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Nosology of genetic skeletal disorders: 2023 revision

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Abstract

The "Nosology of genetic skeletal disorders" has undergone its 11th revision and now contains 771 entries associated with 552 genes reflecting advances in molecular delineation of new disorders thanks to advances in DNA sequencing technology. The most significant change as compared to previous versions is the adoption of the dyadic naming system, systematically associating a phenotypic entity with the gene it arises from. We consider this a significant step forward as dyadic naming is more informative and less prone to errors than the traditional use of list numberings and eponyms. Despite the adoption of dyadic naming, efforts have been made to maintain strong ties to the MIM catalog and its historical data. As with the previous versions, the list of disorders and genes in the Nosology may be useful in considering the differential diagnosis in the clinic, directing bioinformatic analysis of NGS results, and providing a basis for novel advances in biology and medicine.

When the first « Nosology » was compiled and published in 1970, few would have predicted that it would gain such an important role in genetics clinics and research to motivate an 11th revision fifty-two years later. Yet, the reasons that stimulated the first Nosology are the same that uphold the present new revision: coping with the wealth of novel information on the growing number and variety of skeletal phenotypes with a genetic basis and trying to assure a common naming system to facilitate diagnosis and communication.

The recognition of chromosomal aneuploidies at the transition between the 50s and the 60s provided a biological foundation to genetics and ushered in a first golden era of clinical genetics. The Birth Defects Conferences between 1969 and 1971 signaled the awareness and importance of clinical genetics throughout the Sixties and initiated a prolific period in

disease identification, delineation and description. In this context, it became apparent that « chondrodysplasia » was not a single diagnosis, but that many distinct, true-breeding forms existed; for example, diastrophic dysplasia, spondylo-epiphyseal dysplasia congenita, and the so-called “pseudo-Morquio” disorders were distinguished and clinically described. In addition, biochemistry allowed subtypes of clinically similar disorders to be distinguished, the most notable example at the time being the mucopolysaccharidoses. The contribution of radiologic features and radiologists to the delineation of skeletal dysplasias deserves explicit recognition. In many instances, it was the radiographic features and their time dependent evolution (the “fourth dimension” emphasized by the late Andres Giedion) that permitted not only to discriminate between disorders that had outward similarities but also to recognize a gene’s radiographic signature in phenotypically distinct disorders (e.g. Achondrogenesis type 2 and Spondyloepiphyseal dysplasia congenita) and thus create the first gene families (Spranger, 1985) (and see below).

In 1970, the first prototype of the “Nosology” was drafted (“[International nomenclature of constitutional diseases of bone],” 1970; McKusick & Scott, 1971; “A Nomenclature for Constitutional (Intrinsic) Diseases of Bone,” 1971; “[International nomenclature of constitutional bone diseases. Constitutional bone diseases without known pathogenesis],” 1971). At that time, however, the work was called a “Nomenclature” rather than a Nosology; the goal was to bring all scholars to use the same name for the same condition.

Molecular criteria began to inform the Nosology in the 1980s, first with osteogenesis imperfecta and the discovery of genetic variants in collagen 1. The concept of « bone dysplasia families » originating from different pathogenic variants in a single gene was proposed in the 1980s (Spranger, 1985) and confirmed in the 1990s, with the *COL2A1* and *FGFR3* disorders being prominent examples. Ever since, the Nosology has straddled the fence between defining disorders based either on their clinical and radiographic features or on the responsible genes (“International Nomenclature of Constitutional Diseases of Bone,” 1979; “International Nomenclature of Constitutional Diseases of Bone. Revision, May, 1983,” 1983; Beighton et al., 1992; Lachman, 1998; “International Nomenclature and Classification of the Osteochondrodysplasias (1997). International Working Group on Constitutional Diseases of Bone,” 1998; Hall, 2002; Superti-Furga & Unger, 2007; Warman et al., 2011; Bonafe et al., 2015; Mortier et al., 2019).

Traditionally, the nosology has been organized into groups of disorders – initially based on radiographic criteria, then by biochemical criteria (metabolic pathways) and subsequently, more and more, by functional and molecular criteria. The organization into groups has been maintained in the current revision as it helps in finding the disorders relevant for a particular patient of finding. On the other hand, Nature has more complexity than can be captured in the Nosology, and our attempt at classification is necessarily both arbitrary and a simplification, as many disorders might warrant classification in more than one group. Thus, we have elected to drop the term “classification” from the title; this is just a “Nosology”.

Naming problems and the dyadic approach as a way forward

Between 2010 and 2020, the technology of massively parallel sequencing has taken center stage in medical genetics research and diagnostics. Among the many lessons learned from next-generation sequencing (NGS) results are (1) the large number of previously unrecognized rare and ultrarare disorders in each domain of genetic medicine, (2) the phenotypic heterogeneity arising from a single locus is much greater than previously suspected, and (3) for many dyadic entities, individuals who present all the phenotypic criteria as described in the textbooks are the exception rather than the rule.

On this background, it has been proposed that the phenotypic descriptor of a genetic disorder (the « name » of a condition) is no longer sufficient to distinguish the disorder unequivocally. Furthermore, the sequential numbering of conditions with the same name (as applied e.g. for osteogenesis imperfecta or ataxias in Mendelian Inheritance in Man (MIM)) may be unsatisfactory, as a number has no inherent information, making it necessary to consult the numbering reference. As a consequence, it has been suggested that instead of being attributed by a number (or an eponym, see below), the main phenotypic descriptor of a genetic disorder should best be coupled to the name of the underlying gene, allowing for more direct and pertinent information, less prone to ambiguities and errors; the so-called dyadic approach (Biesecker et al., 2021). Of note, the dyadic concept has been pioneered by the editors of the well-known resource GeneReviews starting in 2020 (Dr. M. Adam, personal communication; and Biesecker et al., 2021).

The Nosology has not been immune to the proliferation of numbered lists, such as, for example, in osteogenesis imperfecta (Sillence & Rimoin, 1978; Sillence et al., 1979; Van Dijk & Sillence, 2014). In this 2023 revision, the curators have decided to adopt the dyadic naming approach as it allows for more precision both in the clinic and in the laboratory. However, compromises have been made in some instances to account for the historic evolution of the Nosology, as well as to maintain congruence and interoperability with what is considered the most important reference database for genetic disorders, Mendelian Inheritance in Man (MIM and its online version, OMIM).

The Mendelian Inheritance in Man (MIM) catalog and the Nosology

The late Victor McKusick’s opus, Mendelian Inheritance in Man, remains the single most important general reference database for genetic disorders. The way in which MIM was created and is still curated allows for a detailed documentation of the history of each and every disorder. For the same reason, it is less well-suited to document the changes that occur in the nosography, for instance when one disorder is subsumed under another; several disorders listed in MIM have been subsumed under other conditions in the Nosology, or are altogether not recognized as distinct phenotypic entities in the Nosology (e.g., mesomelic dysplasia, Camera type; MIM 611886). Also, MIM makes extensive use of eponyms to distinguish related but distinct disorders (e.g., Dyggve-Melchior-Clausen disease and Smith-McCort dysplasia); while for others the eponymic descriptors are too similar, leading to diagnostic confusion (e.g., Shprintzen-Goldberg and Goldberg-Shprintzen syndromes represent distinct disorders). MIM’s choice of these eponyms may not reflect the most

significant contribution to the delineation of a phenotypic entity. By adopting the dyadic system, we have elected to describe each disorder with the name of the responsible gene rather than with an eponym. While MIM remains the central reference database, the dyadic system allows the Nosology to group, lump, or dump disorders based on their molecular basis, especially in the light of the lessons of NGS (see above), and is less bound by historical constraints. Nevertheless, the Nosology curators have strived to maintain strong bridges to MIM: MIM numbers are included for all disorders when available, and when not available, the MIM number for the responsible gene is included. Moreover, references are made to the MIM denomination of individual disorders as well as to other MIM disorders arising from pathogenic variants in the same gene.

The Orphanet nomenclature and the Nosology

In the context of a joint collaboration between the ISDS, the European Reference Network on Rare Bone Disorders (ERN-BOND) and Orphanet, co-coordinated by Houda Ali (curator at Orphanet) and Geert Mortier (main curator of the 2019 Nosology), a detailed analysis of the Orphanet database in comparison with the 2019 Nosology, resulted in a list of approx. 248 phenotypic entities that were present in the Orphanet nomenclature of rare diseases but absent in the 2019 Nosology. To be included in the 2023 Nosology, disorders had to have a recognizable phenotype and a clear inheritance pattern or molecular definition. Approximately 30 of these disorders met inclusion criteria and have thus been included in the Nosology. Other disorders in this list had either been described in a single paper without molecular confirmation, or represent historical descriptions with limited available information, reflecting the policy followed by Orphanet to represent all disorders fitting the definition of a rare disease to the advantage of individuals affected by ultrarare presentations, as long as they constitute phenotypically distinct diagnoses (Ref.https://www.orpha.net/orphacom/cahiers/docs/GB/eproc_disease_inventory_R1_Nom_Dis_EP_04.pdf). On the other hand, it became evident that many entries in the list do not seem to represent distinct phenotypic entities in view of the current knowledge and of the Nosology criteria. This has prompted an ongoing revision process by the Orphanet team to review and identify entries that need to be deactivated and subsequently removed from the Orphanet nomenclature of rare diseases.

The Nosology and the ClinGen curation initiative

The ClinGen initiative (https://clinicalgenome.org/affiliation/40065/) is currently working on a set of genes associated with skeletal disorders in order to provide strength of evidence for gene-disease associations, and using strictly verified criteria to assess pathogenicity of variants in genes found to have a definitive association with disease. It has already done so for other groups of genetic disorders, such as the cardiomyopathies and others. Several of the present Nosology curators participate in this effort. However, the sheer number of genes involved in constitutional skeletal conditions is such that the ClinGen section for skeletal dysplasia genes will take time to be completed. In this context, the Nosology, with its list of curated genes and disorders (albeit not to the extent set out in the ClinGen initiative), will remain the best available resource for the foreseeable future. Of note, the ClinGen approach is much more “lumping” than the Nosology, to the extent

that phenotypes due to pathogenic variants at a single locus must have significant qualitative differences to justify separate nosologic entries (phenotypic entities); a simple quantitative difference (typically, more or less severe) is not enough to justify separation. This may lead us to reflect on what constitutes a “dysplasia” or a “syndrome”. Some of us have also contributed to the development of the “Nosology of inborn errors of metabolism” and the subsequent “International Classification of Inherited Metabolic Disorders” (ICIMD) (Ferreira et al., 2019, 2021). That nosology applies the “one gene – one condition” principle, unless there are qualitative differences. However, it is more difficult to apply this principle to the skeletal conditions. For example, children affected by methylmalonic acidemia may have different urinary concentrations of methylmalonic acid but will be considered to have the same disorder (MIM 251000). It would be more difficult to claim that a fetus with achondrogenesis type 1B (MIM 600972) and a child with recessive multiple epiphyseal dysplasia (MIM 226900) have the same disorder, even if the responsible gene is the same and the phenotypes represent opposite ends of severity within the same spectrum, as the morphologic features and clinical prognosis are so radically distinct.

Changes compared to previous revisions

Some changes in the structure of the Nosology deserve to be mentioned. The total number of groups decreased from 42 to 41. This decrease has to do with restructuring of a few groups. Specifically, the previous “Perlecan group” and “Aggrecan group” were incorporated into the new group of “Proteoglycan core protein disorders”, and the former groups of “Neonatal osteosclerotic dysplasias” and of “Other sclerosing bone disorders” were fused into the group of (non-osteopetrotic) “Osteosclerotic disorders”. A new group of “Skeletal disorders of parathyroid hormone signaling cascade” was added to the current Nosology. The two brachydactylies groups (isolated or as part of syndromes; now groups 18 and 19) were found to be more organically placed right after the acromesomelic and acromelic groups (groups 16 and 17).

Several groups were renamed. The group of “Osteopetrosis and related disorders” is now named “Osteopetrosis and related osteoclast disorders”, to highlight the fact that the osteopetroses represent disorders in the number or function of osteoclasts. The “Osteogenesis Imperfecta and decreased bone density group” was renamed “Osteogenesis Imperfecta and bone fragility group” to reflect the fact that skeletal fragility is a hallmark of these disorders irrespective of the bone mineral density (as in fact a small subset of osteogenesis imperfecta patients can have high bone mass). The name of the group of “Overgrowth (tall stature) syndromes with skeletal involvement” was changed to the more encompassing “Overgrowth (tall stature) syndromes and segmental overgrowth”. The group of “Craniosynostosis syndromes” was renamed “Syndromes featuring craniosynostosis”, as although disorders in this group frequently feature craniosynostosis, this finding does not always represent the most salient feature. Other changes in group nomenclature included “Brachydactylies (without extraskeletal manifestations)” to “Isolated brachydactylies”; “Brachydactylies (with extraskeletal manifestations)” to “Brachydactylies as part of syndromes”; “Ciliopathies with major skeletal involvement” to “Skeletal disorders caused by abnormalities of cilia or ciliary signaling”; “Abnormal mineralization group” to “Disorders

of bone mineralization"; and "Ectrodactyly with and without other manifestations" to "Split hand/foot with and without other manifestations".

Some disorders were reassigned. As an example, trichorhinophalangeal dysplasia types 1/3 was moved from the "Acromelic dysplasias" group to the group of "Brachydactylies as part of syndromes".

The total number of disorders increased from 461 to 771, and the number of genes from 437 to 552. Although we are aware of the problems inherent to numeric lists (as discussed above), we have tentatively included a numbering system including the abbreviation "NOS" (for "Nosology, skeletal"), the group number, and a sequential number withing the group, taking care to leave gaps that may allow for the inclusion of disorders in the future. Such a numbering system might prove helpful in cross-referencing with MIM, Orphanet and other databases.

What is the utility of the Nosology?

Since its early revisions, the Nosology has been helpful for pediatricians, geneticists, radiologists, and others as a reminder of the differential diagnosis. Its original structure in groups of disorders with similar radiographic features reflected the diagnostic approach of the clinical geneticist and, even more, of the radiologist, to the osteochondrodysplasias. Over the years, the inclusion of brachydactylies, craniosynostoses, craniofacial dysostoses, syndactylies, limb reductions, and other dysostoses, as well as primordial short stature and overgrowth syndromes has broadened its utility for the differential diagnosis within these groups of disorders. The 2010 revision stated that "*The aim is to provide the Genetics, Pediatrics and Radiology community with a list of recognized genetic skeletal disorders that can be of help in the diagnosis of individual cases, in the delineation of novel disorders, and in building bridges between clinicians and scientists interested in skeletal biology. (…) The Nosology should be useful for the diagnosis of patients with genetic skeletal diseases, particularly in view of the information flood expected with the novel sequencing technologies; in the delineation of clinical entities and novel disorders, by providing an overview of established nosologic entities; and for scientists looking for the clinical correlates of genes, proteins and pathways involved in skeletal biology.*" Thirteen years later, the Nosology may have an additional role in molecular genetic diagnostic testing. In a pre-test setting, the Nosology may inform the decision on which genes to include in a diagnostic panel tailored to a specific clinical situation. Current diagnostic workflows often involve plausibility verification of variants observed in panel or exome sequencing tests (reverse phenotyping). Also, in the post-test setting, the Nosology may be helpful for rapid reference and orientation.

The Nosology is also an illustration of the complexity of the human genome as demonstrated by the sheer number of genes and gene products required for normal skeletal development and growth. The included table with its over 750 entries and its rows and columns is like the musical score for the orchestra of skeletal development and growth that may be an inspiration to geneticists and basic scientists. Perhaps the hybrid nature of the nosology,

combining clinical, radiographic, and molecular criteria, is a strength and not a weakness, allowing colleagues with varied backgrounds an approach to the data.

It is clear that no nosology in medicine is perfect nor complete. They are always dynamic and evolving. However, the frequent citations of previous versions of the Nosology suggest that, despite the many compromises necessary in its preparation the Nosology has been useful to, and widely adopted by, the medical and scientific community. Thanks to the continuous progress in delineating genetic conditions, the Nosology starts its obsolescence at the moment it is published. Nevertheless, may this new version encounter the same benevolent reception, and also be replaced in time by novel and more complete versions.

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	The Nosology of Constitutional Skeletal Disorders: 2023 revision					
Group number/ numer of disorder	**Name of Group / Name of Disorder**	**Inheritance**	***Gene or locus***	**MIM No.**		**Notes**
Group 1	**FGFR3 chondrodysplasias**					
NOS 01–0010	Thanatophoric dysplasia (type 1), FGFR3-related	AD	FGFR3	187600		Includes previous “platyspondylyic dysplasia type San Diego”
NOS 01–0020	Thanatophoric dysplasia (type 2), FGFR3-related	AD	FGFR3	187601		radiographic differences between type 1 and type 2 are correlated to specific *FGFR3* variants
NOS 01–0030	Severe achondroplasia with developmental delay and acanthosis nigricans (SADDAN), FGFR3-related	AD	FGFR3	616482		
NOS 01–0040	Achondroplasia, FGFR3-related	AD	FGFR3	100800		
NOS 01–0050	Hypochondroplasia, FGFR3-related	AD	FGFR3	146000		
	See also group 33 for craniosynostosis syndromes linked to *FGFR3* variants, as well as CATSHL in group 30 and LADD syndrome in group 40 for other *FGFR3*-related phenotypes; rare *FGFR3* missense variants have been reported in idiopathic short stature but a causal link is not yet established and their significance remains unclear					
Group 2	**Type 2 collagen disorders**					
NOS 02–0010	Achondrogenesis, COL2A1-related (formerly type 2, type Langer-Saldino)	AD	COL2A1	200610		Achondrogenesis type 2 and hypochondrogenesis form one phenotypic continuum
NOS 02–0020	Hypochondrogenesis, COL2A1-related	AD	COL2A1	200610		Achondrogenesis type 2 and hypochondrogenesis form one phenotypic continuum
NOS 02–0030	Platyspondylic dysplasia, type Torrance, COL2A1-related	AD	COL2A1	151210		Often variants in the C-propeptide of collagen 2
NOS 02–0040	Spondyloepiphyseal dysplasia congenita (SEDC), COL2A1-related	AD, AR*	COL2A1	183900, 604864		Includes mild SED with premature onset arthrosis, also known as osteoarthrosis with mild chondrodysplasia; includes Namaqualand type hip dysplasia. Mild SED cases may resemble MED (see note). AR*: very rare SED cases with biallelic *COL2A1* variants have been reported
NOS 02–0050	Spondyloepimetaphyseal dysplasia, COL2A1-related	AD	COL2A1	184250, 184253, 184255, 616583		Also known as “SED with marked metaphyseal changes”. Includes SEMD type Strudwick, SMD type Algerian, SED type Stanescu, dysspondyloenchondromatosis, and some cases of SMD “corner fracture” type
NOS 02–0060	Kniest dysplasia, COL2A1-related	AD	COL2A1	156550		
NOS 02–0070	Spondyloperipheral dysplasia, COL2A1-related	AD	COL2A1	271700		Like Torrance dysplasia, often variants in the C-propeptide of collagen 2

	The Nosology of Constitutional Skeletal Disorders: 2023 revision					
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NOS 02–0080	SED with metatarsal shortening, COL2A1-related	AD	COL2A1	609162		Often associated with the p.R275C variant; formerly “Czech dysplasia”
NOS 02–0090	Stickler syndrome, COL2A1-related	AD	COL2A1	108300		Monoallelic loss-of-function variants; See also *COL11A1, COL11A2, COL9A1, COL9A2, COL9A3*
NOS 02–0100	Dysplasia of the proximal femoral epiphyses, COL2A1-related	AD	COL2A1	150600, 608805		Heterogeneous condition, not all cases are due to COL2A1 variants (usually p.G393S; p.G717S; p.G1170S). The condition called “Meyer dysplasia of the hip” is not associated with *COL2A1* variants
	See also the Pseudoachondroplasia-multiple epiphyseal dysplasia group for recessively inherited variants of Stickler syndrome as well as for overlapping phenotypes with normal stature and premature onset arthrosis; as well as Spondylometaphyseal dysplasia Sutcliffe (or “corner fractures” type), *FN1*-related					
Group 3	**Type 11 collagen disorders**					
NOS 03–0010	Stickler syndrome, COL11A1-related	AD, MOS	COL11A1	604841		Can also result from somatic mosaicism for a *COL11A1* variant
NOS 03–0020	Marshall syndrome, COL11A1-related	AD	COL11A1	154780		One report with homozygous p.G901E variant in two affected sibs (PMID 22499343)
NOS 03–0030	Stickler syndrome, COL11A2-related (non-ocular type)	AD	COL11A2	184840		
NOS 03–0040	Fibrochondrogenesis, COL11A1-related	AR, AD	COL11A1	228520		
NOS 03–0050	Fibrochondrogenesis, COL11A2-related	AR, AD	COL11A2	614524		
NOS 03–0060	Otospondylomegaepiphyseal dysplasia (OSMED), recessive type, COL11A2-related	AR	COL11A2	215150		
NOS 03–0070	Otospondylomegaepiphyseal dysplasia (OSMED), dominant type, COL11A2-related	AD	COL11A2	184840		Formerly Weissenbacher-Zweymüller syndrome and Stickler syndrome type 3
	See also Stickler syndrome type 1 in collagen 2 group (Group 2) as well as recessive forms of Stickler syndrome in the Pseudoachondroplasia-Multiple epiphyseal dysplasia group (Group 9)					
Group 4	**Sulfation disorders**					
NOS 04–0010	Achondrogenesis, SLC26A2-related (formerly achondrogenesis type 1B, or type Fraccaro)	AR	SLC26A2	600972		Formerly known as achondrogenesis, type Fraccaro
NOS 04–0020	Atelosteogenesis, SLC26A2-related (formerly atelosteogenesis type 2)	AR	SLC26A2	256050		Includes former entities de la Chapelle dysplasia, McAlister dysplasia, and neonatal osseous dysplasia

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NOS 04–0030	Diastrophic dysplasia, SLC26A2-related	AR	SLC26A2	222600		
NOS 04–0040	Multiple epiphyseal dysplasia, SLC26A2-related (autosomal recessive type, rMED)	AR	SLC26A2	226900		See also multiple epiphyseal dysplasias and pseudoachondroplasia group (group 9)
NOS 04–0050	Spondylo-epi-metaphyseal dysplasia, PAPSS2-related	AR	PAPSS2	612847		Formerly “SEMD Pakistani type”; includes the former “recessive brachyolmia, recessive type” as well as the older entities “Toledo brachyolmia” and “Hobaek brachyolmia”
NOS 04–0060	Chondrodysplasia with congenital joint dislocations, IMPAD1-related	AR	IMPAD1	614078		Some features similar to Catel-Manzke syndrome, *TGDS*-related, as well as to Desbuquois syndrome, *CANT1*-related
NOS 04–0070	Chondrodysplasia with congenital joint dislocations, CHST3-related	AR	CHST3	143095		Includes recessive Larsen syndrome, humero-spinal dysostosis, and SED type Omani
NOS 04–0080	Chondrodysplasia with hypomyelinating leucodystrophy, SLC35B2-related	AR	SLC35B2	see 610788		
NOS 04–0090	Ehlers-Danlos syndrome, musculocontractural type, CHST14-related	AR	CHST14	601776		Includes adducted thumb-clubfoot syndrome
NOS 04–0100	Ehlers-Danlos syndrome, musculocontractural type, DSE-related	AR	DSE	615539		
NOS 04–0110	Osteochondrodysplasia, brachydactyly, and overlapping malformed digits (OCBMD), CHST11-related	AR	CHST11	618167		
NOS 04–0120	Developmental Delay with Corpus Callosum, Skeletal, and Renal Abnormalities, HS2ST1-related	AR	HS2ST1	619194		
	See also Filamin disorders (group 6) and dysplasias with multiple joint dislocations (group 5) for other conditions with dislocations, as well as brachydactyly, *CHSY1*-related, for phalangeal changes reminiscent of the sulfation disorders.					
Group 5	**Dysplasias with multiple joint dislocations**					
NOS 05–0010	Baratela-Scott syndrome, XYLT1-related	AR	XYLT1	615777		May have intellectual disability; formerly Desbuquois dysplasia type 2
NOS 05–0020	Desbuquois dysplasia (with accessory ossification centre in digit 2), CANT1-related	AR	CANT1	251450		
NOS 05–0030	Desbuquois dysplasia (with short metacarpals and elongated phalanges, Kim type), CANT1-related	AR	CANT1	251450		
NOS 05–0040	SEMD with joint laxity (Hall type or leptodactylic type), KIF22-related	AD	KIF22	603546		

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NOS 05–0050	SEMD with joint laxity, EXOC6B-related	AR	EXOC6B	618395		Phenotype resembles SEMD-JL leptodactylic or type Hall (preceding line)
NOS 05–0060	SEMD with joint laxity (Beighton type), B3GALT6-related (Ehlers-Danlos syndrome, spondylodysplastic type 2, EDSSPD2)	AR	B3GALT6	271640		Includes MIM 609465 - Al-Gazali syndrome as neonatal form
NOS 05–0070	Ehlers-Danlos syndrome, spondylodysplastic type 1 (EDSSPD1), B4GALT7-related	AR	B4GALT7	130070		Formerly known as “EDS, progeroid form”; includes Larsen syndrome, La Reunion type; see also *B3GALT6* deficiency above
NOS 05–0080	Multiple joint dislocations, short stature, craniofacial dysmorphisms, and skeletal dysplasia, with or without heart defects, B3GAT3-related	AR	B3GAT3	245600		The phenotype is very variable and has been reported also as “Larsen-like” or as “pseudodiastrophic dysplasia”. Intellectual disability and severe osteopenia with fractures have been observed. The OMIM entry includes older descriptions that are probably unrelated.
NOS 05–0090	Skeletal dysplasia with joint laxity and advanced bone age (SDJLABA), CSGALNACT1-related	AR	CSGALNACT1	618870		
NOS 05–0100	Skeletal dysplasia with joint dislocations and amelogenesis imperfecta, SLC10A7-related	AR	SLC10A7	618363		
	Note: remarkably, this group contains several disorders of glycosaminoglycan synthesis. In spite of this group being named after a clinical feature (dysplasias with joint dislocations), the phenotypes in this group are related to those of the preceding group 4 (sulfation disorders) and of the following group 6 (filamin disorders) justifying its placement here. - See also: Temtamy type brachydactyly, *CHSY1*-related, as well as SEMD with microcephaly, retinal dystrophy and hearing loss, *PISD*-related (Liberfarb syndrome), for other conditions with congenital dislocations, and EDSSPD3, *SLC39A13*-related, in the SEMD group.					
Group 6	**Filamins and related disorders**					
NOS 06–0010	Frontometaphyseal dysplasia, FLNA-related	XL	FLNA	305620		*FLNA* gene also associated with MIM 300049, MIM 300321, MIM 314400, MIM 300048, MIM 300049 (see) and conditions below in this group
NOS 06–0020	Frontometaphyseal dysplasia, MAP3K7-related	AD	MAP3K7	617137		
NOS 06–0030	Frontometaphyseal dysplasia, TAB2-related	AD	TAB2			No MIM entry yet; *TAB2* gene also associated with MIM 614980 - Congenital heart defects, nonsyndromic, 2
NOS 06–0040	Cardiospondylocarpofacial syndrome, MAP3K7-related	AD	MAP3K7	157800		
NOS 06–0050	Melnick-Needles syndrome, FLNA-related	XL	FLNA	309350		Includes osteodysplasty

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NOS 06–0060	Otopalatodigital syndrome type 1 (OPD1), FLNA-related	XL	FLNA	311300		
NOS 06–0070	Otopalatodigital syndrome type 2 (OPD2), FLNA-related	XL	FLNA	304120		
NOS 06–0080	Terminal osseous dysplasia (TOD), FLNA-related	XL	FLNA	300244		Includes digitocutaneous dysplasia
NOS 06–0090	Larsen syndrome, FLNB-related	AD	FLNB	150250		
NOS 06–0100	Atelosteogenesis type 1, FLNB-related	AD	FLNB	108720, 112310		Includes Boomerang dysplasia, Piepkorn dysplasia, and spondylohumerofemoral (giant cell) dysplasia
NOS 06–0110	Atelosteogenesis type 3, FLNB-related	AD	FLNB	108721		
NOS 06–0120	Spondylocarpotarsal synostosis syndrome, FLNB-related	AR	FLNB	272460		
NOS 06–0130	Spondylocarpotarsal synostosis syndrome, RFLNA-related	AR	RFLNA			Entity proven, no MIM entry yet
NOS 06–0140	Spondyocarpotarsal synostosis syndrome with contractures and pterygia, MYH3-related	AD, AR	MYH3	178110, 618469		frequently biallelic loss of function variants; monoallelic missense variants in the *MYH3* gene associated with MIM 193700-Arthrogryposis 2A, and MIM 618436-Arthrogryposis 2B3
NOS 06–0150	Frank-ter Haar syndrome, SH3PXD2B-related	AR	SH3PXD2B	249420		Includes previous Borrone dermatocardioskeletal syndrome
	See also Chondrodysplasia with congenital joint dislocations, *CHST3*-related (“recessive Larsen syndrome”) and the group of dysplasias with multiple dislocations, above (group 5)					
Group 7	**Proteoglycan core proteins disorders**					
NOS 07–0010	Dyssegmental dysplasia, HSPG2-related	AR	HSPG2	224410, 224400		Variable severity; Includes both former Silverman-Handmaker and Rolland-Desbuquois types
NOS 07–0020	Myotonic chondrodystrophy, HSPG2-related (Schwartz-Jampel syndrome)	AR	HSPG2	255800		Variable severity; includes previous Burton dysplasia
NOS 07–0030	Spondylo-epiphyseal dysplasia, ACAN-related (dominant, Kimberley type)	AD	ACAN	608361		
NOS 07–0040	Spondylo-epi-metaphyseal dysplasia, ACAN-related (recessive, aggrecan type)	AR	ACAN	612813		
NOS 07–0050	Short stature with advanced bone age, ACAN-related	AD	ACAN	165800		Sometimes with osteochondritis dissecans; other cases short stature with no skeletal features and normal bone age
NOS 07–0060	SEMD, BGN-related (Camera type)	XL	BGN	300106		The *BGN* gene is also associated with a connective tissue- arterial aneurysms disorder (Meester-Loeys syndrome, MIM300989)

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Group 8	**TRPV4 disorders**					
NOS 08–0010	Metatropic dysplasia, TRPV4-related	AD, MOS	TRPV4	156530		Includes “hyperplastic”, lethal and non-lethal forms. Can also result from somatic mosaicism for a *TRPV4* variant.
NOS 08–0020	Spondyloepimetaphyseal dysplasia, TRPV4-related (Maroteaux type)	AD	TRPV4	184095		Previously known as “Pseudo-Morquio syndrome type 2”. Includes MIM 168400-parastremmatic dwarfism, a phenotypic variation
NOS 08–0030	Spondyloepiphyseal dysplasia, Kozlowski type	AD	TRPV4	184252		
NOS 08–0040	Brachyolmia, TRPV4-related	AD	TRPV4	113500		
NOS 08–0050	Familial digital arthropathy with brachydactyly, TRPV4-related	AD	TRPV4	606835		
	Missense variants in the *TRPV4* gene can be responsible for different types of peripheral neuropathies (see MIM 605427). The *TRPV4* skeletal phenotypes can sometimes be associated with neuropathy.					
Group 9	**Pseudoachondroplasia and the multiple epiphyseal dysplasias**					
NOS 09–0010	Pseudoachondroplasia, COMP-related	AD	COMP	177170		
NOS 09–0020	Multiple epiphyseal dysplasia, COMP-related	AD	COMP	132400		
NOS 09–0030	Multiple epiphyseal dysplasia, MATN3-related	AD	MATN3	607078		
NOS 09–0040	Multiple epiphyseal dysplasia, CANT1-related	AR	CANT1	617719		
NOS 09–0050	Multiple epiphyseal dysplasia, COL9A1-related	AD	COL9A1	614135		
NOS 09–0060	Multiple epiphyseal dysplasia, COL9A2-related	AD	COL9A2	600204		
NOS 09–0070	Multiple epiphyseal dysplasia, COL9A3-related	AD	COL9A3	600969		
NOS 09–0080	Stickler syndrome, recessive type, COL9A1-related	AR	COL9A1	614134		See also groups 2 and 3
NOS 09–0090	Stickler syndrome, recessive type, COL9A2-related	AR	COL9A2	614284		
NOS 09–0100	Stickler syndrome, recessive type, COL9A3-related	AR	COL9A3	120270		
NOS 09–0110	Multiple epiphyseal dysplasia with microcephaly and nystagmus (Lowry-Wood syndrome), RNU4ATAC-related	AR	RNU4ATAC	226960		See also Microcephalic osteodysplastic primordial dwarfism, *RNU4ATAC*-related, as well as Roifman syndrome, *RNU4ATAC*-related, both in the primordial dwarfism group (group 21), for conditions with different severity from the *RNU4ATAC* gene
	See also Multiple Epiphyseal Dysplasia, recessive type, *SLC26A2*-related, as well as ASPED. Some *COL2A1* variants					

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	can make a MED-like phenotype. Some MED or MED-like phenotypes remain genetically unclear.					
Group 10	**Skeletal disorders caused by abnormalities of cilia or ciliary signaling**					
NOS 10–0010	Short rib–polydactyly syndrome (SRPS), DYNC2H1-related	AR	DYNC2H1	613091, 263520		There is significant clinical and radiological overlap between SRP1/3 and ATD. Some forms of both remain unlinked to the known genes. This gene can also be responsible for chondroectodermal dysplasia (Ellis-van Creveld), see below.
NOS 10–0020	Short rib–polydactyly syndrome (SRPS), IFT80-related	AR	IFT80	611263		
NOS 10–0030	Short rib–polydactyly syndrome (SRPS), IFT81-related	AR	IFT81	617895		
NOS 10–0040	Short rib–polydactyly syndrome (SRPS), WDR34-related	AR	WDR34	615633		
NOS 10–0050	Short rib–polydactyly syndrome (SRPS), WDR60-related	AR	WDR60	615503		
NOS 10–0060	Short rib–polydactyly syndrome (SRPS), DYNC2LI1-related	AR	DYNC2LI1	617088		
NOS 10–0070	Short rib–polydactyly syndrome (SRPS), NEK1-related	AR	NEK1	263520		Possibly also digenic inheritance combining *NEK1* with *DYNC2H1* variants
NOS 10–0080	Short rib–polydactyly syndrome (SRPS), IFT122-related	AR	IFT122	269860		
NOS 10–0090	Short rib–polydactyly syndrome (SRPS), WDR19-related	AR	WDR19	614091		*WDR19* is associated with MIM 614091, 614376, 614378, 615633 as well as with nephronopthisis (MIM 614377), Senior-Loken syndrome (MIM 616307) and Mainzer-Saldino syndrome (see below)
NOS 10–0100	Short rib-polydactyly syndrome (SRPS), INTU-related	AR	INTU	617925		
NOS 10–0110	Short rib-polydactyly syndrome (SRPS), TRAF3IP1-related	AR	TRAF3IP1	see 607380		*TRAF3IP1* also known as *IFT154*
NOS 10–0120	Endocrine-cerebro-osteo dysplasia (ECO), CILK1-related	AR	CILK1	612651		
NOS 10–0130	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), DYNC2H1-related	AR	DYNC2H1	613091		
NOS 10–0140	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), DYNC2LI1-related	AR	DYNC2LI1	see 617088		
NOS 10–0150	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), WDR34-related	AR	WDR34	see 615633		
NOS 10–0160	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), TCTEX1D2-related	AR	TCTEX1D2	617405		
NOS 10–0170	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), WDR60-related	AR	WDR60	see 615503		

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NOS 10–0180	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), WDR19-related	AR	WDR19	614376		*WDR19* is associated with MIM 614091, 614376, 614378, 615633 as well as with nephronopthisis (MIM 614377), Senior-Loken syndrome (MIM 616307) and Mainzer-Saldino syndrome (see below)
NOS 10–0190	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT140-related	AR	IFT140	266920		
NOS 10–0200	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), TTC21B-related	AR	TTC21B	613819		Gene also known for nephronophthisis (MIM 613820)
NOS 10–0210	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT122-related	AR	IFT122	see 269860		Subsumed under SRPS (MIM 269860)
NOS 10–0220	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), WDR35-related	AR	WDR35	614091		
NOS 10–0230	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT43-related	AR	IFT43	617866		
NOS 10–0240	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT80-related	AR	IFT80	611623		
NOS 10–0250	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT172-related	AR	IFT172	615630		
NOS 10–0260	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT81-related	AR	IFT81	617895		
NOS 10–0270	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), IFT52-related	AR	IFT52	617102		
NOS 10–0280	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), CFAP410-related	AR	CFAP410	602271		
NOS 10–0290	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), CEP120-related	AR	CEP120	616300		Described in severe cases resembling SRPS; the *CEP120* gene is also associated with Joubert syndrome (MIM 617761)
NOS 10–0300	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), KIAA0586-related	AR	KIAA0586	616546		Gene also associated with Joubert syndrome (MIM 616490)
NOS 10–0310	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), GRK2-related	AR	GRK2	see 109635		
NOS 10–0320	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), TRAF3IP1-related	AR	TRAF3IP1	see 607380		*TRAF3IP1* also known as *IFT154*
NOS 10–0330	Short-rib thoracic dysplasia (formerly asphyxiating thoracic dysplasia - Jeune syndrome), KIAA0753-related	AR	KIAA0753	619479		*KIAA0753* variants also associated with orofaciodigital syndrome (MIM 617127) and with Joubert syndrome (MIM 619476)
NOS 10–0340	Axial spondylometaphyseal dysplasia, CFAP410-related	AR	CFAP410	602271		

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NOS 10–0350	Axial spondylometaphyseal dysplasia, NEK1-related	AR	NEK1	see 252100		
NOS 10–0360	Chondroectodermal dysplasia (Ellis-van Creveld), EVC1-related	AR	EVC1	225500		See also Weyers acrofacial (acrodental) dysostosis (MIM 193530)
NOS 10–0370	Chondroectodermal dysplasia (Ellis-van Creveld), EVC2-related	AR	EVC2			
NOS 10–0380	Chondroectodermal dysplasia (Ellis-van Creveld), WDR35-related	AR	WDR35			
NOS 10–0390	Chondroectodermal dysplasia (Ellis-van Creveld), DYNC2LI1-related	AR	DYNC2LI1	see 617088		
NOS 10–0400	Chondroectodermal dysplasia (Ellis-van Creveld), GLI1-related	AR	GLI1	see 165220		
NOS 10–0410	Chondroectodermal dysplasia (Ellis-van Creveld), SMO-related	AR	SMO	see		A single case with compound heterozygosity missense variants reported
NOS 10–0420	Orofaciodigital syndrome type 4 (Mohr-Majewski), TCTN3-related	AR	TCTN3	258860		
NOS 10–0430	Orofaciodigital syndrome type 2 (Mohr syndrome), NEK1-related	AR	NEK1	252100		
NOS 10–0440	Cranioectodermal dysplasia (Levin-Sensenbrenner), IFT122-related	AR	IFT122	218330		
NOS 10–0450	Cranioectodermal dysplasia (Levin-Sensenbrenner), WDR35-related	AR	WDR35	613610		
NOS 10–0460	Cranioectodermal dysplasia (Levin-Sensenbrenner), WDR19-related	AR	WDR19	614378		*WDR19* is associated with MIM 614091, 614376, 614378, 615633 as well as with nephronopthisis (MIM 614377), Senior-Loken syndrome (MIM 616307) and Mainzer-Saldino syndrome (see below)
NOS 10–0470	Cranioectodermal dysplasia (Levin-Sensenbrenner), IFT40-related	AR	IFT40	see 614620		see short rib thoracic dysplasia, *IFT140*-associated, above
NOS 10–0480	Cranioectodermal dysplasia (Levin-Sensenbrenner), IFT43-related	AR	IFT43	614009		
NOS 10–0490	Joubert syndrome with short-rib thoracic dysplasia, CSPP1-related	AR	CSPP1	615636		in OMIM as “Joubert syndrome type 21”; not all cases have thoracic dysplasia
NOS 10–0500	Atrial defects-polydactyly-multiple congenital malformation syndrome, PRKACA-related	AD	PRKACA	619142		OMIM created the name of “Cardioacrofacial syndrome 1”.
NOS 10–0510	Atrial defects-polydactyly-multiple congenital malformation syndrome, PRKACB-related	AD, MOS	PRKACB	619143		OMIM created the name of “Cardioacrofacial syndrome 2”; one published patient later reclassified as “Ellis-van Creveld syndrome”.
NOS 10–0520	Mainzer-Saldino syndrome, IFT140-related	AR	IFT140	266920		*IFT140* also associated with isolated retinitis pigmentosa (MIM 617781)

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NOS 10–0530	Mainzer-Saldino syndrome, IFT172-related	AR	IFT172			*IFT172* also associated with Bardet-Biedl syndrome (MIM 619471) and isolated retinitis pigmentosa (616394)
NOS 10–0540	Mainzer-Saldino syndrome, WDR19-related	AR	WDR19	see 614376		*WDR19* is also associated with MIM 614091, 614376, 614378, 615633 as well as with nephronopthisis (MIM 614377), and Senior-Loken syndrome (MIM 616307)
NOS 10–0550	Meckel syndrome, MKS1-related	AR	MKS1	249000		
NOS 10–0560	Meckel syndrome, TMEM216-related	AR	TMEM216	603194		
NOS 10–0570	Meckel syndrome, TMEM67-related	AR	TMEM67	607361		
NOS 10–0580	Meckel syndrome, CEP290-related	AR	CEP290	611134		
NOS 10–0590	Meckel syndrome, RPGRIP1L-related	AR	RPGRIP1L	611561		
NOS 10–0600	Meckel syndrome, CC2D2A-related	AR	CC2D2A	612284		
NOS 10–0610	Thoracolaryngopelvic dysplasia (Barnes)	SP		187760		Dominant transmission reported, but diagnostic criteria not stringent. The existence pf this entity is disputed.
	Given the common genetic basis of several disorders in this group and the absence (so far) of clear genotype-phenotype correlations, the distinction between chondroectodermal dysplasia, asphyxiating thoracic dystrophy (see below for name change), short rib-polydactyly syndromes and related conditions is historical and restricted to the clinical phenotypes. - We have followed MIM and used the term “short-rib thoracic dysplasia” instead of “asphyxiating thoracic dysplasia”, to avoid the negative connotation (and inaccuracy) of “asphyxiating”. - See also paternal UPD14 and Cerebro-costo-mandibular syndrome (rib gap syndrome), *SNRPB*-related, both in Group 36. Also, the large phenotypic spectrum of the Bardet-Biedl syndrome has not been included in spite of minor skeletal involvement as the predominant clinical features are non-skeletal.					
Group 11	**Metaphyseal dysplasias**					
NOS 11–0010	Metaphyseal dysplasia Schmid (MCS), COL10A1-related	AD	COL10A1	156500		Pathogenic variants are typically located in the C-terminal domain of the protein.
NOS 11–0020	Cartilage-hair hypoplasia (CHH; metaphyseal dysplasia, McKusick type), RMRP-related	AR	RMRP	250250		The phenotype of CHH is variable and includes MIM 607095-anauxetic dysplasia as well as MIM 250460-metaphyseal dysplasia without hypotrichosis
NOS 11–0030	Metaphyseal dysplasia with short stature (CHH-like), POP1-related	AR	POP1	617396		The clinical spectrum is variable. The denomination of “anauxetic dysplasia 2” in MIM is confusing as anauxetic dysplasia is a variant of Cartilage-Hair Hypoplasia

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NOS 11–0040	Metaphyseal dysplasia with short stature (CHH-like), NEPRO-related	AR	NEPRO	618853		Facial features and hypotrichosis reminiscent of Cartilage-Hair Hypoplasia
NOS 11–0050	Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (Shwachman-Bodian-Diamond syndrome), SBDS-related	AR	SBDS	260400		See also severe spondylodysplastic dysplasia, Sedaghatian-like
NOS 11–0060	Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia (SBDS type 2), EFL1-related	AR	EFL1	617941		
NOS 11–0070	Metaphyseal dysplasia with pancreatic insufficiency and cyclic neutropenia, DNAJC21-related	AR	DNAJC21	617052		Known in OMIM as Bone Marrow Failure Syndrome 3; BMFS3
NOS 11–0080	Shwachman-Diamond like syndrome, SRP54-related	AD	SRP54	618752		Known in OMIM as Neutropenia, severe congenital, 8
NOS 11–0090	Metaphyseal dysplasia Spahr, MMP13-related	AR	MMP13	250400		Recessive, biallelic variants
NOS 11–0100	Metaphyseal anadysplasia, MMP13-related	AD	MMP13	602111		Dominant, monoallelic type; includes SEMD Missouri type
NOS 11–0110	Metaphyseal anadysplasia, MMP9-related	AR	MMP9	613073		
NOS 11–0120	Metaphyseal dysplasia with maxillary hypoplasia, RUNX2-related	AD	RUNX2	156510		Frequently associated with intragenic duplication of exons 3 to 5 or 3 to 6. See also Cleidocranial dysplasia, RUNX2-related (below; MIM 119600), as well as non-syndromic midline craniosynostosis, RUNX2-related, below
	See Rhizomelic spondylo-metaphyseal dysplasia with remission, LBR-related, for another anadysplasia-like disorder					
Group 12	**Spondylometaphyseal dysplasias (SMD)**					
NOS 12–0010	Spondyloenchondrodysplasia with immune dysregulation (SPENCD), ACP5-related	AR	ACP5	607944		
NOS 12–0020	Odontochondrodysplasia (ODCD), TRIP11-related	AR	TRIP11	184260		See also Achondrogenesis, TRIP11-related (formerly type 1A)
NOS 12–0030	Spondylometaphyseal dysplasia Sutcliffe (or “corner fractures” type), FN1-related	AD	FN1	184255		Some cases are linked to *COL2A1* but not the original family
NOS 12–0040	Spondylometaphyseal dysplasia with cone-rod dystrophy, PCYT1A-related	AR	PCYT1A	608940		
NOS 12–0050	Spondylometaphyseal dysplasia with corneal dystrophy, PLCB3-related	AR	PLCB3	618961		
NOS 12–0060	Chondrodysplasia-pseudohermaphroditism syndrome, HHAT-related	AR	HHAT	600092		Also known as Nivelon-Nivelon-Mabille syndrome *(sic)*

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	See also SMD Kozlowski, TRPV4-related, Severe spondylometaphyseal dysplasia (Sedaghatian type), *GPX4*-related, as well as Axial spondylometaphyseal dysplasia, *CFAP410*-related and Axial spondylometaphyseal dysplasia, *NEK1*-related. In addition, there are many reports of sporadic patients with unclassified SMD variants.					
Group 13	**Spondyloepi(meta)physeal dysplasias (SE(M)D)**					
NOS 13–0010	SED tarda, X-linked (SED-XL), TRAPPC2-related	XL	TRAPPC2	313400		
NOS 13–0020	SED with diabetes mellitus (Wolcott-Rallison syndrome), EIF2AK3-related	AR	EIF2AK3	226980		
NOS 13–0030	Dyggve-Melchior-Clausen dysplasia, DYM-related	AR	DYM	223800		
NOS 13–0040	Smith-McCort dysplasia, DYM-related	AR	DYM	607326		
NOS 13–0050	Smith-McCort dysplasia, RAB33B-related	AR	RAB33B	615222		
NOS 13–0060	SEMD, BNIP1-related	AR	BNIP1	see 603291		
NOS 13–0070	SEMD, MATN3-related	AR	MATN3	608728		See also *MATN3*-related MED in group 9
NOS 13–0080	SEMD, DDRGK1-related (Shohat type)	AR	DDRGK1	602557		
NOS 13–0090	SEMD with leucodystrophy, AIFM1-related	XL	AIFM1	300232		
NOS 13–0100	SEMD, RSPRY1-related	AR	RSPRY1	616723		
NOS 13–0110	SEMD, TMEM165-related	AR	TMEM165	614727		Congenital disorder of glycosylation type IIk
NOS 13–0120	SEMD with microcephaly, retinal dystrophy and hearing loss, PISD-related (Liberfarb syndrome)	AR	PISD	618889		Phenotypically variable; in some affected individuals hearing and vision may be unaffected
NOS 13–0130	SEMD, UFSP2-related	AD	UFSP2	142669, 617974		Includes Familial hip dysplasia (Beukes)
NOS 13–0140	SEMD, short limb–abnormal calcification type, DDR2-related	AR	DDR2	271665		See also other dysplasias with stippling
NOS 13–0150	Immuno-osseous dysplasia, SMARCAL1-related (Schimke type)	AR	SMARCAL1	242900		Nephrotic syndrome is an important manifestation; see also EXTL3 deficiency, below
NOS 13–0160	SEMD with immune deficiency and intellectual disability, EXTL3-related	AR	EXTL3	617425		Also known as “Immunoskeletal dysplasia with developmental abnormalities”; includes Omenn syndrome with chondrodysplasia; see also *SMARCAL1*, above
NOS 13–0170	SEMD with immune deficiency, PGM3-related	AR	PGM3	615816		Known in OMIM as “immunodeficiency 23”
NOS 13–0180	SEMD with intellectual disability, NANS-related	AR	NANS	610442		

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NOS 13–0190	SEMD with severe short stature, RPL13-related	AD	RPL13	618728		
NOS 13–0200	SEMD with elevated lysosomal enzymes, MBTPS1-related	AR	MBTPS1	618392		only two unrelated individuals known so far; in OMIM as “Kondo-Fu type”; possible role of lysosomal dysfunction in pathogenesis is unclear
NOS 13–0210	Short stature, skeletal dysplasia, liver failure, optic nerve atrophy and Pelger-Huet anomaly, NBAS-related	AR	NBAS	616483		Combination of clinical features is variable; also known as infantile liver failure syndrome type 2
NOS 13–0220	Short stature, skeletal dysplasia and liver failure, RINT1-related	AR	RINT1	618641		Combination of clinical features is variable; also known as infantile liver failure syndrome type 3
NOS 13–0230	Spondylodysplastic Ehlers-Danlos syndrome (SDEDSS type 3), SLC39A13-related	AR	SLC39A13	612350		*SLC39A13* / ZIP13 zinc transporter
NOS 13–0240	Spondylar and nasal alterations with striated metaphyses (SPONASTRIME dysplasia), TONSL-related	AR	TONSL	271510		Possibly genetically heterogeneous
NOS 13–0250	Spondyloepiphyseal dysplasia, sensorineural hearing loss, impaired intellectual development, and Leber congenital amaurosis (SHILCA) syndrome, NMNAT1-related	AR	NMNAT1	619260		Nonsyndromic Leber congenital amaurosis (LCA9; MIM 608553) is also caused by biallelic *NMNAT1* variants
NOS 13–0260	Platyspondyly (brachyolmia) with amelogenesis imperfecta, LTBP3-related	AR	LTBP3	601216		
NOS 13–0270	Cerebral, ocular, dental, auricular, and skeletal anomalies (CODAS syndrome), LONP1-related	AR	LONP1	600373		Mitochondrial chaperonopathy
NOS 13–0280	Epiphyseal and vertebral dysplasia, microtia, flat nose plus associated malformation (EVEN-PLUS syndrome), HSPA9-related	AR	HSPA9	616854		Mitochondrial chaperonopathy
NOS 13–0290	Cataracts, growth hormone deficiency, sensory neuropathy, sensorineural hearing loss, and skeletal dysplasia (CAGSSS syndrome), IARS2-related	AR	IARS2	616007		
NOS 13–0300	Steel syndrome, COL27A1-related	AR	COL27A1	615155		
NOS 13–0310	Rhizomelic spondylo-metaphyseal dysplasia with remission, LBR-related	AR	LBR	618019		
NOS 13–0320	Rhizomelic spondylo-epi-metaphyseal dysplasia, GNPNAT1-related	AR	GNPNAT1	619598		
	See also: Opsismodysplasia, *INPPL1*-related; Mucopolysaccharidosis type 4, *GALNS*-related (type 4A; Morquio disease), as well as Progressive pseudorheumatoid dysplasia (PPRD), *WISP3*-related					
Group 14	**Severe spondylodysplastic dysplasias**					
NOS 14–0010	Achondrogenesis, TRIP11-related (formerly type 1A)	AR	TRIP11	200600		

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NOS 14–0020	Schneckenbecken dysplasia, SLC35D1-related	AR	SLC35D1	269250		
NOS 14–0030	Severe spondylometaphyseal dysplasia (Sedaghatian type), GPX4-related	AR	GPX4	250220		
NOS 14–0040	Severe spondylometaphyseal dysplasia (SMD Sedaghatian-like), SBDS-related	AR	SBDS	260400		
NOS 14–0050	Opsismodysplasia, INPPL1-related	AR	INPPL1	258480		Includes lethal and milder cases
NOS 14–0060	Spondylometaphyseal dysplasia, PAM16- related	AR	PAM16	613320		
NOS 14–0070	Carbohydrate deficient glycoprotein syndrome, ALG9-related (ALG9-CDG; Gillessen-Kaesbach-Nishimura syndrome)	AR	ALG9	263210, 608776		
	See also: Thanatophoric dysplasia, *FGFR3*-related; achondrogenesis and Torrance dysplasia, *COL2A1*-related; Fibrochondrogenesis, *COL11A1*-related; Achondrogenesis, *SLC26A2*-related; and Metatropic Dysplasia, *TRPV4*-related					
Group 15	**Mesomelic and rhizo-mesomelic dysplasias**					
NOS 15–0010	Dyschondrosteosis (Leri- Weill), SHOX-related	Pseudo-AD	SHOX	127300		Includes Reinhardt-Pfeiffer dysplasia, MIM 191400. Clinical continuum with Idiopathic short stature (MIM 300582)
NOS 15–0020	Mesomelic dysplasia (Langer type), SHOX-related	Pseudo-AR	SHOX	249700		
NOS 15–0030	Omodysplasia, recessive type, GPC6-related	AR	GPC6	258315		
NOS 15–0040	Omodysplasia, dominant type, FZD2-related	AD	FZD2	164745		
NOS 15–0050	Robinow syndrome, WNT5A-related	AD	WNT5A	180700		
NOS 15–0060	Robinow syndrome, DVL1-related	AD	DVL1	616331		
NOS 15–0070	Robinow syndrome, DVL3-related	AD	DVL3	616894		
NOS 15–0080	Robinow syndrome, FZD2-related	AD	FZD2			
NOS 15–0090	Robinow syndrome, recessive type, ROR2-related	AR	ROR2	268310		Includes previous COVESDEM (costo-vertebral segmentation defect with mesomelia); see also brachydactyly type B
NOS 15–0100	Robinow syndrome, recessive type, NXN-related	AR	NXN			
NOS 15–0110	Mesomelic dysplasia, HOXD-related (Kim or Korean type, Kantaputra type, Fryns type)	AD	HOXD	156232		Duplications at HOXD gene cluster locus; phenotypes is variable also within families
NOS 15–0120	Mesomelic dysplasia, Nievergelt type	AD		163400		
NOS 15–0130	Mesomelic dysplasia, Kozlowski-Reardon type	AR		249710		

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NOS 15–0140	Mesomelic dysplasia with acral synostoses (Verloes-David-Pfeiffer type)	AD	SULF1, SLCO5A1	600383		Microdeletion syndrome involving two adjacent genes
NOS 15–0150	Mesomelic dysplasia (Savarirayan type), ID4-related	AD	ID4	605274		Microdeletions on 6p22.3
NOS 15–0160	Mesomelic dysplasia with digital anomalies and intellectual disability (KINSSHIP syndrome), AFF3-related	AD	AFF3	619297		In spite of the acronym, this condition is quite different from both Nievergelt and Savarirayan mesomelic dysplasias
NOS 15–0170	Oculo-skeletal syndrome with rhizomelic shortening, MAB21L2-related	AD	MAB21L2	615877		In OMIM as “Microphthalmia/Coloboma and skeletal dysplasia syndrome”. Skeletal involvement not in all individuals. Two brothers with biallelic variants (AR?) had ocular but no skeletal involvement.
	See also Tibial hemimelia-polysyndactyly-triphalangeal thumb, *ZRS*-related, also consider: mesomelic dysplasia, Camera type (MIM#611886), the status of which remains unconfirmed					
Group 16	**Acromesomelic dysplasias**					
NOS 16–0010	Acromesomelic dysplasia (type Maroteaux), NPR2-related	AR	NPR2	602875		
NOS 16–0020	Acromesomelic dysplasia, PRKG2-related	AR	PRKG2	619636, 619638		Condition associated with biallelic loss of function variants. Three brothers form one family were found to have a spondylo-metaphyseal dysplasia phenotype (in OMIM as “619638 - Spondylometaphyseal dysplasia, Pagnamenta type”. Needs to be confirmed)
NOS 16–0030	Grebe dysplasia, GDF5-related	AR	GDF5	200700		Includes acromesomelic dysplasia Hunter-Thompson type and acromesomelic dysplasia with genital anomalies; see also see other GDF5-related disorders
NOS 16–0040	Grebe dysplasia, BMPR1B-related	AR	BMPR1B	609441		
NOS 16–0050	Fibular hypoplasia and complex brachydactyly (Du Pan), GDF5-related	AR	GDF5	228900		see also other GDF5-related disorders
NOS 16–0060	Fibular hypoplasia and complex brachydactyly (Du Pan), BMPR1B-related	AR	BMPR1B	see 603248		
NOS 16–0070	Acromesomelic dysplasia, Osebold-Remondini type	AD		112910		
Group 17	**Acromelic dysplasias**					
NOS 17–0010	Acrocapitofemoral dysplasia, IHH-related	AR	IHH	607778		See other conditions associated with the *IHH* gene in this table
NOS 17–0020	Geleophysic dysplasia, ADAMTSL2-related	AR	ADAMTSL2	231050		
NOS 17–0030	Geleophysic dysplasia, FBN1-related	AD	FBN1	614185		

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NOS 17–0040	Geleophysic dysplasia, LTBP3-related	AD	LTBP3	617809		
NOS 17–0050	Acromicric dysplasia, FBN1-related	AD	FBN1	102370		Includes acrolaryngeal dysplasia, previously known as Fantasy Island dysplasia or Tattoo dysplasia, and Moore-Federman syndrome
NOS 17–0060	Acromicric dysplasia, LTBP3-related	AD	LTBP3	see 617809		
NOS 17–0070	Weill-Marchesani syndrome, dominant, FBN1-related	AD	FBN1	608328		
NOS 17–0080	Weill-Marchesani syndrome, ADAMTS10-related	AR	ADAMTS10	277600		
NOS 17–0090	Weill-Marchesani syndrome, ADAMTS17-related	AR	ADAMTS17	613195		
NOS 17–0100	Weill-Marchesani syndrome, LTBP2-related	AR	LTBP2	614819		
NOS 17–0110	Myhre dysplasia, SMAD4-related	AD	SMAD4	139210		
NOS 17–0120	Acrodysostosis, PDE4D-related	AD	PDE4D	614613		Includes acroscyphodysplasia (see PMID 30006632)
NOS 17–0130	Acrodysostosis, PRKAR1A-related	AD	PRKAR1A	101800		
NOS 17–0140	Angel-shaped phalango-epiphyseal dysplasia (ASPED)	AD		105835		Possibly related or allelic to brachydactyly type C
NOS 17–0150	Albright hereditary osteodystrophy, GNAS-related	AD	GNAS	103580		Overlaps with progressive osseous heteroplasia
NOS 17–0160	Leri Pleonosteosis, linked to 8q22.1	AD	8q22.1	151200		Duplication at 8q22.1 encompassing GDF6 and SDC2
NOS 17–0170	SED with brachydactyly, MIR140-related	AD	MIR140	618618		Brachydactyly with cone-shaped epiphyses
	See also Cartilage-Hair Hypoplasia, *RMRP*-related, and the brachdydactyly groups, below (groups 18 and 19)					
Group 18	**Brachydactylies (isolated)**					
NOS 18–0010	Brachydactyly type A1, IHH-related	AD	IHH	112500		
NOS 18–0020	Brachydactyly type A2, BMPR1B-related	AD	BMPR1B	112600		
NOS 18–0030	Brachydactyly type A2, BMP2-related	AD	BMP2	112600		Duplication of *BMP2* enhancer
NOS 18–0040	Brachydactyly type A2, GDF5-related	AD	GDF5	112600		See also Grebe dysplasia, GDF5-related; Fibular hypoplasia and complex brachydactyly (Du Pan), GDF5-related; Brachydactyly type C, GDF5-related; and Multiple synostoses syndrome, GDF5-related
NOS 18–0050	Brachydactyly type B1, ROR2-related	AD	ROR2	113000		see also Robinow syndrome/COVESDEM
NOS 18–0060	Brachydactyly type B2, NOG-related	AD	NOG	611377		
NOS 18–0070	Brachydactyly type C, GDF5-related	AD	GDF5	113100		see other GDF5-related disorders

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NOS 18–0080	Brachydactyly type D, HOXD13-related	AD	HOXD13	113200		Brachydactyly type D is often a component of Brachydactyly type E
NOS 18–0090	Brachydactyly type E, HOXD13-related	AD	HOXD13	113300		
NOS 18–0100	Brachydactyly with anonychia (Cooks syndrome), KCNJ2-related	AD	KCNJ2	106995		Duplications of *SOX9/KCNJ2* regulatory region
NOS 18–0110	Preaxial brachydactyly, PAX3 type, linked to 2q35–36	AD	2q35–36			Deletions leading to disruption of TADs and abnormal expression of *PAX3*
	See also brachdactyly, *PTHLH*-related (below)					
Group 19	**Brachydactylies as part of syndromes**					
NOS 19–0010	Trichorhinophalangeal dysplasia types 1/3	AD	TRPS1	190350, 190351		TRPS1 and 3 are a phenotypic spectrum
NOS 19–0020	Langer-Giedion syndrome (Trichorhinophalangeal dysplasia type 2)	AD	TRPS1, EXT1	150230		Microdeletion syndrome; see also multiple cartilaginous exostoses
NOS 19–0030	Catel-Manzke syndrome, TGDS-related	AR	TGDS	616145		
NOS 19–0040	Deafness, onychodystrophy, osteodystrophy, retardation and seizures (DOORS) syndrome	AR	TBC1D24	220500		“Osteodystrophy” and “retardation” are misnomers
NOS 19–0050	Brachydactyly - intellectual disability syndrome, HDAC4-related	AD	HDAC4	600430		The existence of this entity is questionable. *HDAC4* variants alone may not be sufficient to produce either brachydactyly or intellectual disability. Some patients have microdeletions involving contiguous genes (2q37 deletion syndrome). *HDAC4* variants have been associated with a developmental disorder (see MIM 619797)
NOS 19–0060	Hyperphosphatasia with intellectual disability, brachytelephalangy, and distinct face, PIGV-related	AR	PIGV	239300		Several other related defects of GPI synthesis known, most cases not known for skeletal changes; see e.g., MIM 610293 for a summary
NOS 19–0070	Brachydactyly-short stature-hypertension syndrome, PDE3A-related (Bilginturan syndrome)	AD	PDE3A	112410		
NOS 19–0080	Brachydactyly, obesity and intelelctual disability syndrome, PRMT7-related	AR	PRMT7	617157		Phenotype reminiscent of Albright Hereditary Ostedystrophy (AHO), GNAS-related (see above) but recessive. In OMIM as “617157 - Short stature, brachydactyly, intellectual developmental disability, and seizures”
NOS 19–0090	Microcephaly-oculo-digito-esophageal-duodenal syndrome, MYCN-related (Feingold syndrome)	AD	MYCN	164280		
NOS 19–0100	Hand-foot-genital syndrome, HOXA13-related	AD	HOXA13	140000		Includes Guttmacher syndrome

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NOS 19–0110	Rubinstein-Taybi syndrome, CREBBP-related	AD	CREBBP	180849		
NOS 19–0120	Rubinstein-Taybi syndrome, EP300-related	AD	EP300	613684		
NOS 19–0130	Brachydactyly, Temtamy type, CHSY1-related	AR	CHSY1	605282		
NOS 19–0140	Hyperphalangism, characteristic facies, hallux valgus and bronchomalacia (Chitayat syndrome), ERF-related	AD	ERF	617180		typically a monoallelic Y89C substitution
NOS 19–0150	Hypoacusis with facial an digital anomalies (Keipert syndrome), GPC4-related	XL	GPC4	301026		brachytelephalangy is the most consistent skeletal signs
NOS 19–0160	Christian type brachydactyly	AD		112450		
NOS 19–0170	Coffin-Siris syndrome, ARID1A-related	AD	ARID1A	614607		
NOS 19–0180	Coffin-Siris syndrome, ARIB1B-related	AD	ARID1B	135900		Variants in various components of the SWI/SNF complex have been reported in patients with a diagnosis of Coffin-Siris syndrome
NOS 19–0190	Coffin-Siris syndrome, SMARCB1-related	AD	SMARCB1	614608		
NOS 19–0200	Coffin-Siris syndrome, SMARCA4-related	AD	SMARCA4	614609		
NOS 19–0210	Coffin-Siris syndrome, SMARCE1-related	AD	SMARCE1	616938		
NOS 19–0220	Cardiomyopathy and brachydactyly, LMNA-related (Heart-hand syndrome type IV)	AD	LMNA	610140		in OMIM as “Heart-Hand syndrome, Slovenian type”
	See also CDP, X-linked recessive, *ARSE*-related (brachytelephalangic type; CDPX1)					
Group 20	**Bent bones dysplasia group**					
NOS 20–0010	Campomelic dysplasia (CD), SOX9-related	AD	SOX9	114290		Includes acampomelic campomelic dysplasia (ACD), mild campomelic dysplasia (MIM 602196); so-called Ischio-pubic-patellar dysplasia, as well as some cases of isolated Pierre-Robin sequence
NOS 20–0020	Stüve-Wiedemann syndrome, LIFR-related	AR	LIFR	601559		Includes former neonatal Schwartz-Jampel syndrome or SJS type 2
NOS 20–0030	Stüve-Wiedemann syndrome, IL6ST-related	AR	IL6ST	619751		
NOS 20–0040	Kyphomelic dysplasia with facial dysmorphism, KIF5B-related	AD	KIF5B	211350		The name “kyphomelic dysplasia” has been applied to heterogeneous conditions
NOS 20–0050	Bent bone dysplasia, FGFR2-related	AD	FGFR2	614592		
NOS 20–0060	Bent bone dysplasia, LAMA5-related	AR	LAMA5			Biallelic LAMA5 variants are associated with congenital or infantile nephrotic syndrome (MIM

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	Bent bones is an unspecific finding, particularly in a prenatal setting, that can be observed in numerous other conditions, such as those with bone fragility; thus see the OI-bone fragility group (group 26) as well as Hypophosphatasia, *ALPL*-related.					
Group 21	**Primordial dwarfism and slender bones group**					
NOS 21–0010	3-M syndrome, CUL7-related	AR	CUL7	273750		Includes dolichospondylic dysplasia and Yakut short stature syndrome
NOS 21–0020	3-M syndrome, OBSL1-related	AR	OBSL1	612921		
NOS 21–0030	3-M syndrome, CCDC8-related	AR	CCDC8	614205		
NOS 21–0040	Sanjad-Sakati syndrome, recessive, TBCE-related	AR	TBCE	241410		In OMIM as “Kenny-Caffey type 1” but does not correspond to the disorder described by Kenny and Caffey which is the dominant form
NOS 21–0050	Kenny-Caffey syndrome, dominant, FAM111A-related	AD	FAM111A	127000		
NOS 21–0060	Osteocraniostenosis, FAM111A-related	AD	FAM111A	602361		
NOS 21–0070	Hallermann-Streiff syndrome			234100		Usuall sporadic; some cases have phenotypic overlap with Osteocraniostenosis, FAM111A-related
NOS 21–0080	Microcephalic osteodysplastic primordial dwarfism, RNU4ATAC-related	AR	RNU4ATAC	210710		Was MOPD 1/3; usually homozygous variants; includes Taybi-Linder cephaloskeletal dysplasia
NOS 21–0090	Roifman syndrome, RNU4ATAC-related	AR	RNU4ATAC	616651		See other RNU4ATAC-related condition in this table
NOS 21–0100	Microcephalic osteodysplastic primordial dwarfism, PCNT-related	AR	PCNT	210720		Was MOPD2, Majewski type
NOS 21–0110	Microcephalic osteodysplastic primordial dwarfism, ATR-related	AR	ATR	210600		In MIM as Seckel syndrome 1
NOS 21–0120	Microcephalic osteodysplastic primordial dwarfism, RBBP8-related	AR	RBBP8	606744		In MIM as Seckel syndrome 2. The RBBP8 gene is also associated with Jawad syndrome (microcephaly with intellectual disability and digital anomalies; MIM 251255)
NOS 21–0130	Microcephalic osteodysplastic primordial dwarfism, CEP152-related	AR	CEP152	613823		In MIM as Seckel syndrome 5. The CEP152 gene also causes primary microcephaly (MIM 614852)
NOS 21–0140	Microcephalic osteodysplastic primordial dwarfism, DNA2-related	AR	DNA2	615807		In MIM as Seckel syndrome 8. The DNA2 gene is also associated with autosomal dominant progressive external ophthalmoplegia with mitochondrial DNA deletions (MIM 615156)
NOS 21–0150	Microcephalic osteodysplastic primordial dwarfism, TRAIP-related	AR	TRAIP	616777		In MIM as Seckel syndrome 9

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NOS 21–0160	Microcephalic osteodysplastic primordial dwarfism, NSMCE2-related	AR	NSMCE2	617253		In MIM as Seckel syndrome 10
NOS 21–0170	Microcephalic osteodysplastic primordial dwarfism, CENPE-related	AR	CENPE	see 616051		In MIM as autosomal recessive primary microcephaly
NOS 21–0180	Microcephalic osteodysplastic primordial dwarfism, CRIPT-related	AR	CRIPT	615789		In MIM as short stature with microcephaly and distinctive facies
NOS 21–0190	Microcephalic osteodysplastic primordial dwarfism, XRCC4-related	AR	XRCC4	616541		In MIM as short stature, microcephaly and endocrine dysfunction
NOS 21–0200	Microcephalic osteodysplastic primordial dwarfism, or microcephaly-short stature-micromelia-limb abnormalities, DONSON-related	AR	DONSON	251230, 617604		Milder affected patients may fall into the Meier-Gorlin syndrome spectrum
NOS 21–0210	IMAGE syndrome (intrauterine growth retardation, metaphyseal dysplasia, adrenal hypoplasia, and genital anomalies)	AD	CDKN1C	614732		Gene also known to cause Beckwith-Wiedemann syndrome (MIM 130650). IMAGE-associated variants are clustered in the PCNA-binding region and are maternally transmitted (gene is imprinted with preferential maternal expression)
NOS 21–0220	IMAGE syndrome / FILS syndrome, POLE-related	AR	POLE	618336, 615139		The phenotype is variable and may include immune deficiency (OMIM 615139)
NOS 21–0230	Saul-Wilson syndrome, COG4-related	AD	COG4	618150		
NOS 21–0240	Short stature, facial dysmorphism, skeletal and dental anomalies syndrome, SCUBE3-related	AR	SCUBE3	619184		in OMIM as “short stature, facial dysmorphism, and skeletal anomalies with or without cardiac anomalies 2”
NOS 21–0250	Ear-patella-primordial short stature syndrome (Meier-Gorlin), ORC4-related	AR	ORC1	224690		
NOS 21–0260	Ear-patella-primordial short stature syndrome (Meier-Gorlin), ORC4-related	AR	ORC4	613800		
NOS 21–0270	Ear-patella-primordial short stature syndrome (Meier-Gorlin), ORC6-related	AR	ORC6	613803		
NOS 21–0280	Ear-patella-primordial short stature syndrome (Meier-Gorlin), CDT1-related	AR	CDT1	605525		
NOS 21–0290	Ear-patella-primordial short stature syndrome (Meier-Gorlin), CDC6-related	AR	CDC6	613805		A single case reported so far
NOS 21–0300	Ear-patella-primordial short stature syndrome (Meier-Gorlin), CDC45-related	AR	CDC45	603465		
NOS 21–0310	Ear-patella-primordial short stature syndrome (Meier-Gorlin), MCM3-related	AR	MCM3	see 602693		

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NOS 21–0320	Ear-patella-primordial short stature syndrome (Meier-Gorlin), MCM5-related	AR	MCM5	602696		
NOS 21–0330	Ear-patella-primordial short stature syndrome (Meier-Gorlin), MCM7-related	AR	MCM7	see 600592		
NOS 21–0340	Ear-patella-primordial short stature syndrome (Meier-Gorlin), GMNN-related	AD	GMNN	613804		
NOS 21–0350	Ear-patella-primordial short stature syndrome (Meier-Gorlin) with craniosynostosis, GINS2-related	AD	GINS2	see 610609		A single case reported so far
Group 22	**Lysosomal Storage Diseases with Skeletal Involvement**					
NOS 22–0010	Mucopolysaccharidosis type 1, IDUA-related	AR	IDUA	607014, 607015, 607016		was Type 1H-Hurler syndrome, type 1S-Scheie syndrome
NOS 22–0020	Mucopolysaccharidosis type 2, IDS-related	XL	IDS	309900		known as Hunter syndrome
NOS 22–0030	Mucopolysaccharidosis type 3, SGSH-related (type 3A)	AR	SGSH	252900		known as Sanfilippo A syndrome
NOS 22–0040	Mucopolysaccharidosis type 3, NAGLU-related (type 3B)	AR	NAGLU	252920		known as Sanfilippo B syndrome
NOS 22–0050	Mucopolysaccharidosis type 3, HSGNAT-related (type 3C)	AR	HSGNAT	252930		known as Sanfilippo C syndrome
NOS 22–0060	Mucopolysaccharidosis type 3, GNS-related (type 3D)	AR	GNS	252940		known as Sanfilippo D syndrome
NOS 22–0070	Mucopolysaccharidosis type 4, GALNS-related (type 4A)	AR	GALNS	253000		known as Morquio A syndrome
NOS 22–0080	Mucopolysaccharidosis type 4, GLB1-related (type 4B)	AR	GLB1	253010		known as Morquio B syndrome
NOS 22–0090	Mucopolysaccharidosis type 6, ARSB-related	AR	ARSB	253200		known as Maroteaux-Lamy syndrome
NOS 22–0100	Mucopolysaccharidosis type 7, GUSB-related	AR	GUSB	253220		known as Sly syndrome
NOS 22–0110	Mucopolysaccharidosis type 10, ARSK-related	AR	ARSK	610011		
NOS 22–0120	Mucopolysaccharidosis-plus syndrome, VPS33A-related	AR	VPS33A	617303		
NOS 22–0130	Fucosidosis, FUCA-related	AR	FUCA	230000		
NOS 22–0140	alpha-Mannosidosis, MAN2B1-related	AR	MAN2B1	248500		
NOS 22–0150	beta-Mannosidosis, MANBA-related	AR	MANBA	248510		
NOS 22–0160	Aspartylglucosaminuria, AGA-related	AR	AGA	208400		
NOS 22–0170	Gangliosidosis GM1, GLB1-related	AR	GLB1	230500		Several forms, see also mucopolysaccharidosis type 4B (Morquio B) above
NOS 22–0180	Sialidosis, NEU1-related	AR	NEU1	256550		Several forms of different severity

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NOS 22–0190	Galactosialidosis, PPGB-related	AR	PPGB	256540		Several forms of different severity
NOS 22–0200	Sialic acid storage disease (SIASD), SLC17A5-related	AR	SLC17A5	269920		
NOS 22–0210	Multiple sulfatase deficiency, SUMF-related	AR	SUMF1	272200		
NOS 22–0220	Mucolipidosis II (I-cell disease), GNPTAB-related	AR	GNPTAB	252500		the old entity of Pacman dysplasia is the prenatal manifestation of mucolipidosis II with hyperparathyroidism
NOS 22–0230	Mucolipidosis III (Pseudo-Hurler polydystrophy), GNPTAB-related	AR	GNPTAB	252600		
NOS 22–0240	Mucolipidosis III (Pseudo-Hurler polydystrophy), GNPTG-related	AR	GNPTG	252605		in general somewhat milder phenotype than the GNPTAB-related form
NOS 22–0250	Mucolipidosis, GCAF-related	AR	CGAF	619345		The gene was previously known as TMEM251 and encodes for a “GNTAP cleavage and activity factor” (see GNTAP, above)
NOS 22–0260	Gaucher disease, GBA-related	AR	GBA	230800		Long-standing Gaucher disease can have bone changes that are different from the “dysostosis multiplex” pattern seen in other lysosomal diseases in this group
	See also familial arthritis with hyaluronidase deficiency (“mucopolysaccharidosis type 9”), *HYAL1*-related; SEMD with elevated lysosomal enzymes, *MBTPS1*-related, above; as well as Farber disease, *ASAH1*-related, below.					
Group 23	**Chondrodysplasia punctata (CDP) group**					
NOS 23–0010	CDP, X-linked recessive, ARSE-related (brachytelephalangic type; CDPX1)	XL	ARSE	302950		
NOS 23–0020	CDP, X-linked dominant, EBP-related (Conradi-Hünermann type; CDPX2)	XL	EBP	302960		
NOS 23–0030	Congenital hemidysplasia, ichthyosis, limb defects (CHILD) syndrome, NSDHL-related	XL	NSDHL	308050		
NOS 23–0040	Keutel syndrome, MGP-related	AR	MGP	245150		
NOS 23–0050	Greenberg dysplasia, LBR-related	AR	LBR	215140		Includes hydrops-ectopic calcification-moth-eaten appearance dysplasia (HEM) and dappled diaphyseal dysplasia; possibly includes also the ultrarare entity designed as Astley-Kendall dysplasia. See also the non-lethal condition associated with *LBR*, above
NOS 23–0060	Rhizomelic CDP, PEX7-related	AR	PEX7	215100		
NOS 23–0070	Rhizomelic CDP, DHPAT-related	AR	DHPAT	222765		

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NOS 23–0080	Rhizomelic CDP, AGP5-related	AR	AGPS	600121		
NOS 23–0090	Rhizomelic CDP, FAR1-related	AR	FAR1	616154		MIM calls this entity “peroxisomal fatty acyl-CoA reductase 1 disorder”; skeletal phenotype milder than other rCDP forms. The *FAR1* gene is also associated with cataracts, spastic paraparesis, and speech delay (MIM 619338, AD)
NOS 23–0100	Rhizomelic CDP, PEX5-related	AR	PEX5	616716		
NOS 23–0110	CDP tibial-metacarpal type			118651		Some cases possibly caused by maternal auto-immune disease
	Note: stippling can occur in several syndromes such as Zellweger cerebro-hepato-renal syndrome (see OMIM for the many genetic types), Smith-Lemli-Opitz (MIM 270400), in Mucolipidosis II (I-cell disease), *GNPTAB*-related, mild forms of Raine dysplasia, *FAM20C*-related, and others. See also SEMD short limb-abnormal calcification type, *DDR2*-related. Stippling in the fetus is also observed as a consequence of maternal auto-immune disease, sometimes presenting as “CDP tibial-metacarpal type”.					
Group 24	**Osteopetrosis and related osteoclast disorders**					
NOS 24–0010	Osteopetrosis, neonatal or infantile form, TCIRG1-related	AR	TCIRG1	259700		
NOS 24–0020	Osteopetrosis, neonatal or infantile form, CLCN7-related	AR	CLCN7	611490		
NOS 24–0030	Osteopetrosis, neonatal or infantile form, SNX10-related	AR	SNX10	615085		
NOS 24–0040	Osteopetrosis, infantile form, with nervous system involvement, OSTM1-related	AR	OSTM1	259720		Includes former osteopetrosis with infantile neuraxonal dysplasia (MIM 600329)
NOS 24–0050	Osteopetrosis, infantile form, osteoclast-poor with immunoglobulin deficiency, TNFRSF11A-related	AR	TNFRSF11A	612301		See also below in this group, Dysosteosclerosis, TNFRSF11A-related, as well as MIM 602080-familial expansile osteolysis
NOS 24–0060	Osteopetrosis, intermediate form, TCIRG1-related	AR	TCIRG1	259700		
NOS 24–0070	Osteopetrosis, intermediate form, TNFSF11-related	AR	TNFSF11	259710		
NOS 24–0080	Osteopetrosis, intermediate form, PLEKHM-related	AR	PLEKHM1	611497		
NOS 24–0090	Osteopetrosis, intermediate form, CLCN7-related	AR	CLCN7	259710		
NOS 24–0100	Osteopetrosis, late-onset, dominant form, CLCN7-related	AD	CLCN7	166600		
NOS 24–0110	Osteopetrosis with renal tubular acidosis, CA2-related	AR	CA2	259730		
NOS 24–0120	Osteopetrosis with ectodermal dysplasia and immune defect (OLEDAID), IKBKG-related	XL	IKBKG	300301		

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NOS 24–0130	Osteopetrosis, moderate form, SLC4A2-related	AR	SLC4A2	see 109280		a single adult patient reported, phenotype may evolve
NOS 24–0140	Osteopetrosis, moderate form with defective leucocyte adhesion, FERMT3-related	AR	FERMT3	612840		In OMIM as Leucocyte Adhesion Deficiency 3 (LAD3) - MIM 612840
NOS 24–0150	Osteopetrosis, moderate form with defective leucocyte adhesion, RASGRP2-related	AR	RASGRP2	615888		OMIM only includes Bleeding Disorder, Platelet type, 18 (MIM 615888) for this gene
NOS 24–0160	Osteosclerotic metaphyseal dysplasia, LRKK1-related	AR	LRRK1	615198		The name may be misleading as the condition is best described as a form of osteopetrosis
NOS 24–0170	Pyknodysostosis, CTSK-related	AR	CTSK	265800		In some individuals, the features of pyknodyostosis are absent and the disorder mimics osteopetrosis
NOS 24–0180	Dysosteosclerosis, SLC29A3-related	AR	SLC29A3	224300		
NOS 24–0190	Dysosteosclerosis, TNFRSF11A-related	AR	TNFRSF11A	224300		This entity probably forms a spectrum with Osteopetrosis, intermediate form, TNFSF11-related (above)
NOS 24–0200	Dysosteosclerosis with degenerative encephalopathy and brain malformation, CSF1R-related	AR	CSF1R	618476		In OMIM as “Brain abnormalities, neurodegeneration and dysosteosclerosis (BANDDOS)”; gene also associated with MIM 221820 -Leukoencephalopathy with spheroids.
	Note: osteomesopyknosis (MIM 166450) may represent a form of osteopetrosis. In a pattern similar to the ciliary disorders, the phenotypes from individual loci are variable and may overlap with those of other loci.					
Group 25	**Osteosclerotic disorders**					
NOS 25–0010	Desmosterolosis, DHCR4-related	AR	DHCR24	602398		See also other sterol-metabolism related conditions
NOS 25–0020	Raine dysplasia, FAM20C-related	AR	FAM20C	259775		Variable severity, many cases are perinatal severe, some cases show survival to adulthood; then often combined with FGF23 elevation and hypophosphatemic rickets
NOS 25–0030	Caffey disease, COL1A1-related	AD	COL1A1	114000		Rare specific variants in *COL1A1.* See also osteogenesis imperfecta related to collagen 1 genes.
NOS 25–0040	Caffey dysplasia (severe variants with prenatal onset)	AR?		114000		
NOS 25–0050	Dysplastic cortical hyperostosis, Kozlowski-Tsuruta type					A few sporadic cases known, phenotype consistent, molecular basis unknown
NOS 25–0060	Dysplastic cortical hyperostosis, Al-Gazali type			601356		Only a few cases known. Im OMIM as “Lethal short-limb skeletal dysplasia, Al Gazali type”. Not to be confused with “Al-Gazali syndrome”, a rare variant of *B3GALT6* disorders (see above)

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NOS 25–0070	Osteopoikilosis, LEMD3-related	AD	LEMD3	166700		Includes Buschke-Ollendorff syndrome (same OMIM entry)
NOS 25–0080	Melorheostosis with osteopoikilosis, LEMD3-related	AD	LEMD3	166700		Includes mixed sclerosing bone dysplasia
NOS 25–0090	Melorheostosis, MAP2K1-related	SP	MAP2K1	155950		Possibly locus heterogeneity
NOS 25–0100	Osteopathia striata with cranial sclerosis (OSCS), AMER1-related	XL	AMER1	300373		
NOS 25–0110	Pyle disease, SFRP4-related	AR	SFRP4	265900		The name “metaphyseal dysplasia, Pyle type” is misleading (no growth plate dysplasia) and should be avoided
NOS 25–0120	Craniometaphyseal dysplasia, ANKH-related	AD	ANKH	123000		Dominant type
NOS 25–0130	Craniometaphyseal dysplasia, GJA1-related	AR	GJA1	218400		Recessive type
NOS 25–0140	Diaphyseal dysplasia Camurati-Engelmann, TGFB1-related	AD	TGFB1	131300		Gain-of-function variants
NOS 25–0150	Hyperostosis-Hyperphosphatemia syndrome, GALNT3-related	AR	GALNT3	211900		Formerly hyperphosphatemic tumoral calcinosis type 1
NOS 25–0160	Hyperostosis-Hyperphosphatemia syndrome, FGF23-related	AR	FGF23	617993		Formerly hyperphosphatemic tumoral calcinosis type 2
NOS 25–0170	Hyperostosis-Hyperphosphatemia syndrome, KL-relathed	AR	KL	617994		Formerly hyperphosphatemic tumoral calcinosis type 3
NOS 25–0180	Cerebellar hypoplasia-endosteal sclerosis, POLR3B-related	AR	POLR3B	213002		
NOS 25–0190	Hematodiaphyseal dysplasia Ghosal, TBXAS1-related	AR	TBXAS1	231095		
NOS 25–0200	Hypertrophic osteoarthropathy, HPGD-related	AR	HPGD	259100		Includes cranio-osteoarthropathy, some cases of recessive pachydermoperiostosis, as well as recessively inherited isolated digital clubbing (MIM 119900)
NOS 25–0210	Hypertrophic osteoarthropathy, SLCO2A1-related	AD, AR	SLCO2A1	614441		
NOS 25–0220	Oculodentoosseous dysplasia (ODOD), GJA1-related, dominant, mild type	AD	GJA1	164200		
NOS 25–0230	Oculodentoosseous dysplasia (ODOD) GJA1-related, recessive, severe type	AR	GJA1	257850		Possibly homozygous form of mild ODOD
NOS 25–0240	Osteoectasia with hyperphosphatasia (juvenile Paget disease), OPG-related	AR	OPG	239000		
NOS 25–0250	Osteosclerosis, LRP5-related	AD	LRP5	144750, 607634		Includes previous AD osteopetrosis type 1 (OPTA1)
NOS 25–0260	Sclerosteosis, SOST-related	AR	SOST	269500		see also sclerosteosis, SOST-related, below
NOS 25–0270	Sclerosteosis, LRP4-related	AR	LRP4	614305		
NOS 25–0280	Endosteal hyperostosis, van Buchem type, SOST-related	AR	SOST	239100		Specific 52 kb deletion downstream of *SOST*

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NOS 25–0290	Endosteal hyperostosis, Worth type	AD	LRP5	144750		
NOS 25–0300	Craniodiaphyseal dysplasia, SOST-related	AD	SOST	122860		Presumed dominant negative variant
NOS 25–0310	Craniodiaphyseal dysplasia, SP7-related	AR	SP7	see 606633		one family reported; SP7 variants also associated with Osteogenesis imperfecta (MIM 613849), see below
NOS 25–0320	Trichodentoosseous dysplasia, DLX3-related	AD	DLX3	190320		
NOS 25–0330	Diaphyseal medullary stenosis with malignant fibrous histiocytoma, MTAP-related	AD	MTAP	112250		Also known as Hardcastle disease
NOS 25–0340	Craniotubular dysplasia, TMEM53-related	AR	TMEM53	619727		
NOS 25–0350	Craniometadiaphyseal dysplasia, Wormian bone type	AR		269300		
NOS 25–0360	Lenz-Majewski hyperostotic dysplasia, PTDSS1-related	AD	PTDSS1	151050		
NOS 25–0370	Osteochondrodysplasia with hypertrichosis (Cantu syndrome), ABCC9-related	AD	ABCC9	239850		
NOS 25–0380	Familial Paget disease of bone, SQSTM1-related	AD	SQSTM1	167250		
NOS 25–0390	Inclusion body myopathy, Paget disease of bone and frontotemporal dementia	AD	VCP	167320		Monoallelic variants in the VCP gene are also associated with MIM 616687-Charcot-Marie-Tooth disease 2Y, and with MIM 613954-Frontotemporal dementia and/or amyotrophic lateral sclerosis 6.
NOS 25–0400	Endosteal hyperostosis, oligodontia, short stature, facial dysmorphism and intellectual disability, POLR3GL-related	AR	POLR3GL	619234		Phenotypic elements will need to be evaluated more precisely; one patient reported as Wiedemann-Rautenstrauch-syndrome-like
NOS 25–0410	Metaphyseal dysplasia, Braun-Tinschert type	AD		605946		
NOS 25–0420	Trichothiodystrophy with axial osteosclerosis	AR				A subset of patients with trichothiodystrophy have marked osteosclerosis but have not been molecularly characterized so far
	See also the chondrodysplasia punctata group (group 23); as well as familial expansile osteolysis, *TNFRSF11A*-related (below); and Trichothiodystrophy with central osteosclerosis (PMID 15148554)					
Group 26	**Osteogenesis Imperfecta and bone fragility group**					
NOS 26–0010	Osteogenesis imperfecta, non-deforming (Sillence type 1), COL1A1-related	AD	COL1A1	166200		Usually with persistently blue sclerae, can have signs of connective tissue weakness (in MIM as OI type I)
NOS 26–0020	Osteogenesis imperfecta, non-deforming (Sillence type 1), COL1A2-related	AD	COL1A2	166200		Usually with persistently blue sclerae, can have signs of connective tissue weakness (in MIM as OI type I)

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NOS 26–0030	Osteogenesis imperfecta, severe perinatal form (Sillence type 2) COL1A1-related	AD	COL1A1	166210		Formerly “perinatal lethal”; in OMIM as OI type II
NOS 26–0040	Osteogenesis imperfecta, severe perinatal form (Sillence type 2), COL1A2-related	AD	COL1A2	166210		Formerly “perinatal lethal”; in OMIM as OI type II
NOS 26–0050	Osteogenesis imperfecta, severe perinatal form (Sillence type 2), CRTAP-related	AR	CRTAP	610682		Formerly “perinatal lethal”; in OMIM as OI type VII
NOS 26–0060	Osteogenesis imperfecta, severe perinatal form (Sillence type 2), P3H1-related	AR	P3H1	610915		Formerly “perinatal lethal”; in OMIM as OI type VIII
NOS 26–0070	Osteogenesis imperfecta, severe perinatal form (Sillence type 2), PPIB-related	AR	PPIB	259440		Formerly “perinatal lethal”; in OMIM as OI type IX
NOS 26–0080	Osteogenesis imperfecta, progressively deforming (Sillence type 3), COL1A1-related	AD	COL1A1	259420		In OMIM as OI type III
NOS 26–0090	Osteogenesis imperfecta, progressively deforming (Sillence type 3), COL1A2-related	AD	COL1A2	259420		In OMIM as OI type III
NOS 26–0100	Osteogenesis imperfecta, progressively deforming (Sillence type 3), IFITM5-related	AD	IFITM5	610967		in OMIM OI type III; phenotype is distinct but is some instances can mimin OI type III
NOS 26–0110	Osteogenesis imperfecta, progressively deforming (Sillence type 3), SERPINF1-related	AR	SERPINF1	613982		In OMIM as OI type VI
NOS 26–0120	Osteogenesis imperfecta, progressively deforming (Sillence type 3), CRTAP-related	AR	CRTAP	610682		In OMIM OI type VII
NOS 26–0130	Osteogenesis imperfecta, progressively deforming (Sillence type 3), P3H1-related	AR	P3H1	610915		In OMIM OI type VIII
NOS 26–0140	Osteogenesis imperfecta, progressively deforming (Sillence type 3), PPIB-related	AR	PPIB	see 259440		In OMIM OI type IX
NOS 26–0150	Osteogenesis imperfecta, progressively deforming (Sillence type 3), SERPINH1-related	AR	SERPINH1	613848		In OMIM OI type X
NOS 26–0160	Osteogenesis imperfecta, progressively deforming (Sillence type 3), FKBP10-related	AR	FKBP10	610968		In OMIM OI type XI
NOS 26–0170	Osteogenesis imperfecta, progressively deforming (Sillence type 3), TMEM38B-related	AR	TMEM38B	615066		In OMIM OI type XIV
NOS 26–0180	Osteogenesis imperfecta, progressively deforming (Sillence type 3), BMP1-related	AR	BMP1	614856		In OMIM OI type XIII
NOS 26–0190	Osteogenesis imperfecta, progressively deforming (Sillence type 3), WNT1-related	AR	WNT1	615220		In OMIM as OI type XV. Biallelic variants; monoallelic variants may result in AD osteoporosis.
NOS 26–0200	Osteogenesis imperfecta, progressively deforming (Sillence type 3), CREB3L1-related	AR	CREB3L1	616229		In OMIM as OI type XVI. Has severe joint laxity and scoliosis, Ehlers-Danlos-like

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NOS 26–0210	Osteogenesis imperfecta, progressively deforming (Sillence type 3), SPARC-related	AR	SPARC	616507		In OMIM as OI type XVII
NOS 26–0220	Osteogenesis imperfecta, progressively deforming (Sillence type 3), TENT5A-related	AR	TENT5A	617952		In OMIM as OI type XVIII
NOS 26–0230	Osteogenesis imperfecta, progressively deforming (Sillence type 3), MBTPS2-related	XLR	MBTPS2	301014		In OMIM as OI type XIX
NOS 26–0240	Osteogenesis imperfecta, progressively deforming (Sillence type 3), MESD-related	AR	MESD	618644		In OMIM as OI type XX
NOS 26–0250	Osteogenesis imperfecta, progressively deforming (Sillence type 3) with neurodevelopmental features, KDELR2-related	AR	KDELR2	619131		In OMIM as OI type XXI. Frequency of neurodevelopmental delay not clear yet.
NOS 26–0260	Osteogenesis imperfecta, progressively deforming (Sillence type 3), CCD134-related	AR	CCD134	619795		In OMIM as OI typeXXII
NOS 26–0270	Osteogenesis imperfecta, moderate form (Sillence type 4), COL1A1-related	AD	COL1A1	166220		In OMIM as OI type IV
NOS 26–0280	Osteogenesis imperfecta, moderate form (Sillence type 4), COL1A2-related	AD	COL1A2	166220		In OMIM as OI type IV
NOS 26–0290	Osteogenesis imperfecta, moderate form (Sillence type 4), WNT1-related	AR	WNT1	see 166220		In OMIM as OI type XV
NOS 26–0300	Osteogenesis imperfecta, moderate form (Sillence type 4), IFITM5-related	AD	IFITM5	166220		in OMIM OI type IV
NOS 26–0310	Osteogenesis imperfecta, moderate form (Sillence type 4), CRTAP-related	AR	CRTAP	see 610682		In OMIM as OI type VII
NOS 26–0320	Osteogenesis imperfecta, moderate form (Sillence type 4), PPIB-related	AD	PPIB	see 259440		In OMIM as OI type IX
NOS 26–0330	Osteogenesis imperfecta, moderate form (Sillence type 4), FKBP10-related	AR	FKBP10	see 610968		In OMIM as OI type XI
NOS 26–0340	Osteogenesis imperfecta, moderate form (Sillence type 4), SP7-related	AR	SP7	613849		In OMIM as OI type XII
NOS 26–0350	Osteogenesis imperfecta with calcification of interosseous membranes and/or hypertrophic callus (OI type 5), IFITM5-related	AD	IFITM5	610967		When calcification of intraosseous membranes or hypertrophic callus are not observed, may mimic progressively deforming or moderate OI (Sillence types 3 and 4)
NOS 26–0360	Osteogenesis imperfecta with craniosynostosis (Cole-Carpenter syndrome), P4HB-related	AD	P4HB	112240		Craniosynostosis is not well documented in this condition in spite of the name.
NOS 26–0370	Osteogenesis imperfecta with craniosynostosis (Cole-Carpenter syndrome), SEC24D-related	AR	SEC24D	616294		Was Cole-Carpenter syndrome 2. Possibly misnomer, as most patients do not have craniosynostosis but rather large fontanels.

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NOS 26–0380	Osteoporosis – X-linked form, PLS3-related	XL	PLS3	300910		
NOS 26–0390	Osteoporosis – X-linked form, MBPTS2-related	XL	MBTPS2	301014		In OMIM as OI type XIX; gene also associated with MIM 300918, MIM308205, MIM 308800
NOS 26–0400	Osteoporosis – dominant form, WNT1-related	AD	WNT1	615220		OMIM OI type XV
NOS 26–0410	Osteoporosis – AD form, LRP5-related	AD	LRP5	166710, 601884		Monoallelic variants; biallelic variants result in MIM 259770 osteoporosis-pseudoglioma (see below); this gene is also associated with hyperostotic forms (see below) as well as with MIM 601813 - exudative vitreoretinopathy, as well as MIM 617875 - polycystic liver disease
NOS 26–0420	Osteoporosis -AD form, ARHGAP25-related	AD	ARHGAP25	see 610587		
NOS 26–0430	Bruck syndrome type 1 (BS1), FKBP10-related	AR	FKBP10	259450		See autosomal recessive OI, above; intrafamilial variability between OI type 3, arthrogryposis and Bruck syndrome 1 is documented
NOS 26–0440	Bruck syndrome type 2 (BS2), PLOD2-related	AR	PLOD2	609220		
NOS 26–0450	Osteoporosis-pseudoglioma syndrome, LRP5-related	AR	LRP5	259770		When eye involvement is absent, may mimic progressively deforming or moderate OI (Sillence types 3 and 4)
NOS 26–0460	Bone fragility with calvarial “doughnut” lesions, SGSM2-related	AD	SGMS2	126550		Overlap with a spondylo-metaphyseal dysplasia phenotype
NOS 26–0470	Spondylo-ocular dysplasia, XYLT2-related	AR	XYLT2	605822		
NOS 26–0480	Gnathodiaphyseal dysplasia, ANO5-related	AD	ANO5	166260		Gene also associated with OMIM 613319-Miyoshi muscular dystrophy 3, and OMIM 611307-recessive limb-girdle muscular dystrophy 12
NOS 26–0490	Osteoporosis with developmental delay and microcephaly, COPB2-related	AD	COPB2	619884		Clinically variable, microcephaly in some cases only
NOS 26–0500	Geroderma osteodysplasticum, GORAB-related	AR	GORAB	231070		
NOS 26–0510	Cutis laxa, PYCR1-related	AR	PYCR1	612940		Autosomal recessive form, type 2B (ARCL2B). Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum
NOS 26–0520	Cutis laxa, ATP6V0A2-related	AR	ATP6V0A2	278250, 219200		Autosomal recessive form, type 2A (ARCL2A); wrinkly skin syndrome. Skeletal features overlapping with progeroid EDS and geroderma osteodysplasticum
NOS 26–0530	Wiedemann-Rautenstrauch syndrome, POLR3A-related	AR	POLR3A	264090		Gene also associated with MIM 607694-Leukodystrophy, hypomyelinating, with or without oligodontia and/or hypogonadotropic hypogonadism

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NOS 26–0540	Singleton-Merten dysplasia, IFIH-related	AD	IFIH1	182250		Gene also associated with MIM 615846-Aicardi-Goutieres syndrome 7, and OMIM 619773-Immunodeficiency 95
NOS 26–0550	Singleton-Merten dysplasia, DDX58-related	AD	DDX58	616298		
	Note: some of the recently discovered OI variants are limited to very small numbers of patients, so the association with OI "Sillence type 3" is tentative and may be too restrictive as more severe or milder phenotypes will emerge in the future. See also: Short stature, skeletal dysplasia, liver failure, optic nerve atrophy and Pelger-Huet anomaly, *NBAS*-related, above (Group 13); as well as all the Loeys-Dietz syndrome variants and the Snyder-Robinson syndrome, *SMS*-related, in Group 31.					
Group 27	**Disorders of bone mineralisation**					
NOS 27–0010	Hypophosphatasia, ALPL-related, recessive (biallelic) forms	AR	ALPL	241500		Includes perinatal, infantile and juvenile forms
NOS 27–0020	Hypophosphatasia, ALPL-related, dominant (monoallelic) form	AD	ALPL	146300		Includes juvenile and adult forms as well as odontohypophosphatasia
NOS 27–0030	Hypophosphatemic rickets, PHEX-related	XL	PHEX	307800		X-linked, most common form
NOS 27–0040	Hypophosphatemic rickets, FGF23-related	AD	FGF23	193100		Autosomal dominant
NOS 27–0050	Hypophosphatemic rickets, DMP1-related	AR	DMP1	241520		Autosomal recessive (ARHR1)
NOS 27–0060	Hypophosphatemic rickets, ENPP1-related	AR	ENPP1	613312		Autosomal recessive (ARHR2)
NOS 27–0070	Hypophosphatemic rickets, SGK3-related	AD	SGK3	see 607591		Autosomal dominant
NOS 27–0080	Hypophosphatemic rickets with hypercalciuria, CLCN5-related	XL	CLCN5	300554		X-linked; part of Dent's disease complex (progressive proximal renal tubulopathy with hypercalciuria, low molecular weight proteinuria, and nephrocalcinosis; MIM 300009)
NOS 27–0090	Hypophosphatemic rickets with hypercalciuria, SLC34A3-related	AR	SLC34A3	241530		Autosomal recessive (HHRH)
NOS 27–0100	Vitamin D-dependent rickets, CYP27B1-related	AR	CYP27B1	264700		Formerly type 1A
NOS 27–0110	Vitamin D-dependent rickets, CYP2R1-related	AR	CYP2R1	600081		Formerly type 1B
NOS 27–0120	Vitamin D-dependent rickets, VDR-related	AR	VDR	277440		Formerly type 2A
NOS 27–0130	Vitamin D-dependent rickets, CYP3A4-related	AD	CYP3A4	619073		Formerly type 3; specific monoallelic variants that increase enzyme activity leading to rapid degradation of active Vitamin D
NOS 27–0140	Vitamin D-dependent rickets, HNRNPC-related	AD?	HNRNPC	see 164020		Formerly type 2B; molecular basis (supposed HNRNPC dominant negative) from a single patient

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NOS 27–0150	Familial hyperparathyroidism, CDC73-related	AD	CDC73	145000, 145001		With or without jaw tumors
NOS 27–0160	Familial hyperparathyroidism linked to chromosome 2	AD	2p14-p13.3	610071		Linkage studies; no gene identified
NOS 27–0170	Familial hyperparathyroidism, GCM2-related	AD	GCM2	617343		Variants in this gene also cause familial isolated hypoparathyroidism (MIM 618883)
NOS 27–0180	Neonatal hyperparathyroidism, CASR-related	AR, AD	CASR	239200		“Severe” form (but see below, transient form also CASR-related). Variants in the *CASR* gene can also result in autosomal dominant hypocalcemia (MIM 601198)
NOS 27–0190	Neonatal hyperparathyroidism, TRPV6-related	AR	TRPV6	618188		Transient form
NOS 27–0200	Familial hypocalciuric hypercalcemia with transient neonatal hyperparathyroidism, CASR-related	AD	CASR	145980		Other forms of familial hypocalciuric hypercalcemia do not show significant skeletal phenotypes
NOS 27–0210	Calcium pyrophosphate deposition disease (familial chondrocalcinosis), ANKH-related	AD	ANKH	118600		Loss-of-function variants (see als craniometaphyseal dysplasia, dominant type)
NOS 27–0220	Calcium pyrophosphate deposition disease (familial chondrocalcinosis), TNFRSF11B-related	AD	TNFRSF11B	see 602643		Apparently monoallelic gain-of-function variants
NOS 27–0230	Cutaneous skeletal hypophosphatemia syndrome	MOS	HRAS			Somatic mosaicism for activating variants in *HRAS* with elevated FGF23 levels
NOS 27–0240	Cutaneous skeletal hypophosphatemia syndrome	MOS	NRAS			Somatic mosaicism for activating variants in *NRAS* with elevated FGF23 levels
	Note: Hyperparathyroidism due to parathyroid adenoma occurs in a number of genetic disorders, e.g. in Multiple Endocrine Neoplasias (see MIM for variants) - See also Group 28, below, as well as Raine dysplasia, *FAM20C*-related					
Group 28	**Skeletal disorders of parathyroid hormone signaling cascade**					
NOS 28–0010	Metaphyseal dysplasia, Jansen type, PTHR1-related	AD	PTHR1	156400		Caused by activating variants
NOS 28–0020	Metaphyseal dysplasia, Csukasi-Krakow type, SIK3-related	AR	SIK3	618162		disruption of mTOR signalling downstream of the PTH receptor
NOS 28–0030	Blomstrand dysplasia, PTHR1-related	AR	PTHR1	215045		Caused by recessive (biallelic) loss-of-function variants
NOS 28–0040	Eiken dysplasia, PTHR1-related	AR	PTHR1	600002		Caused by recessive (biallelic) hypomorphic variants
NOS 28–0050	Brachydactyly, PTHLH-related (brachdactyly type E2)	AD	PTHLH	613382		Haploinsufficiency; with or without short stature
NOS 28–0060	Osteolysis, PTHLH-related	AD	PTHLH			Duplications of *PTHLH* causing acro-osteolysis; see also group 30 and group 18

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	Note: see also Acrodysostosis, *PDE4D*-related and *PRKAR1A*-related, above; and Albright hereditary osteodystrophy, *GNAS*-related. Monoallelic loss-of-function variants in *PTHR1* lead to primary failure of tooth eruption (MIM 125350)					
Group 29	**Osteolysis group**					
NOS 29–0010	Familial expansile osteolysis, TNFRSF11A-related	AD	TNFRSF11A	174810, 602080		Includes early-onset familial Paget disease of bone. See other *TNFRSF11A*-related phenoytpes in Group 24
NOS 29–0020	Mandibuloacral dysplasia, LMNA-related	AR	LMNA	248370		See also Progeria (in this group), *LMNA*-related cardiomyopathy and brachydactyly (Group 19) as well as many other conditions in MIM related to *LMNA*
NOS 29–0030	Mandibuloacral dysplasia, ZMPSTE24-related	AR	ZMPSTE24	608612		
NOS 29–0040	Mandiculoacral dysplasia, MTX2-related	AR	MTX2	619127		
NOS 29–0050	Progeria, Hutchinson-Gilford type, LMNA-related	AD	LMNA	176670		
NOS 29–0060	Multicentric osteolysis, nodulosis and arthropathy (MONA), MMP2-related	AR	MMP2	259600		Includes Winchester-Torg syndrome and nodulosis-arthropathy-osteolysis syndrome
NOS 29–0070	Multicentric osteolysis, nodulosis and arthropathy (MONA), MMP14-related	AR	MMP14	277950		A biallelic homozygous *MMP14* variant seen in the original Winchester syndrome family
NOS 29–0080	Hajdu-Cheney syndrome, NOTCH2-related	AD	NOTCH2	102500		Includes the Serpentine fibula-polycystic kidney syndrome (SFPKS)
NOS 29–0090	Multicentric carpal-tarsal osteolysis with and without nephropathy, MAFB-related	AD	MAFB	166300		
NOS 29–0100	Penttinen syndrome, PDGFRB-related	AD	PDGFRB	601812		See also MIM 601812-Kosaki overgrowth syndrome
NOS 29–0110	Nestor Guillermo progeria syndrome, BANF1-related	AR	BANF1	603811		
NOS 29–0120	Farber disease, ASAH1-related	AR	ASAH1			The chronic, adult form of Farber disease can present as osteolysis
	Note: several neurologic conditions may cause acroosteolysis. See also Osteolysis, *PTHLH*-related (above), Pyknodysostosis, *CTSK*-related; cleidocranial dysplasia, *RUNX2*-related; Keutel syndrome, *MGP*-related; Singleton-Merten dysplasia, *IFIH*-related; and Singleton-Merten dysplasia, *DDX58*-related					
Group 30	**Disorganized development of skeletal components group**					
NOS 30–0010	Multiple cartilaginous exostoses (MCE), EXT1-related (multiple osteochondromas, MO)	AD	EXT1	133700		

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NOS 30–0020	Multiple cartilaginous exostoses (MCE), EXT2-related (multiple osteochondromas, MO)	AD	EXT2	133700		
NOS 30–0030	Cherubism, SH3BP2-related	AD	SH3BP2	118400		
NOS 30–0040	Fibrous dysplasia, polyostotic form (McCune-Albright syndrome), GNAS-related	MOS	GNAS	174800		Somatic mosaicism for gain-of-function variants; includes Mazabraud syndrome with intramuscular myxomas
NOS 30–0050	Progressive osseous heteroplasia (POH), GNAS-related	AD	GNAS	166350		Germline loss-of-function of paternal allele
NOS 30–0060	Metachondromatosis, PTPN11-related	AD	PTPN11	156250		Loss-of-function variants (in contrast to Noonan syndrome) with loss of heterozygosity in lesional tissue
NOS 30–0070	Osteoglophonic dysplasia, FGFR1-related	AD	FGFR1	166250		Craniosynostosis is also an important feature (group 34)
NOS 30–0080	Fibrodysplasia ossificans progressiva (FOP), ACVR1-related	AD	ACVR1	135100		Most cases sporadic but dominant transmission documented
NOS 30–0090	Neurofibromatosis type 1, NF1-related	AD	NF1	162200		
NOS 30–0100	Cherubism with gingival fibromatosis (Ramon syndrome)	AR		266270		Some similarities to primary intraosseous vascular malformation, ELMO2-related (see below)
NOS 30–0110	Dysplasia epiphysealis hemimelica (Trevor)	SP		127800		Some familial cases reported (“familial Trevor disease”) but probably represent a different condition
NOS 30–0120	Lipomembraneous osteodystrophy with leukoencephalopathy, TREM2-related (Nasu-Hakola)	AR	TREM2	618193		Also known as presenile dementia with bone cysts
NOS 30–0130	Lipomembraneous osteodystrophy with leukoencephalopathy, TYROBP-related (Nasu-Hakola)	AR	TYROBP	221770		Also known as presenile dementia with bone cysts
NOS 30–0140	Enchondromatosis, IDH1-related (Ollier disease)	MOS	IDH1	166000		Somatic mosaicism for specific *IDH1* variants. See also MIM 147700 and 137800
NOS 30–0150	Enchondromatosis, IDH2-related (Ollier disease)	MOS	IDH2	166000		Somatic mosaicism for *IDH2* variants; significantly rarer than IDH1 variants. See also MIM 147650 and 613657, D-2-hydroxyglutaric aciduria 2
NOS 30–0160	Enchondromatosis with hemangiomas, IDH1-related (Maffucci disease)	MOS	IDH1	614569		Somatic mosaicism for specific IDH1 variants. See also MIM 147700 and 137800
NOS 30–0170	Enchondromatosis with hemangiomas, IDH2-related (Maffucci disease)	MOS	IDH2	614569		Somatic mosaicism for IDH2 variants; significantly rarer than IDH1 variants. See also MIM 147650 and 613657, D-2-hydroxyglutaric aciduria 2
NOS 30–0180	Metaphyseal chondromatosis with D-2-hydroxyglutaric aciduria, IDH1-related	MOS	IDH1	614875		Includes so-called cheirospondyloenchondromatosis. Somatic mosaicism for *IDH1* variants. Possibly also *IDH2* variants but not yet well documented
NOS 30–0190	Primary intraosseous vascular malformation, ELMO2-related	AR	ELMO2	606893		

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NOS 30–0200	Osteofibrous dysplasia, MET-related	AD, SP	MET	607278		Possibly corresponding to the former “Campanacci dysplasia”
NOS 30–0210	Genochondromatosis	AD		137360		“Geno” from Greek “knee”, but upper limbs also affected. Probably includes the condition known as Vaandrager-Peña syndrome
NOS 30–0220	Gorham-Stout disease and familial diffuse angiomatosis of bone	SP (MOS?), AD		see 123880		Gorham-Stout is often severe and mostly sporadic. Somatic *KRAS* variants have been found in rare cases. In contrast, milder cases may be familial (“familial diffuse cystic angiomatosis of bone”; see OMIM 123880).
	Note: *PTEN*-related disorders are not included because the overgrowth is restricted to macrocephaly.- See also: Proteus syndrome, *AKT1*-related; Spondyloenchondrodysplasia with immune dysregulation (SPENCD), *ACP5*-related; Spondyloepimetaphyseal dysplasia, *COL2A1*-related (“SED with marked metaphyseal changes”, including dysspondyloenchondromatosis); Cutaneous skeletal hypophosphatemia syndrome, *HRAS*- related and *NRAS*-related. Some patients with *SOX6* variants have osteochondromas.					
Group 31	**Overgrowth (tall stature) syndromes and segmental overgrowth**					
NOS 31–0010	Marfan syndrome, FBN1-related	AD	FBN1	154700		See also as differential diagnosis: homocystinuria and marfanoid habitus with ID (Lujan Fryns syndrome): *MED12*; *ZDHHC9*; *UPF3B*
NOS 31–0020	Congenital contractural arachnodactyly (Beals-Hecht syndrome), FBN2-related	AD	FBN2	121050		
NOS 31–0030	Loeys-Dietz syndrome, TGFBR1-related	AD	TGFBR1	609192		Osteopenia with propensity to fractures may be observed in all variants of the Loeys-Dietz syndrome
NOS 31–0040	Loeys-Dietz syndrome, TGFBR2-related	AD	TGFBR2	610168		
NOS 31–0050	Loeys-Dietz syndrome, TGFB2-related	AD	TGFB2	614816		
NOS 31–0060	Loeys-Dietz syndrome, TGFB3-related	AD	TGFB3	615582		
NOS 31–0070	Loeys-Dietz syndrome, SMAD2-related	AD	SMAD2	619656		
NOS 31–0080	Loeys-Dietz syndrome, SMAD3-related	AD	SMAD3	613795		
NOS 31–0090	Weaver syndrome, EZH2-related	AD	EZH2	277590		Some cases reported with *NSD1*, *EED* and *SUZ12* variants
NOS 31–0100	Cohen-Gibson (Weaver-like) syndrome, EED-related	AD	EED	617561		

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NOS 31–0110	Imagawa-Matsumoto (Weaver like) syndrome, SUZ12-related	AD	SUZ12	606245		
NOS 31–0120	Sotos syndrome, NSD1-related	AD	NSD1	117550		
NOS 31–0130	Sotos syndrome, APC2-related	AR	APC2	617169		
NOS 31–0140	Malan (Sotos-like) syndrome, NFIX-related	AD	NFIX	614753		
NOS 31–0150	Luscan-Lumish syndrome, SETD2-related	AD	SETD2	616831		
NOS 31–0160	Tatton-Brown-Rahman syndrome, DNMT3A-related	AD	DNMT3A	615879		
NOS 31–0170	Marshall-Smith syndrome, NFIX-related	AD	NFIX	602535		See also Malan syndrome. The localization of the monoallelic variants determine the Malan vs. Marshall-Smith phenotype
NOS 31–0180	Beckwith-Wiedemann syndrome	AD	11p15.5 region	130650		Variant or deletion of imprinted genes within the chromosome 11p15.5 region
NOS 31–0190	Simpson-Golabi-Behmel syndrome, GPC3-related	XL	GPC3	312870		
NOS 31–0200	Proteus syndrome, AKT1-related	MOS	AKT1	176920		
NOS 31–0210	Hypoinsulinemic hypoglycemia with hemihypertrophy (HIHGHH), AKT2-related	AD	AKT2			Gene also associated with OMIM 125853 diabetes mellitus type II
NOS 31–0220	Congenital ipomatous overgrowth, vascular Malformations, epidermal Nevi, spinal/skeletal anomalies/scoliosis (CLOVES) syndrome, PIK3CA-related	MOS	PIK3CA	612918		Also named PIK3CA-related overgrowth syndrome (PROS); somatic variants; see MIM 171834
NOS 31–0230	Fibroadipose hyperplasia, PIK3CA-related	MOS	PIK3CA	see 171834		See MIM 171834 for the many conditions associated with somatic *PIK3CA* variants
NOS 31–0240	Snyder-Robinson syndrome (intellectual disability, tall stature, osteoporosis and fractures), SMS-related	XLR	SMS	309583		
NOS 31–0250	Overgrowth syndrome with 2q37 translocations	SP	NPPC	see 600296		Overgrowth probably caused by overexpression of *NPPC*
NOS 31–0260	Tall stature with long halluces, NPR2-related	AD	NPR2	615923		Monoallelic gain-of-function variants in *NPR2*; in OMIM as epiphyseal chondrodysplasia, Miura type
NOS 31–0270	Tall stature with long halluces, NPR3-related	AR	NPR3	619543		Biallelic loss-of-function variants in *NPR3*; in OMIM as Boudin-Mortier syndrome
NOS 31–0280	Moreno-Nishimura-Schmidt syndrome	SP		608811		
NOS 31–0290	Camptodactyly, tall stature and hearing loss syndrome (CATSHL), FGFR3-related	AD, AR	FGFR3	610474		Original family with monoallelic (dominant negative?) variant; a second family with biallelic variants (see group 1)
NOS 31–0300	Kosaki overgrowth syndrome, PDGFRB-related	AR	PDGFRB	616592		See also MIM 601812-Pentinnen syndrome

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NOS 31–0310	Segmental odontomaxillary dysplasia, ACTB-related	MOS	ACTB	see 102630		See PMID 32585735; see also MIM 243310-Baraitser-Winter syndrome
	See also: Shprintzen-Goldberg syndrome, *SKI*-related, in the craniosynostosis group. Note: this category does not include disorders that cause overgrowth secondary to vascular malformations.					
Group 32	**Genetic inflammatory or rheumatoid-like osteoarthropathies**					
NOS 32–0010	Progressive pseudorheumatoid dysplasia (PPRD), WISP3-related	AR	WISP3	208230		Also known as SED with progressive arthropathy
NOS 32–0020	Chronic infantile neurologic cutaneous articular syndrome (CINCA), CIAS1-related (neonatal onset multisystem inflammatory disease (NOMID))	AD	CIAS1	607115		
NOS 32–0030	Sterile multifocal osteomyelitis, periostitis, and pustulosis (CINCA/NOMID-like), IL1RN-related	AR	IL1RN	147679		
NOS 32–0040	Chronic recurrent multifocal osteomyelitis with congenital dyserythropoietic anemia (CRMO with CDA; Majeed syndrome), LPIN2-related	AR	LPIN2	609628		
NOS 32–0050	Familial juvenile arthritis with hyaluronidase deficiency, HYAL1-related	AR	HYAL1	601492		Also known as mucopolysaccharidosis type 9, although clinically no storage
NOS 32–0060	Hyaline Fibromatosis Syndrome, ANTXR2-related	AR	ANTXR2	236490, 228600		Previously known as Infantile systemic hyalinosis, Juvenile Hyaline Fibromatosis, and Puretic syndrome
	Farber disease, *ASAH1*-related (osteolysis group 29, and MIM 228000) shows phenotypic overlap with the conditions in this group.					
Group 33	**Cleidocranial dysplasia and related disorders**					
NOS 33–0010	Cleidocranial dysplasia, RUNX2-related	AD	RUNX2	119600		See also MIM 156510-metaphyseal dysplasia with maxillary hypoplasia, as well as non-syndromic midline craniosynostosis, RUNX2-related, below
NOS 33–0020	Cleidocranial-like dysplasia, CBFB-related	AD	CBFB	see 121360		See also MIM 601626, familial leukemia
NOS 33–0030	CDAGS syndrome (craniosynostosis, delayed fontanel closure, parietal foramina, imperforate anus, genital anomalies, skin eruption), RNU12-related	AR	RNU12	603116		
NOS 33–0040	Yunis-Varon dysplasia, FIG4-related	AR	FIG4	216340		Gene also causes OMIM 612577 amyotrophic lateral sclerosis 11, and OMIM 611228 CMT disease 4J

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NOS 33–0050	Yunis-Varon dysplasia, VAC14-related	AR	VAC14			Only one case of VAC14-related Yunis-Varon reported so far, so association needs to be confirmed. Gene also associated with OMIM 617054 Striatonigral degeneration, childhood-onset (several patients reported)
NOS 33–0060	Parietal foramina, MSX2-related	AD	MSX2	168500		
NOS 33–0070	Parietal foramina, ALX4-related	AD	ALX4	609597		See also Frontonasal dysplasia type 1
NOS 33–0080	Parietal foramina with cleidocranial dysplasia, MSX2-related	AD	MSX2	168550		*MSX2* variants also cause craniosynostosis Boston type
	See also: Pyknodysostosis, *CTSK*-related; Cutis laxa, *ATP6V0A2*-related; Mandibuloacral dysplasia, *LMNA*-related; Progeria, Hutchinson-Gilford type, *LMNA*-related; and Hajdu-Cheney syndrome, *NOTCH2*-related, for similar clavicular defects or osteolysis. See also Crane-Heise syndrome (MIM 218090), the nosologic status of which remains unclear.					
Group 34	**Syndromes featuring craniosynostosis**					
NOS 34–0010	Pfeiffer syndrome, FGFR1-related	AD	FGFR1	101600		Most have *FGFR1* p.P252R variant; Includes Jackson-Weiss syndrome (MIM 123150)
NOS 34–0020	Pfeiffer syndrome, FGFR2-related	AD	FGFR2	101600		
NOS 34–0030	Apert syndrome, FGFR2-related	AD	FGFR2	101200		
NOS 34–0040	Craniosynostosis with cutis gyrata (Beare-Stevenson), FGFR2-related	AD	FGFR2	123790		Notably p.S372Y or p.Y375C variants
NOS 34–0050	Crouzon syndrome, FGFR2-related	AD	FGFR2	123500		
NOS 34–0060	Crouzon-like craniosynostosis with acanthosis nigricans, FGFR3-related	AD	FGFR3	612247		Defined by specific *FGFR3* p.A391E variant; also known as Crouzonodermoskeletal syndrome
NOS 34–0070	Craniosynostosis, Muenke type, FGFR3-related	AD	FGFR3	602849		Defined by specific *FGFR3* p.P250R variant
NOS 34–0080	Antley-Bixler syndrome, POR-related	AR	POR	201750		
NOS 34–0090	Craniosynostosis Boston type, MSX2-related	AD	MSX2	604757		Heterozygous p.P148H variant in a two families
NOS 34–0100	Saethre-Chotzen syndrome, TWIST1-related	AD	TWIST1	101400		Variants in *FGFR3*, *FGFR2* and *TCF12* have been reported to cause phenotypes resembling Saethre-Chotzen syndrome
NOS 34–0110	Shprintzen-Goldberg syndrome, SKI-related	AD	SKI	182212		
NOS 34–0120	Baller-Gerold syndrome, RECQL4-related	AR	RECQL4	218600		see other phenotypes associated with RECQL4 variants, above
NOS 34–0130	Carpenter syndrome, RAB23-related	AR	RAB23	201000		

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NOS 34–0140	Carpenter syndrome, MEGF8-related	AR	MEGF8	614976		
NOS 34–0150	Craniosynostosis, TCF12-related	AD	TCF12	615314		Frequently coronal craniosynostosis
NOS 34–0160	Craniosynostosis, SIX1-related	AD	SIX1	see 601205		Frequently sagittal and lambdoid synostosis. See also MIM 608389 - Branchiootic syndrome 3, and 605192-Deafness, autosomal dominant 23, for other SIX1-related phenotypes
NOS 34–0170	Complex craniosynostosis, ERF-related	AD	ERF	600775		Variants in *ERF* also cause Chitayat hyperphalangism syndrome (Group 19)
NOS 34–0180	Non-syndromic midline (metopic / sagittal) craniosynostosis, SMAD6-related	AD?	SMAD6	617439		Rare *SMAD6* variants and a common *BMP2* polymorphism may interact to produce craniosynostosis; subject disputed
NOS 34–0190	Non-syndromic midline craniosynostosis, RUNX2-related	AD	RUNX2			Gain-of-function variants, duplications, triplications
NOS 34–0200	Structural brain anomalies with impaired ID and craniosynostosis / craniosynostosis type 6	AD	ZIC1	618736		
NOS 34–0210	Craniosynostosis and dental anomalies (CRSDA), IL11RA-related	AR	IL11RA	614188		
NOS 34–0220	Craniosynostosis, retained deciduous teeth and intellectual disability, IL6ST-related	AR	IL6ST	see 600694		Single case reported, with preserved LIF signaling. See Stüve-Wiedemann syndrome, *IL6ST*-related (above, group 24) as well as *IL6ST*-MIM 600694 for other phenotypes associated with *IL6ST*
NOS 34–0230	Cutis laxa with craniosynostosis, short stature, brachydactyly, and syndactyly, LTBP1-related	AR	LTBP1	619451		
NOS 34–0240	Bohring-Opitz syndrome, ASXL1-related	AD	ASXL1	605039		
NOS 34–0250	Craniosynostosis, radiohumeral fusion and other skeletal defects, CYP26B1-related	AR	CYP26B1	614416		*CYP26B1* is a retinoid acid-degrading enzyme, pathogenesis involves retinoic acid-associated morphogenesis
NOS 34–0260	Cardiac, facial and digital anomalies with developmental delay (CAFDADD), TRAF7-related	AD	TRAF7	618164		Multisuture craniosynostosis is one of the features
NOS 34–0270	Craniosynostosis, hypertrichosis, progeroid appearance, bone dysplasia, characteristic face (Fontaine progeroid syndrome, Gorlin-Chaudhry-Moss syndrome), SLC25A24-related	AD	SLC25A24	612289		
NOS 34–0280	Curry-Jones syndrome, SMO-related	MOS	SMO	601707		Activating variant c.1234C>T (p.L412F)
NOS 34–0290	3MC syndrome, MASP1-related	AR	MASP1	257920		Craniosynostosis in 20–30%
NOS 34–0300	3MC syndrome, COLEC11-related	AR	COLEC11	265050		Craniosynostosis in 20–30%
NOS 34–0310	3MC syndrome, COLEC10-related	AR	COLEC10	248340		Craniosynostosis in 20–30%

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NOS 34–0320	Weiss-Kruszka syndrome, ZNF462-related	AD	ZNF462	618619		Metopic ridging or CSO (metopic, lambdoid, 9/24)
NOS 34–0330	Au-Kline syndrome, HNRNPK-related	AD	HNRNPK	616580		Craniosynostosis and vertebral anomalies in a significant proportion of cases
NOS 34–0340	Char syndrome, TFAP2B-related	AD	TFAP2B	169100		Mainly with loss-of-function variants
NOS 34–0350	Syndrome with developmental and speech delay, dysmorphic facies, craniosynostosis and T-cell abnormalities	AD	BCL11B	618092		Craniosynostosis in some affected individuals
	Craniosynostosis is not rare and may have a non-genetic pathogenesis in many cases. It can also occur secondarily in any form of rickets. Conditions in which craniosynostosis is an occasional feature have not been included. - See also: cranioectodermal dysplasia (several types in the ciliopathy group); SEMD, *RSPRY1*-related; osteocraniostenosis, *FAM111A*-related; Osteogenesis imperfecta with craniosynostosis (Cole-Carpenter syndrome), *P4HB*-related; CDAGS syndrome, *RNU12*-related; syndactyly (Lueken type, with or without craniosynostosis), *IHH*-related; and Multiple synostoses syndrome, *FGF9*-related. Craniosynostosis can also be present in Loeys-Dietz syndromes, Meier-Gorlin syndrome, *CDC45*-related and *GINS2*-related; Hypophosphatasia, *ALPL*-related; Hypophosphatemic rickets, *PHEX*-related; Greig cephalopolysyndactyly syndrome, GLI3-related; and others.					
Group 35	**Craniofacial Dysostoses**					
NOS 35–0010	Mandibulofacial dysostosis, TCOF1-related (Treacher-Collins, Franceschetti-Klein)	AD	TCOF1	154500		
NOS 35–0020	Mandibulofacial dysostosis, POLR1B-related (Treacher-Collins, Franceschetti-Klein)	AD	POLR1B	618939		
NOS 35–0030	Mandibulofacial dysostosis, POLR1C-related (Treacher-Collins, Franceschetti-Klein)	AR	POLR1C	248390		
NOS 35–0040	Mandibulofacial dysostosis, POLR1D-related (Treacher-Collins, Franceschetti-Klein)	AD, AR	POLR1D	613717		
NOS 35–0050	Mandibulofacial dysostosis with limb deficiencies, POLR1A-related (Cincinnati type)	AD	POLR1A	616462		The original description was “acrofacial dysostosis: a mandibulofacial dysostosis with limb anomalies”. The limb anomalies are variable
NOS 35–0060	Mandibulofacial dysostosis with microcephaly, EFTUD2-related (Guion-Almeida type)	AD	EFTUD2	610536		
NOS 35–0070	Mandibulofacial dysostosis with alopecia, EDNRA-related	AD	EDNRA	616367		

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NOS 35–0080	Burns-McKeown syndrome, TXNL4A-related	AR	TXNL4A	608572		Some pathogenic variants are in the promoter region; severity is variable
NOS 35–0090	Postaxial acrofacial dysostosis, DHODH-related (Miller syndrome)	AR	DHODH	263750		
NOS 35–0100	Acrofacial dysostosis, SF3B4-related (Nager syndrome)	AD, AR	SF3B4	154400, 201170		Both monoallelic and biallelic variants are at the basis of a spectrum that also includes the former “Rodriguez type” of acrofacial dysostosis
NOS 35–0110	Agnathia-Otocephaly complex, PRRX1-related	AD, AR	PRRX1	202650		
NOS 35–0120	Frontonasal dysplasia, ALX3-related	AR	ALX3	136760		
NOS 35–0130	Frontonasal dysplasia, ALX4-related	AR	ALX4	613451		
NOS 35–0140	Frontonasal dysplasia, ALX1-related	AR	ALX1	613456		
NOS 35–0150	Frontonasal dysplasia, SIX2-related	AD	SIX2	see 604994		
NOS 35–0160	Frontonasal dysplasia with additional malformations (Sweeney-Cox syndrome), TWIST1-related	AD	TWIST1	617746		Results from specific amino acid substitutions in TWIST1
NOS 35–0170	Craniofrontonasal syndrome, EFN1B-related	XL	EFNB1	304110		
NOS 35–0180	Acromelic frontonasal dysostosis, ZSWIM6-related	AD	ZSWIM6	603671		
NOS 35–0190	Richieri-Costa-Pereira syndrome, EIF4A3-related	AR	EIF4A3	268305		
NOS 35–0200	Auriculocondylar syndrome, GNAI3-related (type 1)	AD	GNAI3	602483		
NOS 35–0210	Auriculocondylar syndrome, PLCB4-related (type 2)	AR, AD	PLCB4	614669		
NOS 35–0220	Auriculocondylar syndrome, EDN1-related (type 3)	AR	EDN1	615706		
NOS 35–0230	Orofaciodigital syndrome type I, OFD1-related	XL	OFD1	311200		
NOS 35–0240	Weyers acrofacial (acrodental) dysostosis, EVC1-related	AD	EVC1	193530		See also group 10
NOS 35–0250	Weyers acrofacial (acrodental) dysostosis, EVC2-related	AD	EVC2	193530		See also group 10
NOS 35–0260	Teebi hypertelorism syndrome, SPECCIL-related	AD	SPECC1L	145420		
NOS 35–0270	Craniolenticulosutural dysplasia, SEC23A-related	AR, AD	SEC23A	607812		Monoallelic and biallelic inheritance observed
NOS 35–0280	Faciogenital dysplasia, FGD1-related (Aarskog-Scott syndrome)	XL	FGD1	305400		
NOS 35–0290	Baraitser-Winter syndrome, ACTB-related	AD	ACTB	243310		
NOS 35–0300	Baraitser-Winter syndrome, ACTG1-related	AD	ACTG1	614583		
NOS 35–0310	Cerebrofaciothoracic dysplasia, TMCO1-related	AR	TMCO1	213980		
NOS 35–0320	Opitz GBBB syndrome, MID1-related	XL	MID1	300000		

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NOS 35–0330	Arhinia microphthalmia syndrome, SMCHD1-related (Bosma)	AD	SMCHD1	603457		
NOS 35–0340	Acrofrontofacionasal dysostosis	AR		201180		
NOS 35–0350	Hemifacial microsomia	SP, AD		164210		Includes Goldenhar syndrome and Oculo-Auriculo-Vertebral spectrum; genetically heterogeneous; SF3B2 haploinsufficiency identified in ~3% of sporadic and ~25% of familial cases; in some cases a microduplication on 14q23.1
	See also Orofaciodigital syndrome type 4 (Mohr-Majewski), *TCTN3*-related; Endocrine-cerebro-osteo dysplasia (ECO), *CILK1*-related; the Cerebro-Costo-Mandibular syndrome, SNRPB-related (group 36, below); and Robinow syndrome (see variants in group 15)					
Group 36	**Vertebral and costal dysostoses**					
NOS 36–0010	Currarino syndrome, MNX1-related	AD	MNX1	176450		Possible clinical o)verlap with caudal regression syndrome (see MIM 600145; the role of heterozygous variants in *VANGL1* remains to be confirmed)
NOS 36–0020	Spondylocostal dysostosis, DLL3-related	AR	DLL3	277300		Possible role of CNVs in *TBX6* in modulating the phenotype?
NOS 36–0030	Spondylocostal dysostosis, MESP2-related	AR	MESP2	608681		
NOS 36–0040	Spondylocostal dysostosis, LFNG-related	AR	LFNG	609813		
NOS 36–0050	Spondylocostal dysostosis, HES7-related	AR	HES7	613686		
NOS 36–0060	Spondylocostal dysostosis, TBX6-related	AR, AD	TBX6	122600		Possible role of CNVs in *TBX6*
NOS 36–0070	Spondylocostal dysostosis, RIPPLY2-related	AR	RIPPLY2	616566		
NOS 36–0080	Vertebral segmentation defect (congenital scoliosis) with variable penetrance, MESP2-related	AD	MESP2	608681		
NOS 36–0090	Vertebral segmentation defect (congenital scoliosis) with variable penetrance, HES7-related	AD	HES7	613686		
NOS 36–0100	Short stature, cervical segmentation defects, and developmental delay, CDK10-related	AR	CDK10	617694		
NOS 36–0110	Klippel-Feil syndrome, GDF6-related	AD	GDF6	118100		Role of *GDF6* variants in Klippel-Feil syndrome as well as in AD spondylothoracic dysostosis remains unclear
NOS 36–0120	Klippel-Feil syndrome, MEOX1-related	AR	MEOX1	214300		
NOS 36–0130	Klippel-Feil syndrome, GDF3-related	AD	GDF3	613702		

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NOS 36–0140	Klippel-Feil syndrome, MYO18B-related	AR	MYO18B	616549		
NOS 36–0150	Cervico-oculo-acoustic (Wildervanck) syndrome	SP		314600		Congenital perceptive deafness, Klippel-Feil anomaly (see 118100), and abducens palsy with retractio bulbi
NOS 36–0160	Cerebro-costo-mandibular syndrome (rib gap syndrome), SNRPB-related	AD	SNRPB	117650		
NOS 36–0170	Cerebro-costo-mandibular-like syndrome, COG1-related	AR	COG1	611209		Also known as CDG IIg
NOS 36–0180	Diaphanospondylodysostosis, BMPER-related	AR	BMPER	608022		Includes ischiospinal dysostosis, a term that has been used for milder cases
NOS 36–0190	Spondylo-megaepiphyseal-metaphyseal dysplasia (SMMD), NKX3–2-related	AR	NKX3–2	613330		
NOS 36–0200	NAD deficiency syndrome, HAAO-related	AR	HAAO	617660		With associated cardiac, limb and renal defects; VACTERL-like
NOS 36–0210	NAD deficiency syndrome, KYNU-related	AR	KYNU	617661		In some cases VACTERL-like
NOS 36–0220	NAD deficiency syndrome, NADSYN1-related	AR	NADSYN1	618845		In some cases VACTERL-like
NOS 36–0230	VATER/VACTERL association	SP		192350		
NOS 36–0240	VACTERL association with hydrocephalus (VACTERL-H), FANCB-related	XL	FANCB	300514		*FANCB*-related Fanconi anemia may present in hemizygous males with the VACTERL-hydrocephalus phenotype
NOS 36–0250	VACTERL association with hydrocephalus (VACTERL-H), ZIC3-related	XL	ZIC3	314390		
NOS 36–0260	Uniparental disomy, paternal, for chromosome 14 (UPD14; Kagami-Ogata syndrome)	SP	14q32?	608149		Imprinted genes at 14q32 may have a role in this complex phenotype with skeletal malformations such as “coat-hanger ribs”
	VACTERL is nowadays defined as a “Recurrent Constellation of Embryonic Malformations” (RCEM; see Adam et al, AJMG 2020) without a single genetic basis. It may be mimicked by NAD deficiency syndrome, Fanconi anemia and others. The diagnosis is supported by negative genetic analysis. - See also Spondylocarpotarsal synostosis syndrome, FLNB-related and RFLNA-related, Robinow syndrome (variants in group 15), and Cerebrofaciothoracic dysplasia, TMCO1-related (Group 35)					
Group 37	**Patellar dysostoses**					
NOS 37–0010	Ischiopatellar dysplasia (small patella syndrome), TBX4-related	AD	TBX4	147891		See MIM 601360 - posterior amelia for the biallelic phenotype
NOS 37–0020	Nail-patella syndrome, LMX1B-related	AD	LMX1B	161200		

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NOS 37–0030	Genitopatellar syndrome, KAT6B-related	AD	KAT6B	606170		
	See also Meier-Gorlin syndromes in the primordial dwarfism group (group 21), and the Pseudoachondroplasia/MED group (Group 9) for conditions with patellar changes; see also ischio-pubic-patellar dysplasia as mild expression of campomelic dysplasia, *SOX9*-related; RAPADILINO syndrome, *RECQL4*-related. Patellar hypoplasia is variably present in Clubfoot with or without deficiency of long bones and/or mirror-image polydactyly, *PITX1*-related.					
Group 38	**Limb hypoplasia – reduction defects group**					
NOS 38–0010	Ulnar-mammary syndrome, TBX3-related	AD	TBX3	181450		
NOS 38–0020	Holt-Oram syndrome, TBX5-related	AD	TBX5	142900		
NOS 38–0030	Holt-Oram/Ulnar Mammary blended phenotype	AD	TBX3, TBX5			CNVs involving both *TBX3* and *TBX5* may result in combined phenotype
NOS 38–0040	Posterior Amelia, TBX4-related	AR	TBX4	601360		See also ischiopatellar syndrome for the monoallelic TBX4-related phenotype
NOS 38–0050	Cornelia de Lange syndrome, NIPBL-related	AD	NIPBL	122470		
NOS 38–0060	Cornelia de Lange syndrome, SMC1A-related	XL	SMC1A	300590		
NOS 38–0070	Cornelia de Lange syndrome, SMC3-related	AD	SMC3	610759		
NOS 38–0080	Cornelia de Lange syndrome, RAD21-related	AD	RAD21	614701		
NOS 38–0090	Cornelia de Lange syndrome, HDAC8-related	XL	HDAC8	300882		
NOS 38–0100	Thrombocytopenia-absent radius (TAR) syndrome, RBM8A-related	AR	RBM8A	274000		Deletion and common SNP on other allele that has regulatory function
NOS 38–0110	Thrombocythemia with distal limb defects, THPO-related	AD	THPO	187950		Distal limb defects postulated as consequence of vascular occlusions
NOS 38–0120	Okihiro syndrome (Duane syndrome with radial ray anomaly), SALL4-related	AD	SALL4	607323		Includes IVIC syndrome
NOS 38–0130	Cousin syndrome, TBX15-related	AR	TBX15	260660		
NOS 38–0140	Roberts syndrome, ESCO2-related	AR	ESCO2	268300		
NOS 38–0150	Tibial hemimelia-polysyndactyly-triphalangeal thumb (Werner syndrome), ZRS-related	AD	ZRS	188740		Monoallelic variants in *ZRS*, a limb-specific enhancer of *SHH* that is located within intron 5 of the *LMBR1* gene
NOS 38–0160	Clubfoot with or without deficiency of long bones and/or mirror-image polydactyly, PITX1-related	AD	PITX1	119800		In some patients bilateral patellar hypoplasia (see group 37)

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NOS 38–0170	Acheiropodia, LMBR1-related	AR	LMBR1	200500		The Brazilian founder allele is deletion spanning exon 4 of *LMBR1* that probably affects the activity of *ZRS*, the limb-specific enhancer of *SHH*. In a further patient, biallelic deletion of exons 1 to 16 of *LMBR1*, including the *ZRS*
NOS 38–0180	Engrailed-1 related dorsoventral syndrome (ENDOVES), limb-brain type	AR	EN1	619218		One single patient with a biallelic frameshift variant described
NOS 38–0190	Engrailed-1 related dorsoventral syndrome (ENDOVES), limb-only type	AR	MAENLI	619217		*MAENLI* is a lncRNA regulating *EN1* expression
NOS 38–0200	Tetra-amelia, WNT3-related	AR	WNT3	273395		
NOS 38–0210	Tetra-amelia, RSPO2-related	AR	RSPO2	618021		
NOS 38–0220	Limb reduction syndrome, WNT7A-related	AR	WNT7A	276820, 228930		Includes former Al-Awadi Raas-Rothschild limb-pelvis hypoplasia-aplasia as well as Fuhrmann syndrome
NOS 38–0230	RAPADILINO syndrome, RECQL4-related	AR	RECQL4	266280		See also Baller-Gerold syndrome, *RECQL4*-related. See MIM 266280 for explanation of the RAPADILINO acronym
NOS 38–0240	Rothmund-Thompson syndrome, RECQL4-related	AR	RECQL4	268400		
NOS 38–0250	Rothmund-Thompson syndrome, ANAPC1-related	AR	ANAPC1	618625		
NOS 38–0260	Rothmund-Thompson syndrome, DNA2-related	AR	DNA2			
NOS 38–0270	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), ARHGAP31-related	AD	ARHGAP31	100300		
NOS 38–0280	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), DOCK6-related	AR	DOCK6	614219		
NOS 38–0290	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), RBPJ-related	AD	RBPJ	614814		
NOS 38–0300	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), DLL4-related	AR	DLL4	616589		
NOS 38–0310	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), EOGT-related	AD	EOGT	615297		
NOS 38–0320	Adams-Oliver syndrome (aplasia cutis congenita and transverse limb defects), NOTCH1-related	AD	NOTCH1	616028		
NOS 38–0330	B-cell immunodeficiency-limb anomaly-urogenital malformation syndrome (BILU syndrome), TOP2B-related	AD	TOP2B	609296		Also known as Hoffmann syndrome (see MIM 609296)
NOS 38–0340	Scapulo-iliac dysplasia (Kosenow syndrome)	AD		169550		
NOS 38–0350	Hypoglossia-hypodactylia (Hanhart syndrome)	SP		103300		

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NOS 38–0360	Poland syndrome	SP, AD		173800		Most commonly sporadic and probably non-genetic; some familial cases reported but no specific gene identified so far
NOS 38–0370	Femoral facial syndrome (FFS)	SP		134780		Some phenotypic overlap with FFU syndrome (below)
NOS 38–0380	Femur-fibula-ulna syndrome (FFU)	SP		228200		
NOS 38–0390	Fibular aplasia, tibial campomelia, and oligosyndactyly syndrome (FATCO)	SP		246570		
NOS 38–0400	Tibial hemimelia (isolated)	SP		275220		Possibly non-genetic etiology
NOS 38–0410	Sirenomelia	SP				Rare cases reported as associated with monoallelic *CDX2* variants with variable expressivity
NOS 38–0420	Fanconi anemia	*AR*	(several)	227650		The complex genetic basis of Fanconi anemia and its complementation groups and loci is acknowledged but not further listed in this Nosology; please refer to MIM or to specialized reviews
	There is overlap between this group and the split hand-foot malformation group. - *See also* Baller-Gerold syndrome, *RECQL4*-related; Congenital hemidysplasia, ichthyosis, limb defects (CHILD) syndrome, *NSDHL*-related; as well as the mesomelic and acromesomelic dysplasias groups (above). Some entities in this group (e.g. the Femoral-Facial syndrome and the Femur-fibula-ulna (FFU) syndromes) might be considered “” (RCEM; see the note to VACTERL in Group 36)					
Group 39	**Split hand/foot with and without other manifestations**					
NOS 39–0010	Ankyloblepharon-ectodermal dysplasia-cleft palate (AEC)	AD	TP63	106260		see other TP63-related disorders in this group (below)
NOS 39–0020	Ectrodactyly-ectodermal dysplasia cleft-palate syndrome Type 3 (EEC3)	AD	TP63	604292		
NOS 39–0030	Ectrodactyly-ectodermal dysplasia-macular dystrophy syndrome (EEM)	AR	CDH3	225280		
NOS 39–0040	Limb-mammary syndrome (including ADULT syndrome)	AD	TP63	603543		
NOS 39–0050	Split hand-foot malformation, isolated form, type 4 (SHFM4)	AD	TP63	605289		
NOS 39–0060	Split hand-foot malformation, isolated form, type 1 (SHFM1)	AD	DLX5	220600		Structural variations at locus; also regulatory variants affecting exons of *DYNC1I1* that regulate *DLX5*; association with deafness in a single family may be coincidental; a recessive *DLX5* syndrome may exist
NOS 39–0070	Split hand-foot malformation, isolated form, type 1 (SHFM1)	AD	DLX6	183600		

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Group number/ numer of disorder	**Name of Group / Name of Disorder**	**Inheritance**	***Gene or locus***	**MIM No.**		**Notes**
NOS 39–0080	Split hand-foot malformation, isolated form, type 3 (SHFM3)	AD	10q24	246560		Duplications at 10q24 encompassing *LBX1*, *BTRC*, *POLL*, *DPCD* and *FBXW4*
NOS 39–0090	Split hand-foot malformation, isolated form, type 6 (SHFM6)	AR	WNT10B	225300		
NOS 39–0100	Split-foot malformation with mesoaxial polydactyly (SFMMP)	AR	ZAK	616890		
NOS 39–0110	Split-hand-foot malformation with or without long bone deficiency (SHFLD), BHLHA9-related	AD	BHLHA9	612576		Duplications at 17p13.3 that include *BHLHA9*. Phenotypic penetrance is less than 50% and shows markedly variable expressivity; includes the so-called Gollop-Wolfgang complex
NOS 39–0120	Hartsfield syndrome, FGFR1-related	AD	FGFR1	615465		
NOS 39–0130	Split hand-foot malformation, EPS15L-related	AD	EPS15L1			Structural variants (deletions) at this locus; one consanguineous family with homozygous point variant in *EPS15L1* but inheritance still unclear
NOS 39–0140	Aplasia cutis congenita with ectrodactyly, UBA2-related	AD	UBA2			19q13.11 deletions may also cause this phenotype. In OMIM as “aplasia cutis congenita with ectrodactyly skeletal syndrome” (a redundant name)
NOS 39–0150	Focal dermal hypoplasia (Goltz Syndrome), PORCN-related	XLD	PORCN	305600		
Group 40	**Polydactyly-Syndactyly-Triphalangism group**					
NOS 40–0010	Preaxial polydactyly, SHH-related	AD	SHH	174400		Formerly preaxial polydactyly type 1 and type 2 (with triphalangeal thumb); regulatory domain variant or duplication of *ZRS* (limb enhancer of *SHH)*
NOS 40–0020	Preaxial polydactyly, GLI1-related	AR	GLI1	174400		
NOS 40–0030	Preaxial polydactyly, GLI3-related	AD	GLI3	174700		
NOS 40–0040	Preaxial polydactyly type 3 (PPD3)	AD		174600		
NOS 40–0050	Mirror-image polydactyly of hands and feet (Laurin-Sandrow syndrome), SHH-related	AD	SHH	135750		Duplication of *ZRS* (limb enhancer of *SHH*)
NOS 40–0060	Postaxial polydactyly, GLI1-related	AR	GLI1	618123		
NOS 40–0070	Greig cephalopolysyndactyly syndrome, GLI3-related	AD	GLI3	175700		
NOS 40–0080	Pallister-Hall syndrome, GLI3-related	AD	GLI3	146510		
NOS 40–0090	Hypothalamic hamartomas and polydactyly (Pallister-Hall-like) syndrome, SMO-related	AR	SMO	241800		
NOS 40–0100	Culler-Jones syndrome, GLI2-related	AD	GLI2	615849		Hypopituitarism
NOS 40–0110	Synpolydactyly, FBLN1-related	AD	FBLN1	608180		

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NOS 40–0120	Synpolydactyly, HOXD13-related	AD	HOXD13	186000		
NOS 40–0130	Postaxial polydactyly, isolated (type A10), KIAA0825-related	AR	KIAA0825	618498		
NOS 40–0140	Townes-Brocks syndrome, SALL1-related	AD	SALL1	107480		
NOS 40–0150	Lacrimo-auriculo-dento-digital syndrome (LADD), FGFR2-related	AD	FGFR2	149730		
NOS 40–0160	Lacrimo-auriculo-dento-digital syndrome (LADD), FGFR3-related	AD	FGFR3	149730		
NOS 40–0170	Lacrimo-auriculo-dento-digital syndrome (LADD), FGF10-related	AD	FGF10	149730		
NOS 40–0180	Acrocallosal syndrome, KIF7-related	AR	KIF7	200990		
NOS 40–0190	Acro-pectoral-vertebral dysplasia (F-syndrome), WNT6-related	AD	WNT6	102510		Structural variations of locus resulting in ectopic activation of *WNT6*
NOS 40–0200	Cenani-Lenz syndactyly, LRP4-related	AR	LRP4	212780		
NOS 40–0210	Cenani-Lenz-like syndactyly, GREM/FMN1-related	AD	GREM1, FMN1	see 212780		Monoallelic duplication of both *GREM1* and *FMN1* loci (one individual)
NOS 40–0220	Oligosyndactyly, radio-ulnar synostosis, hearing loss and renal defects syndrome, FMN1-related	AR	FMN1			Biallelic deletion of the *FMN1* gene (one individual)
NOS 40–0230	Mesoaxial synostotic syndactyly with phalangeal reduction (Malik-Percin), BHLHA9-related	AD	BHLHA9	609432		
NOS 40–0240	STAR syndrome (syndactyly of toes, telecanthus, anal and renal malformations), FAM58A-related	XLD	FAM58A	300707		X-linked dominant (only affected females known, possibly lethal in males)
NOS 40–0250	Syndactyly type 1 (III-IV)	AD		185900		
NOS 40–0260	Syndactyly type 3 (IV-V), GJA1-related	AD	GJA1	186100		
NOS 40–0270	Syndactyly type 4 (I-V) Haas type, SHH-related	AD	SHH	186200		Duplication of *ZRS* (limb enhancer of *SHH*)
NOS 40–0280	Syndactyly type 5 (Brachydactyly-Syndactyly syndrome; syndactyly with metacarpal and metarsal fusion), HOXD13-related	AD	HOXD13	186300, 610713		
NOS 40–0290	Syndactyly (Lueken type, with or without craniosynostosis), IHH-related	AD	IHH	185900		Duplication of *IHH* and regulatory region on 2q35; includes syndactyly with craniosynostosis (Philadelphia type)
NOS 40–0300	Metacarpal 4–5 fusion, FGF16-related	XLR	FGF16	309630		
NOS 40–0310	Syndactyly with microcephaly and mental retardation (Filippi syndrome), CKAP2L-related	AR	CKAP2L	272440		

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NOS 40–0320	Synpolydactyly plus syndrome, MAPKAPK5-related	AR	MAPKAPK5	619869		In OMIM as neurocardiofaciodigital syndrome
	Note: the Smith-Lemli-Opitz syndrome can present with polydactyly and/or syndactyly. The different variants of Meckel syndrome can have polydactyly and are included under the ciliopathies (see there). The Bardet-Biedl syndromes may have polydactyly as a secondary feature and have not been included in this neither in this group nor in the ciliopathies. - See also Clubfoot with or without deficiency of long bones and/or mirror-image polydactyly, *PITX1*-related. The entity called “Crossed polysyndactyly” not included as unclear whether or not it is a distinct entity.					
Group 41	**Defects in joint formation and synostoses**					
NOS 41–0010	Multiple synostoses syndrome, NOG-related	AD	NOG	186500, 186570		Includes: Stapes ankylosis with broad thumbs and toes, Tarsal-Carpal coalition syndrome, proximal Symphalangism 1A; see also Brachydactyly type B2, *NOG*-related, in the brachydactyly group
NOS 41–0020	Multiple synostoses syndrome, GDF5-related	AD	GDF5	610017		see other *GDF5*-related disorders
NOS 41–0030	Multiple synostoses syndrome, FGF9-related	AD	FGF9	612961		
NOS 41–0040	Multiple synostoses syndrome, GDF6-related	AD	GDF6	617898		
NOS 41–0050	Liebenberg syndrome, PITX1-related	AD	PITX1	186550		Structural variants encompassing the *H2AFY* gene resulting in ectopic activation of *PITX1* in upper limb
NOS 41–0060	Short stature, auditory atresia, mandibular hypoplasia, skeletal abnormalities (SAMS) syndrome, GSC-related	AR	GSC	602471		
NOS 41–0070	Radio-ulnar synostosis with amegakaryocytic thrombocytopenia, HOXA11-related	AD	HOXA11	605432		
NOS 41–0080	Radio-ulnar synostosis with amegakaryocytic thrombocytopenia, MECOM-related	AD	MECOM	616738		
NOS 41–0090	Radio-ulnar synostosis with microcephaly (Giuffré-Tsukahara syndrome)			603438		X-linked recessive inheritance suggested
	See also Spondylocarpotarsal synostosis syndrome, *FLNB*-related and *RFLNA*-related; Cardiospondylocarpofacial syndrome, *MAP3K7*-related; mesomelic dysplasia with acral synostoses (Verloes-David-Pfeiffer type); Baller-Gerold syndrome, *RECQL4*-related; and Antley-Bixler syndrome, *POR*-related					

The numbering system (first column) includes “NOS” for “Nosology, skeletal”, followed by the group number and the number of the disorder. The abbreviations are as follows: in the disorder names, SED in spondylo-ephyseal dysplasia; SEMD is spondylo-epi-metaphyseal dysplasia; MED is multiple epiphyseal dysplasia; CDP is chondrodysplasia punctata. In the “Inheritance” column: AD = autosomal

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recessive, AR = autosomal recessive, XL = X-linked, MOS = somatic mosaicism, SP = sporadic and inheritance unknown. Pseudo-AD and Pseudo-AR refers to genes in the pseudoautosomal regions of chromosome X and Y. The "MIM No." column shows the MIM number of the disorder; when the number is preceded by "see", the MIM number is that of the underlying gene.