)	AD	156530				
<b>4. Short-rib dysplasia (SRP) (with or without polydactyly) group</b>						
SRP type I/III	AR	263530 263510				
SRP type II	AR	263520				
SRP type IV	AR	269860				

Asphyxiating thoracic dysplasia (Jeune)	AR	208500			
Chondroectodermal Dyplasia (Ellis-van Creveld dysplasia)	AR	225500	4p16	EVC	EVC
Thoracolumbar dysplasia	AD	187760			
<b>5. Atelosteogenesis-Omodysplasia group</b>					
Atelosteogenesis type I (includes "Boomerang dysplasia")	SP	108720			
Omodysplasia I (Maroteaux)	AD	164745			
Omodysplasia II (Borochowitz)	AR	258315			
Atelosteogenesis Type III	AD	108721			
de la Chapelle dysplasia	AR				
<b>6. Diastrophic dysplasia group</b>					
Achondrogenesis 1B	AR	600972	5q32-q33	DTDST	Sul. transporter
Atelosteogenesis type II	AR	256050	5q32-q33	DTDST	Sul. transporter
Diastrophic dysplasia	AR	222600	5q32-q33	DTDST	Sul. transporter
Autosomal Recessive MED	AR	226900	5q32-q33	DTDST	Sul. transporter
			see also: Group 11		
<b>7. Dyssegmental dysplasia group</b>					
Dyssegmental dysplasia, Silverman-Handmaker type	AR	224410	1p36.1	PLC (HSPG2)	Perlecan
Dyssegmental dysplasia, Rolland-Desbuquois type	AR	224400			
<b>8. Type II collagenopathies</b>					
Achondrogenesis II (Langer-Saldino)	AD	200610	12q13.1-q13.3	COL2A1	Type II collagen
Hypochondrogenesis	AD	200610	12q13.1-q13.3	COL2A1	Type II collagen
Spondyloepiphyseal dysplasia (SED) congenita	AD	183900	12q13.1-q13.3	COL2A1	Type II collagen
Spondyloepimetaphyseal dysplasia (SEMD) Strudwick type	AD	184250	12q13.1-q13.3	COL2A1	Type II collagen
Kniest dysplasia	AD	156550	12q13.1-q13.3	COL2A1	Type II collagen
SED Namaqualand Type	AD		12q13.1-q13.3	COL2A1	Type II collagen
SED with brachydactyly	AD		12q13.1-q13.3	COL2A1	Type II collagen
Mild SED with premature onset arthrosis	AD		12q13.1-q13.3	COL2A1	Type II collagen
Stickler dysplasia Type I	AD	108300	12q13.1-q13.3	COL2A1	Type II collagen
<b>9. Type XI collagenopathies</b>					

Stickler dysplasia Type II	AD	184840	heterogeneous with or without ocular involvement	1p21	COL11A1	Type XI collagen
Marshall syndrome	AD			6p21.3	COL11A2	Type XI collagen
Otospondylomegapiphyseal dysplasia (OSMED)	AR	215150	Recessive haploinsufficiency mutations	6p21.3	COL11A2	Type XI collagen
Otospondylomegapiphyseal dysplasia (OSMED)	AD	215150	Dominant mutations; also called Weissenbach-Zweymüller or Stickler dysplasia without ocular involvement	6p21.3	COL11A2	Type XI collagen
<b>10. Other spondyloepi-(meta)-physeal [SE(M)D] dysplasias</b>						
X-linked SED tarda	XLD	313400		Xp22.2-p22.1	SEDT	SEDLIN
SEMD Handigodu Type	AD					
Progressive pseudorheumatoid dysplasia	AR	208230		6q22-q23	WISP3	WNT1-inducible signaling pathway protein
Dyggve-Melchior-Clausen dysplasia	AR	223800				
Wolcott-Rallison dysplasia	AR	226980		2p12	EIF2AK3	EIF2AK3
Immuno-osseous dysplasia (Schimke)	AR	242900		2q34-q36	SMARCAL1	SMARCAL1
Schwartz-Jampel syndrome	AR	255800	includes Burton dysplasia and Kyphomelic dysplasia; see also dyssegmental dysplasiaSilverman-Handmaker (see group 7)	1p36.1	PLC (HSPG2)	Perlecan
SEMD with joint laxity (SEMDJL)	AR	271640				
SEMD with dislocations (Hall) (leptodactylic Type)						
Sponastrime dysplasia	AR	271510				
SEMD short limb - abnormal calcification Type	AR	271665	see also: Group 12			
SEMD Pakistani Type	AR	603005	see: opsismodysplasia Group 2	10q23-24	PAPSS2	PAPSS2

### 11. Multiple epiphyseal dysplasias & pseudoachondroplasia

Pseudoachondroplasia	AD	177170	see also: Groups 8/10	19p12-13.1	COMP	COMP
Multiple epiphyseal dysplasia (MED)	AD	132400	see also: recessive MED in Group 6	19p13.1	COMP	COMP
(Fairbanks and Ribbing types)	AD	120210		6q13	COL9A1	Type IX collagen
	AD	600204		1p32.2-33	COL9A2	Type IX collagen
	AD	600969		20q13.3	COL9A3	Type IX collagen
	AD	602109		2p23-24	MATN3	matrilin 3
Familial hip dysplasia (Beuke)	AD	142669		4q35		

### 12. Chondrodysplasia punctata (CDP) (stippled epiphyses group)

Rhizomelic CDP Type 1	AR	215100		6q22-q24	PEX7	PTS2 peroxisomal biogenesis receptor
Rhizomelic CDP Type 2	AR	222765		1q42	DHPAT	DHAPAT
Rhizomelic CDP Type 3	AR	600121		2q31	AGPS	ADHAPS
Zellweger syndrome	AR	214100		7q11.23	PEX1	Peroxin-1
	AR	214100		8q21.1	PEX2	Peroxin-2
	AR	214100		6q23	PEX3	Peroxin-3
	AR	214100		12p13.3	PEX5 (PXR1)	Peroxin-5
	AR	214100		6p21.1	PEX6	Peroxin-6
	AR	214100		17q11.2	PEX12	Peroxin-12
CDP Conradi-Hünemann Type	XLD	300205		Xp11	EBP	EBP
CDP X-linked recessive Type (brachytelephalangic)	XLR	302950 302940		Xp22.3	ARSE	Arylsulfatase E
CDP Tibia-metacarpal Type	AD	118651				
CHILD (limb reduction ichthyosis)	XLD	308050		Xp11	EBP	EBP
CHILD (limb reduction ichthyosis)	XLD	308050		Xq28	NSDHL	NAD(P)H steroid dehydrogenase like protein
Hydrops-ectopic calcification- motheaten appearance HEM (Greenberg dysplasia)	AR	215140				
Dappled diaphyseal dysplasia	AR					

### 13. Metaphyseal dysplasias

Jansen Type	AD	156400		3p22-p21.1	PTHR1	PTHR/PTHRP
Schmid Type	AD	156500		6q21-q22.3	COL10A1	Type X collagen
Cartilage-Hair-Hypoplasia (McKusick)	AR	250250		9p21-p12	RMRP	RNA subunit of RMRP RNA'ase
Metaphyseal dysplasia without hypotrichosis	AR	250460		9p21-p12	RMRP	RNA subunit of RMRP RNA'ase
Metaphyseal anadysplasia (various types)	AD/ XLD	309645				
Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachman Diamond)	AR	260400		7p11-q11		

Adenosine deaminase (ADA) deficiency	AR	102700		20q-13.11	ADA	Adenosine deaminase
Metaphyseal chondrodysplasia Spahr Type	AR	250400				
Acroscyphodysplasia (various types)	AR	250215				
<b>14. Spondylometaphyseal dysplasias (SMD)</b>						
Spondylometaphyseal dysplasia Kozlowski Type	AD	184252				
Spondylometaphyseal dysplasia (Sutcliffe/corner fracture Type)	AD	184255				
SMD with severe genu valgum (includes Schmidt and Algerian Types)	AD	184253				
					see also: SMD Sedaghatian Type (Group 2)	
<b>15. Brachyolmia spondylodysplasias</b>						
Hobaek (includes Toledo Type)	AR	271530-630				
Maroteaux type	AR					
Autosomal dominant type	AD	113500				
<b>16. Mesomelic dysplasias</b>						
Dychondrosteosis (Leri-Weill)	Pseudo AD	127300		Xpter-p22.32	SHOX	Short stature homeobox protein
Langer type (homozygous dychondrosteosis)	Pseudo AR	249700	Homozygous dominant	Xpter-p22.32	SHOX	Short stature homeobox protein
Nievergelt Type	AD	163400				
Kozlowski-Reardon Type	AR					
Reinhardt-Pfeiffer Type	AD	191400				
Werner Type	AD	188770				
Robinow Type, dominant	AD	180700				
Robinow Type, recessive	AR	268310		9q22	ROR2	Receptor tyrosine kinase-like orphan recept
Mesomelic dysplasia with synostoses	AD	600383				
Mesomelic dysplasia Kantaputra Type	AD	156232		2q24-q32		
Mesomelic dysplasia Verloes Type	AD	600383				
Mesomelic dysplasia Savarirayan Type						
<b>17. Acromelic dysplasias</b>						
Acromicric dysplasia	AD	102370				
Geleophysic dysplasia	AR	231050				
Myhre dysplasia		139210				
Weill-Marchesani dysplasia	AR	277600				

Trichorhinophalangeal dysplasia Types I/III	AD	190350190351	8q24.12	TRPS1	
Trichorhinophalangeal dysplasia Type II (Langer-Giedion)	AD	150230	8q24.11-q24.13	TRPS1 EXT1 (contiguous gene deletion)	
Brachydactyly type A1	AD	112500	2q35		
Brachydactyly type A2	AD	112600			
Brachydactyly type A3		112700			
Brachydactyly type B	AD	113000	9q22	ROR2	Receptor tyrosine kinase-like orphan receptor
Brachydactyly type C	AD	113100	20q11	CDMP1	cartilage derived morphogenic protein 1
	AD		12q24		
Brachydactyly type D	AD	113200			
Brachydactyly type E	AD	113000			
Pseudohypoparathyroidism (Albright Hereditary Osteodystrophy)	AD	103580	20q13	GNAS1	guanine nucleotide binding protein of adenylylating subunit
Acrodysostosis	SP(AD)	101800			
Saldino-Mainzer dysplasia	AR	266920			
Brachydactyly-hypertension dysplasia (Bilginturan)	AD	112410	12p12.2-p11.2	HTNB	
Craniofacial conodysplasia	AD				
Angel-shaped phalango-epiphyseal dysplasia (ASPED)	AD	105835			
Camptodactyly arthropathy coxa vara pericarditis (CACP)	AR	208250	1q25-31	PRG4	Proteoglycan-4
<b>18. Acromesomelic dysplasias</b>					
Acromesomelic dysplasia Type Maroteaux	AR	201250	9p13-p12		
Acromesomelic dysplasia Type Campailla-Martinelli	AR				
Acromesomelic dysplasia Type Ferraz/Ohba	AD				
Acromesomelic dysplasia Type Osebold Remondini	AD	112910			
Grebe dysplasia	AR	200700	20q11.2	CDMP1	cartilage derived morphogenic protein 1
Cranioectodermal dysplasia	AR	218330			
<b>19. Dysplasias with predominant membranous bone involvement</b>					
Cleidocranial dysplasia	AD	119600	6p21	CBFA1/RUNX-2	core binding factor $\alpha$ 1-subunit
Yunis-Varon dysplasia	AR	216340			
Parietal foramina (isolated)	AD	168500	11p11.2	ALX4	Aristaless-like 4
Parietal foramina (isolated)	AD	168500	5q34-q35	MSX2	Muscle segment homeobox 2
<b>20. Bent-bone dysplasia group</b>					

Campomelic dysplasia	AD	114290		17q24.3-q25.1	SOX9	SOX9
Cumming syndrome	AR	211890				
Stüve-Wiedemann dysplasia	AR	601559				
			see also			
			Antley-Bixler			
			syndrome			
<b>21. Multiple dislocations with dysplasias</b>						
Larsen syndrome	AD	150250		3p21.1-p14.1		
Larsen-like syndromes (including La Reunion Island)	AR	245600				
Desbuquois dysplasia	AR	251450				
Pseudodiastrophic dysplasia	AR	264180				
			see also: Group			
			10			
<b>22. Dysostosis multiplex group</b>						
Mucopolysaccharidosis IH	AR	252800		4p16.3	IDA	$\alpha$ -1-Iduronidase
Mucopolysaccharidosis IS	AR	252800		4p16.3	IDA	$\alpha$ -1-Iduronidase
Mucopolysaccharidosis II	XLR	309900		Xq27.3-q28	IDS	Iduronate-2-sulfatase
Mucopolysaccharidosis IIIA	AR	252900		17q25.3	HSS	Heparan sulfate sulfatase
Mucopolysaccharidosis IIIB	AR	252920		17q21		N-Ac- $\alpha$ -D-glucosaminidase
Mucopolysaccharidosis IIIC	AR	252930				Ac-Coa: $\alpha$ -glucosamine-N-acetyltransferase
Mucopolysaccharidosis IIID	AR	252940		12q14	GNS	N-Ac-glucosamine-6- sulfatase
Mucopolysaccharidosis IVA	AR	253000		16q24.3	GALNS	Galactosamine-6-sulfatase
Mucopolysaccharidosis IVB	AR	230500	See also: GM1-Gangliosidosis	3p21.33	GLBI	$\beta$ -Galactosidase
Mucopolysaccharidosis VI	AR	253200		5q13.3	ARSB	Arylsulfatase B
Mucopolysaccharidosis VII	AR	253220		7q21.11	GUSB	$\beta$ -Glucuronidase
Fucosidosis	AR	230000		1p34	FUCA	$\alpha$ -Fucosidase
a-Mannosidosis	AR	248500		19p13.2-q12	MAN	$\alpha$ -Mannosidase
b-Mannosidosis	AR	248510		4q22-q25	MANB	$\beta$ -Mannosidase
Aspartylglucosaminuria	AR	208400		4q32-q33	AgA	Aspartylglucosaminidase
GM1 Gangliosidosis, several forms	AR	230500	See also: MPS IV B	3p21.33	GLB1	$\beta$ -Galactosidase
Sialidosis, several forms	AR	256550		6p21.3	NEU	$\alpha$ -Neuraminidase
Sialic acid storage disease	AR	269920		6q14-q15	SIASD	
Galactosialidosis, several forms	AR	256540		20q13.1	PPGB	$\beta$ -Galactosidase protective protein
Multiple sulfatase deficiency	AR	272200				Multiple sulfatases
Mucopolipidosis II	AR	252500		4q21-23	GNPTA	N-Ac-Glucosamine-phosphotransferase
Mucopolipidosis III	AR	252600		4q21-23	GNPTA	N-Ac-Glucosamine-phosphotransferase
			see also:			
			Groups			
			8,10,11,14			

### 23. Osteodysplastic slender bone group

Type I microcephalic osteodysplastic dysplasia	AR	210710
Type II microcephalic osteodysplastic dysplasia	AR	210720
Microcephalic osteodysplastic dysplasia (Saul Wilson).	AR	210730

### 24. Dysplasias with decreased bone density

Osteogenesis imperfecta I (normal teeth)	AD	166200	17q21-q22	COL1A1	Type I collagen
Osteogenesis Imperfecta I (normal teeth)		166200	7q22.1	COL1A2	Type I collagen
Osteogenesis imperfecta I (opalescent teeth)	AD	166240	7q22.1	COL1A2	Type I collagen
	AD	166240	7q22.1	COL1A2	Type I collagen
Osteogenesis imperfecta II	AD	166210	17q21-q22	COL1A1	Type I collagen
	AD	166210	7q22.1	COL1A2	Type I collagen
	AD	259400	17q21-q22	COL1A1	Type I collagen
Osteogenesis imperfecta III	AD	259420	17q21-q22	COL1A1	Type I collagen
	AD	259420	7q22.1	COL1A2	Type I collagen
	AR	259420	7q22.1	COL1A2	Type I collagen
	AR	259420			
Osteogenesis imperfecta IV (normal teeth)	AD	166220	7q22.1	COL1A2	Type I collagen
	AD	166220	17q	COL1A1	Type I collagen
Osteogenesis imperfecta IV (opalescent teeth)	AD	166220	7q22.1	COL1A2	Type I collagen
	AD	166220	17q21-q22	COL1A1	Type I collagen
Osteogenesis Imperfecta V					
Osteogenesis Imperfecta VI					
Cole-Carpenter dysplasia	SP	112240			
Bruck dysplasia I	AR	259450	17p12		
Bruck dysplasia II					
Singleton-Merton dysplasia	AR				
Osteopenia with radiolucent lesions of the mandible	AD	166260			
Osteoporosis-pseudoglioma dysplasia	AR	259770	11q12-q13	LRP5	Low density lipoprotein receptor-related protein
Geroderma osteodysplasticum	AR	231070			
Idiopathic juvenile osteoporosis	SP	259750			

### 25. Dysplasias with defective mineralization

Hypophosphatasia- perinatal lethal and infantile forms	AR	241500	1p36.1-p34	ALPL	alkaline phosphatase
Hypophosphatasia adult form	AD	146300	1p36.1-p34	ALPL	alkaline phosphatase
Hypophosphatemic rickets	XLD	307800	Xp22.2-p22.1	PHEX	Phosphate regulating endopeptidase

	AD	193100		12p13.3	FGF23	Fibroblast growth factor 23
Neonatal hyperparathyroidism	AR	239200		3q21-q24	CASR	Calcium-sensing receptor
Transient neonatal hyperparathyroidism with hypocalciuric hypercalcemia	AD	145980	Some families not linked to this locus	3q21-q24	CASR	Calcium-sensing receptor

## 26. Increased bone density without modification of bone shape

Osteopetrosis						
Infantile form	AR	259700		11q13.4-q13.5	TC1RG1	vacuolar proton pump
	AR			16p13	CLCN7	Chloride channel 7
With infantile neuroaxonal dysplasia	AR?	600329				
Delayed forms	AD	166600				
Intermediate form (possibly heterogeneous)	AR	259710				
With renal tubular acidosis (carbonic anhydrase II deficiency)	AR	259730		8q22	CA2	carbonic anhydrase II
Dysosteosclerosis	AR	224300				
With ectodermal dysplasia and immune defect (OLEDAID)	XL	300301		Xq28	IKBKG (NEMO)	NF-kB signalling
Osteomesopyknosis	AD	166450				
Cranial osteosclerosis with bamboo hair (Netherton)	AR	256500				
Pyknodysostosis	AR	265800		1q21	CTSK	cathepsin K
Osteosclerosis Stanescu type	AD	122900				
Osteopathia striata (isolated)	SP					
Osteopathia striata with cranial sclerosis	AD/XL	166500				
	D?					
Melorheostosis	SP	155950				
Osteopoikilosis	AD	166700				
Mixed sclerosing bone dysplasia	SP					

## 27. Increased bone density with diaphyseal involvement

Diaphyseal dysplasia	AD	131300		19q13.1-13.3	TGFb1	transforming growth factor beta 1
Camurati Engelmann						
Diaphyseal dysplasia with anemia (Ghosal)	AR	231095				
Craniodiaphyseal dysplasia	?AR	218300	122860			
Lenz Majewski dysplasia		151050				
Endosteal hyperostosis						
van Buchem type	AR	239100		17q11.2	SOST	Sclerostin
Sclerosteosis	AR	269500		17q11.2	SOST	Sclerostin
Worth type	AD	144750				
Sclero-osteo-cerebellar dysplasia	AR	213002				
Kenny Caffey dysplasia Type I	AR	244460		1q41-q42		
Kenny Caffey dysplasia Type II	AD	127000				

Osteoectasia with hyperphosphatasia (Juvenile Paget disease)	AR	239000			
Diaphyseal medullary stenosis with bone malignancy	AD	112250	9p21-p22		
Oculodentoosseous dysplasia	AR	257850			
	AD	164200	6q22-24		
Trichodentoosseous dysplasia	AD	190320	17q21	DLX3	Distal-less 3 protein
<b>28. Increased bone density with metaphyseal involvement</b>					
Pyle dysplasia	AR	265900			
Cranio metaphyseal dysplasia					
Severe type	AR	218400			
Mild type	AD	123000	5p15.2-p14.2	ANKH	Pyrophosphate channel
			see also: Group 29		
<b>29. Craniotubular digital dysplasias</b>					
Frontometaphyseal dysplasia	XLR	305620			
Osteodysplasty, Melnick-Needles	XLD	309350			
Precocious osteodysplasty (terHaar dysplasia)	AR	249420			
Otopalatodigital syndrome Type I	XLD	311300	Xq28		
Otopalatodigital syndrome Type II	XLR	304120			
			see also: Group 28		
<b>30. Neonatal severe osteosclerotic dysplasias</b>					
Blomstrand dysplasia	AR	215045	3p22-p21.1	PTHR1	PTH/PTH-RP
Raine dysplasia	AR	259775			
Prenatal onset Caffey disease	AD	114000			
	?AR				see also: Mucopolipidosis II
Astley-Kendall dysplasia	AR				
<b>31. Disorganized development of cartilaginous and fibrous components of the skeleton</b>					
Dysplasia epiphysealis hemimelica	SP	127800			
Multiple cartilaginous exostoses	AD	133700	8q23-q24.1	EXT1	exostosin-1
	AD	133701	11p12-p11	EXT2	exostosin-2
	AD	600209	19p		
Enchondromatosis, Ollier	SP	166000			
Enchondromatosis with hemangiomata (Maffucci)	SP	166000			
Spondyloenchondromatosis	AR	271550			
Spondyloenchondromatosis with basal ganglia calcification	AR				
Dysspondyloenchondromatosis					

Metachondromatosis	AD	156250			
Osteoglophonic dysplasia	AD	166250			
Enchondromatosis	AD	166000			
Carpotarsal osteochondromatosis	AD	127820			
Fibrous dysplasia (McCune-Albright and others)	SP	174800	20q13	GNAS1	guanine nucleotide-binding protein, $\alpha$ subu
Jaffe Campanacci	SP				
Fibrodysplasia ossificans progressiva	AD	135100	4q27-31		
Cherubism	AD	118400	4p16.3	SH3BP2	SH3 domain-binding protein 2
Cherubism with gingival fibromatosis	AR	135300			
<b>32. Osteolyses</b>					
<u>Multicentric -hands and feet</u>					
Multicentric carpal-tarsal osteolysis with and without nephropathy	AD	166300			
Shinohara carpal-tarsal osteolysis					
Winchester syndrome	AR	277950			
Torg syndrome	AR	259600	16q12-21	MMP2	MMP2
<u>Distal phalanges</u>					
Hadju-Cheney syndrome	AD	102500			
Mandibuloacral syndrome	AR	248370			
<u>Diaphyses and metaphyses</u>					
Familial expansile osteolysis	AD	174810	18q21.1-q22	TNFRSF11A	RANK
Juvenile hyaline fibromatosis (includes systemic juvenile hyalinosis)	AD	228600			
<b>33. Patella dysplasias</b>					
Nail patella dysplasia	AD	161200	9q34.1	LMX1B	LIM homeobox transcription factor 1
Scypho-patellar dysplasia	AD				
Ischiopubic patellar dysplasia	AD	147891			
Genitopatellar syndrome					
Ear patella short stature syndrome (Meier Gorlin)	AR	224690			