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Supplemental Data

Clinical Diagnostics in Human Genetics with Semantic Similarity Searches in Ontologies

Sebastian Köhler, Marcel H. Schulz, Peter Krawitz, Sebastian Bauer, Sandra Dölken, Claus E. Ott, Christine Mundlos, Denise Horn, Stefan Mundlos, Peter N. Robinson

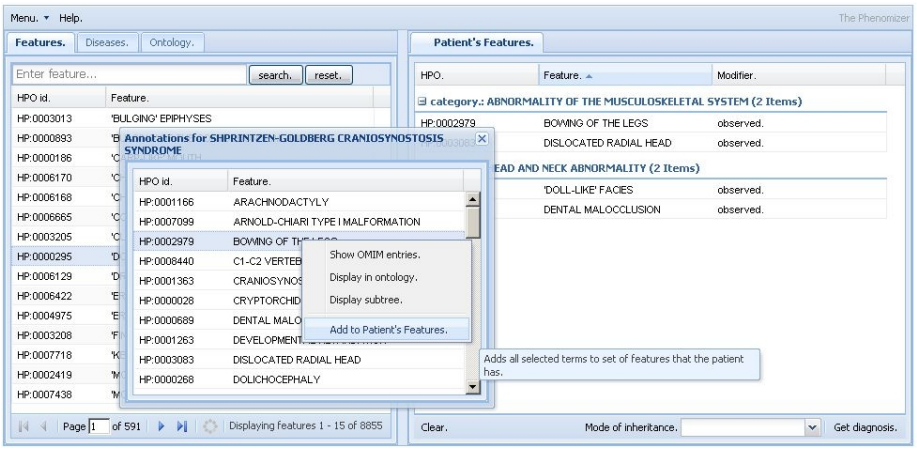

Figure S1: **Screenshot of the *Phenomizer* web-application.** We have implemented our methods using Web 2.0 technologies including the Google Web Toolkit (GWT) (http://code.google.com/webtoolkit/) and GWT-Ext (http://www.gwt-ext.com) in the form of a freely available, web-application called the *Phenomizer*, which can be used for searching for Mendelian disorders. The data is fetched asynchronously (AJAX) from our Tomcat-webserver, where most of the computations are performed. Thus, for the user our application is very lightweight and requires no installation. Users require just a standard web-browser such as Firefox, Internet Explorer ($\geq$ IE6), or Safari and an internet connection. The application is thus independent of the user's operating system. For each query, the similarity to each disease in the database (currently, the 4,813 diseases listed in OMIM) is calculated. Therefore, we report multiple-testing corrected P-values. The default multiple-correction method for the *Phenomizer* is that of Benjamini and Hochberg [1], but users can choose among several other multiple-testing corrections, which are calculated using R [2] on the server side.

Description	*Numerical Frequency*
very rare	0.01
rare	0.05
occasional	0.075
main	0.25
frequent	0.33
typical	0.5
common	0.5
hallmark	0.9

Table S1: **Conversion of textual description of feature-frequencies into numerical values.** In some cases, the literature consulted to construct the frequency tables shown in Tables S2-S45 dod not contain numerical estimates of the frequencies of clinical features, but rather general descriptions of their frequency such as "common" or "rare". For these features, we used the numerical values given in this table.

HPO Term	Term ID	Frequency
Delayed motor milestones	HP:0002130	100.00%
Absent speech	HP:0001617	100.00%
Gait ataxia	HP:0007240	100.00%
Severe mental retardation	HP:0001261	100.00%
EEG abnormalities	HP:0002353	92.00%
Blue irides	HP:0000635	88.00%
Seizures	HP:0001250	86.00%
Blond hair	HP:0002214	65.00%
Strabismus	HP:0000486	42.00%
Hypopigmentation of the skin	HP:0001010	39.00%
Mild cortical atrophy on CT or MRI	HP:0006823	33.00%
Deep set eyes	HP:0000490	main
Maxillary hypoplasia	HP:0000327	main
Microbrachycephaly	HP:0002258	main
Hypotonia	HP:0001318	main
Macrostomia *and* Macroglossia *and* Widely spaced teeth	HP:0000181 *and* HP:0000203 *and* HP:0000687	main
Mandibular prognathism	HP:0000303	main
Inappropriate laughter	HP:0000748	main
Scoliosis	HP:0002650	occasional
Hyperreflexia	HP:0001282	occasional
Nystagmus	HP:0000639	occasional
Inheritance: Isolated cases (Imprinting defect)		

Table S2: **Angelman Syndrome [MIM 105830].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Abnormality of the pyramidal tracts	HP:0002062	68/69
Cerebral atrophy, progressive	HP:0002422	66/69
Increased CSF interferon alpha	HP:0009709	31/33
Basal ganglia calcifications	HP:0002135	64/69
Microcephaly	HP:0000252	59/69
Chronic CSF lymphocytosis	HP:0009704	51/65
Leukoencephalopathy	HP:0002352	53/69
Extrapyramidal signs	HP:0002071	42/69
Hepatosplenomegaly	HP:0001433	13/23
Nystagmus	HP:0000639	11/21
Feeding difficulties	HP:0002022	35/69
Encephalopathy, progressive	HP:0002448	typical
Truncal hypotonia	HP:0002320	typical
Poor head control	HP:0002421	typical
Seizures	HP:0001250	50%
Deep white matter hypodensities	HP:0007321	typical
Dystonia	HP:0001332	typical
Strabismus	HP:0000486	6/21
Chilblain lesions	HP:0009710	5/21
Liver dysfunction	HP:0004394	11/69
Fever	HP:0001945	11/69
Inheritance: Autosomal recessive		

Table S3: **Aicardi-Goutières Syndrome.** Feature frequencies according to [4] and [5].

HPO Term	Term ID	Frequency
Carpal bone fusion	HP:0001192	100.00%
Absent or hypoplastic thumbs	HP:0002950	100.00%
Absent carpals, metacarpals, and phalanges	HP:0005056	100.00%
Craniosynostosis	HP:0002685	100.00%
Aplasia/hypoplasia of the radius	HP:0006501	77.00%
Short ulna	HP:0002998	68.00%
Bowed ulna	HP:0003031	68.00%
Low-set, posteriorly rotated ears	HP:0000368	64.00%
Mental retardation	HP:0001249	50.00%
Micrognathia	HP:0000210	50.00%
Abnormality of the anus	HP:0004378	40.00%
Genitourinary abnornmality	HP:0000119	35.00%
Microstomia	HP:0000160	32.00%
Downward slanting palpebral fissures	HP:0000494	32.00%
Prominent nasal bridge	HP:0000426	32.00%
Flattened forehead	HP:0004425	27.00%
cardiac abnormality	HP:0001627	25.00%
Growth retardation	HP:0001510	main
Sudden death	HP:0001699	20.00%
spina bifida occulta	HP:0003298	occasional
Strabismus	HP:0000486	occasional
hearing loss, conductive	HP:0000405	occasional
limited elbow movement	HP:0002996	occasional
cleft palate	HP:0000175	occasional
myopia	HP:0000545	occasional
bifid uvula	HP:0000193	occasional
midfacial capillary hemangioma	HP:0007611	occasional
rib fusion	HP:0000902	occasional
limited knee movement	HP:0005192	occasional
abnormalities of the vertebrae	HP:0003468	occasional
limited shoulder movement	HP:0006467	occasional
polymicrogyria	HP:0002126	occasional
Hydrocephalus	HP:0000238	occasional
Epicanthal folds	HP:0000286	occasional
Seizures	HP:0001250	occasional
scoliosis	HP:0002650	occasional
anomalous splenoportal venous system	HP:0005201	occasional
choanal stenosis	HP:0000452	occasional
Patellar hypoplasia	HP:0003065	occasional
Humeral hypoplasia	HP:0005792	occasional
hypoplastic nasal alae	HP:0000430	occasional
optic atrophy	HP:0000648	occasional
agenesis of corpus callosum	HP:0001274	occasional
Inheritance: autosomal recessive		

Table S4: **Baller Gerold Syndrome [MIM 218600].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Retinal dystrophy	HP:0000556	100.00%
Abnormality of the kidneys	HP:0000077	95.00%
Small penis *and* Decreased testicular size	HP:0000038 *and* HP:0008734	88.00%
Obesity	HP:0001513	83.00%
Speech delay	HP:0002117	77.00%
Myopia	HP:0000545	75.00%
Astigmatism	HP:0000483	63.00%
Hypertension	HP:0000822	60.00%
Postaxial polydactyly	HP:0001162	58.00%
Nystagmus	HP:0000639	52.00%
Brachydactyly	HP:0001156	50.00%
Behavioral disturbances	HP:0000715	33.00%
Cataract *or* Congenital primary aphakia	HP:0000518 *or* HP:0007707	30.00%
Short, broad feet	HP:0001773	main
Asthma	HP:0002099	25.00%
Poor coordination *and* Gait imbalance	HP:0002370 *and* HP:0002141	main
Syndactyly	HP:0001159	main
Mental deficiency	HP:0001267	main
Glaucoma	HP:0000501	22.00%
Retinitis pigmentosa	HP:0000510	8.00%
Clinodactyly	HP:0001157	occasional
Macrocephaly	HP:0000256	occasional
Cardiac abnormality	HP:0001627	occasional
Diabetes insipidus	HP:0000873	occasional
Biliary tract abnormality	HP:0001080	occasional
Diabetes mellitus	HP:0000819	occasional
Vaginal atresia	HP:0000148	occasional
Ataxia	HP:0001251	occasional
Hirsutism	HP:0001007	occasional
Dental abnormality	HP:0000164	occasional
Hearing loss	HP:0000365	occasional
Abnormality of the ovaries	HP:0000137	occasional
Hepatic fibrosis	HP:0001395	occasional
Inheritance: autosomal recessive (heterogeneous,sometimes triallelic inheritance)		

Table S5: **Bardet Biedl Syndrome [MIM 209900].** Feature frequencies according to [3] and [6].

HPO Term	Term ID	Frequency
Low posterior hairline	HP:0002162	92.00%
Low-set posteriorly rotated ears *and/or* Overfolded ears *and/or* Malformed ears	HP:0000368 *and/or* HP:0001758 *and/or* HP:0000377	38/42
Abnormality of upper lip	HP:0000177	90.00%
Nasolacrimal duct obstruction	HP:0000579	29/39
Male: Undescended testes	HP:0000797	73.00%
Proximally placed thumbs	HP:0001170	72.00%
Short neck	HP:0000470	66.00%
Elbow contractures	HP:0002987	64.00%
Hearing loss	HP:0000365	60.00%
Telecanthus	HP:0000506	58.00%
Atrophic skin *and* Aplasia cutis congenita *and* Scarring	HP:0001077 *and* HP:0001057 *and* HP:0000987	57.00%
Myopia *and/or* Ptosis *and/or* Nystagmus	HP:0000545 *and/or* HP:0000508 *and/or* HP:0000639	57.00%
Dental abnormalities	HP:0000164	56.00%
Transverse palmar crease	HP:0000945	51.00%
Micrognathia	HP:0000210	50.00%
Upslanting palpepral fissures	HP:0000582	48.00%
Prenatal growth deficiency	HP:0001515	16/34
Coloboma	HP:0000589	16/35
Microphthalmos *or* Anophthalmia	HP:0000568 *or* HP:0000528	44.00%
Hypoplastic superior helix	HP:0008559	43.00%
Mild mental retardation	HP:0001256	15/36
Postnatal growth retardation	HP:0001514	13/34
Hearing loss, conductive	HP:0000405	14/38
Male: Hypospadias	HP:0000047	33.00%
Strabismus	HP:0000486	11/36
Gastrooesophageal reflux	HP:0002020	30.00%
Myopia	HP:0000545	9/32
Ptosis	HP:0000508	10/36
Cataract	HP:0000518	8/33
Premature graying of hair	HP:0002216	9/38
Dolichocephaly	HP:0000268	9/39
Seizures	HP:0001250	23.00%
Fith finger clinodactyly	HP:0001158	8/38
Supra-auricular sinuses	HP:0008606	15.00%
Hearing loss, sensorineural	HP:0000407	occasional
Renal agenesis	HP:0000104	occasional
Preaxial polydactyly	HP:0001177	occasional
Lower lip pits	HP:0000196	occasional
Agenesis of cerebellar vermis	HP:0002335	occasional
White forelock	HP:0002211	occasional
Microtia	HP:0000393	occasional
Abnormality of the scalp	HP:0001965	occasional
Broad nasal tip	HP:0000455	occasional
Cleft palate	HP:0000175	occasional
Microcephaly	HP:0000252	occasional
Gastroesophagial obstruction *and/or* duplication of internal organs *and/or* malrotation of colon	HP:0002020 *and/or* HP:0005217 *and/or* HP:0004785	occasional
Pyloric stenosis	HP:0002021	occasional
Posterior auricular pit	HP:0004464	occasional
Inheritance: Autosomal dominant		

Table S6: **Branchiooculofacial syndrome [MIM 113620].** Feature frequencies according to [3] and [7].

HPO Term	Term ID	Frequency
Hearing loss	HP:0000365	90.0%
Preauricular pit	HP:0000392	80.0%
Renal dysplasia	HP:0000110	65.0%
Branchial fistula *or* Branchial cyst	HP:0009795 *or* HP:0009796	50.0%
Cup-shaped ears	HP:0000378	45.00%
Abnormal form of ears	HP:0000377	35.0%
External auditory canal stenosis	HP:0000402	30.0%
Abnormality of the middle ear *and/or* Abnormality of the inner ear	HP:0000370 *and/or* HP:0000359	main
Lacrimal duct aplasia or stenosis	HP:00007993	10.0%
Long narrow facies	HP:0000318	occasional
Microdontia	HP:0000691	occasional
Euthyroid goiter	HP:0009798	occasional
Preauricular skin tag	HP:0000384	occasional
Cleft palate	HP:0000175	occasional
High-arched palate	HP:0000156	occasional
Lacrimation abnormality	HP:0000632	occasional
Bifid uvula	HP:0000193	occasional
abnormality of the cerebrum	HP:0002060	occasional
Cranial nerve VII palsy	HP:0007212	occasional
Cholesteatoma	HP:0009797	occasional
Intestinal malrotation	HP:0002026	occasional
Congenital hip dislocation	HP:0001374	occasional
Inheritance: Autosomal dominant		

Table S7: **Branchiootorenal syndrome 1 [MIM 113650].** Note that Branchiootorenal syndrome 1 is also known as Melnick-Fraser syndrome. Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Cortical thickening of long bone diaphyses	HP:0005791	82/87
Asthenic habitus	HP:0001533	hallmark
Increased bone mineral density	HP:0004350	26/29
Limb pain	HP:0009763	63/92
Sclerotic skull base	HP:0002694	32/59
Poor appetite	HP:0004396	typical
Amyotrophy	HP:0003202	typical
Easy fatigability	HP:0003388	32/72
Headaches	HP:0002315	9/22
Muscle weakness	HP:0001324	36/92
Decreased subcutaneous fat	HP:0001002	10/47
Delayed puberty	HP:0000823	1/6
Deafness	HP:0000404	10/67
Inheritance: Autosomal dominant		

Table S8: **Camurati-Engelmann disease [MIM 131300].** Feature frequencies according to [8].

HPO Term	Term ID	Frequency
Accessory index finger phalanges	HP:0004107	100.00%
Cleft palate	HP:0000175	78.00%
Postnatal growth retardation	HP:0001514	75.00%
Micrognathia	HP:0000210	72.00%
Bilateral single palmar creases	HP:0007598	40.00%
Coarctation of aorta	HP:001680	39.00%
Fifth finger clinodactyly	HP:0001158	39.00%
Ventricular septal defect	HP:0001629	39.00%
overriding aorta	HP:00002623	39.00%
Dextrocardia	HP:0001651	39.00%
Abnormal form of ears	HP:0000377	33.00%
Joint dislocations	HP:0002722	occasional
Umbilical hernia	HP:0001537	occasional
Developmental delay	HP:0000754	occasional
Abnormality of the vertebral column	HP:0000925	occasional
Short neck	HP:0000470	occasional
Joint laxity	HP:0001388	occasional
Prenatal growth deficiency	HP:0001515	occasional
Cleft lip	HP:0000204	occasional
Pectus excavatum/carinatum	HP:0006708	occasional
Talipes equinovarus	HP:0001762	occasional
Inguinal hernia	HP:0000023	occasional
Seizures	HP:0001250	occasional
Camptodactyly	HP:0001160	occasional
Abnormality of the ribs	HP:0000772	occasional
Facial palsy	HP:0002517	occasional
Cryptorchidism	HP:0000028	occasional
Inheritance: X-linked recessive and isolated cases		

Table S9: **Catel-Manzke Syndrome 1 [MIM 302380].** Feature frequencies according to [3].

HPO Term	Term ID		Frequency
Mental retardation	HP:0001249		100.00%
Small ears *and/or* Cup-shaped ears *and/or* Lop ears *and/or*	HP:0000409	*and/or*	90.00%
Sensorineural deafness *and/or* Mixed hearing loss	HP:0000378	*and/or*	
	HP:0000394	*and/or*	
	HP:0000374	*and/or*	
	HP:0000410		
Clinical anopthalmia *or* Iris coloboma *or* Retinal coloboma	HP:0001485 *or* HP:0000612 *or* HP:0000480		85.00%
Tetralogy of Fallot *and/or* Patent ductus arteriosus *and/or* Double outlet right ventricle *and/or* Ventricular spetal defect *and/or* Atrial septal defect *and/or* Right aortic arch	HP:0001636		77.50%
Male: Hypoplastic male genitalia	HP:0008721		75.00%
Postnatal growth retardation	HP:0001514		70.00%
Choanal atresia	HP:0000453		58.00%
Arrhinencephaly	HP:0002139		main
Hypogonadotropic hypogonadism	HP:0000044		main
Scoliosis	HP:0002650		occasional
Abnormality of the nipples	HP:0004404		occasional
Growth hormone deficiency	HP:0000824		occasional
Sloping shoulders	HP:0001556		occasional
Ptosis	HP:0000508		occasional
Polydactyly *and/or* Ectrodactyly *and/or* Hypoplastic thumb	HP:0001161	*and/or*	occasional
and/or Abnormal palmar dermatoglyphics	HP:0001171	*and/or*	
	HP:0009628	*and/or*	
	HP:0001018		
Micrognathia	HP:0000210		occasional
Cranial nerve abnormality	HP:0001291		occasional
Anal atresia *or* Anal stenosis	HP:0002023 *or* HP:0002025		occasional
Abnormality of the ribs	HP:0000772		occasional
Hemivertebrae	HP:0002937		occasional
Feeding difficulties	HP:0002022		occasional
Hypertelorism	HP:0000316		occasional
Renal hypoplasia *or* Renal agenesis	HP:0000089 *or* HP:0000104		occasional
Omphalocele	HP:0001539		occasional
Webbed neck	HP:0000465		occasional
Cleft palate	HP:0000175		occasional
Cleft lip	HP:0000204		occasional
Microcephaly	HP:0000252		occasional
Tracheoesophageal fistula	HP:0002575		occasional
Inheritance: Autosomal dominant, isolated cases			

Table S10: **CHARGE Syndrome [MIM 214800].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Mental retardation	HP:0001249	30/30
Broad hands *and* Tapered fingers	HP:0001169 *and* HP:0001182	30/30
Broad nose *and* Thick nasal septum	HP:0000445 *and* HP:0009746	25/25
Hypertelorism *and* Telecanthus	HP:0000316 *and* HP:0000506	29/29
Heavy arched eyebrows *and* Coarse facial features	HP:0007804 *and* HP:0000280	27/27
Short stature	HP:0001509	29/30
Thick, everted lower lip	HP:0009086	27/28
Drumstick' terminal phalanges	HP:0006129	24/25
Transverse palmar creases	HP:0000954	16/17
Downward slanting palpebral fissures	HP:0000494	23/27
Hypodontia	HP:0000688	16/19
Pectus excavatum *or* Pectus carinatum	HP:0000767 *or* HP:0000768	20/25
Delayed skeletal maturation	HP:0002750	15/19
Kyphoscoliosis	HP:0002751	21/28
Thickened calvarium	HP:0002684	14/22
Seizures	HP:0001250	8/17
Inheritance: X-linked dominant		

Table S11: **Coffin-Lowry Syndrome [MIM 303600].** Feature frequencies according to [9].

HPO Term	Term ID	Frequency
Hypoplastic to absent fifth finger- and toenails	HP:0008398	33/33
Pervasive developmental disorder	HP:0000729	31/31
Full lips	HP:0000170	28/32
Coarse facial features	HP:0000280	27/31
Feeding difficulties	HP:0002022	25/29
Wide mouth	HP:0000154	23/27
Lumbosacral hirsutism	HP:0009747	25/30
Flattened nasal bridge *and* broad nasal tip	HP:0000425 *and* HP:0000455	24/29
Sparse scalp hair	HP:0002209	23/28
Thick eyebrows	HP:0000574	23/30
Postnatal growth retardation	HP:0001514	14/19
Delayed skeletal maturation	HP:0002750	11/15
Microcephaly	HP:0000252	21/30
Recurrent upper and lower respiratory tract infections	HP:0002873	14/22
Intrauterine growth retardation	HP:0001511	typical
Delayed dentition	HP:0000684	typical
Hypoplastic corpus callosum *and/or* Dandy-Walker malformation	HP:0002079 *and/or* HP:0001305	typical
Short stature	HP:0001509	typical
Patent ductus arteriosus *or* Tetralogy of Fallot *or* Ventricular septum defect *or* Atrial septal defect	HP:0001643 *or* HP:0001636 *or* HP:0001629 *or* HP:0001631	9/22
Scoliosis	HP:0002650	6/17
Inheritance: Autosomal recessive		

Table S12: **Coffin-Siris Syndrome [MIM 135900].** Feature frequencies according to [10].

HPO Term	Term ID	Frequency
Mental retardation	HP:0001249	100.00%
Pes planus	HP:0001763	97.00%
Microcephaly	HP:0000252	28/31
Feeding difficulties	HP:0002022	27/33
Leukopenia	HP:0001182	78.00%
Short stature	HP:0001509	21/33
Neonatal hypotonia	HP:0001319	56.00%
Myopia	HP:0000545	typical
Delayed motor milestones	HP:0002130	typical
Prominent nasal bridge	HP:0000426	typical
Truncal obesity developing in mid-childhood	HP:0008874	typical
Beaked nose	HP:0000444	typical
Short philtrum	HP:0000322	typical
Chorioretinal dystrophy	HP:0001135	typical
Thick eyebrows	HP:0000574	typical
Narrow hand	HP:0004283	typical
Prominent upper central incisors	HP:0000675	typical
Downward slanting palpebral fissures	HP:0000494	typical
Delayed puberty	HP:0000823	40.00%
Impaired vision	HP:0000505	35.00%
Hyperextensible joints	HP:0001378	frequent
Laryngomalacia	HP:0001601	frequent
Low birth weight	HP:0001518	frequent
Mild thoracic scoliosis	HP:0004615	31.00%
Mild lumbar lordosis	HP:0004560	31.00%
Inheritance: Autosomal recessive		

Table S13: **Cohen Syndrome [MIM 216550].** Feature frequencies according to [11].

HPO Term	Term ID		Frequency
Marfanoid habitus *and* arachnodactyly	HPO:0001519 HPO:0001166	*and*	86.00%
Elbow contractures	HP:0002987		86.00%
Knee contractures	HP:0002978		81.00%
Camptodactyly	HP:0001160		78.00%
Poorly defined conchae	HP:0008602		75.00%
Hypoplastic calf muscles	HP:0008962		65.00%
Kyphoscoliosis	HP:0002751		46.00%
Talipes equinovarus	HP:0001762		32.00%
Frontal bossing	HP:0000254		29.00%
Scaphocephaly *and/or* Brachycephaly *and/or* Dolichocephaly *and/or* frontal bossing	HP:0000258 HP:0000248 HP:0000268 HP:0000254	*and/or* *and/or* *and/or*	29.00%
Micrognathia	HP:0000210		26.00%
Hip contractures	HP:0003273		26.00%
Ulnar deviation of fingers	HP:0001120		main
Relatively short neck	HP:0005992		main
Mitral valve regurgitation	HP:0001653		main
Metatarsus varus	HP:0001840		main
Myopia	HP:0000545		occasional
Aortic root dilatation	HP:0002616		occasional
Atrial septal defect	HP:0001631		occasional
Pectus excavatum/carinatum	HP:0006708		occasional
Iris coloboma	HP:0000612		occasional
Mitral valve prolapse	HP:0001634		occasional
Keratoconus	HP:0000563		occasional
Ventricular septal defect	HP:0001629		occasional
Dislocation of patella	HP:0002999		occasional
Inheritance: Autosomal dominant			

Table S14: **Congenital Contractural Arachnodactyly (CCA; Beals Hecht Syndrome [MIM 121050].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Hypertonicity	HP:0002388	100.00%
Delayed skeletal maturation	HP:0002750	100.00%
Long, curly eyelashes	HP:0000500	99.00%
Broad bushy eyebrows *and* Synophrys	HP:0004546 *and* HP:0000664	98.00%
Long philtrum *and* Thin upper lip *and* Downturned corners of mouth	HP:0000343 *and* HP:0000219 *and* HP:0002714	94.00%
Microbrachycephaly	HP:0002258	93.00%
Micromelia	HP:0002983	93.00%
Low posterior hairline	HP:0002162	92.00%
Late eruption of teeth	HP:0006328	86.00%
3-4 toe syndactyly	HP:0004691	86.00%
High-arched palate	HP:0000156	86.00%
Anteverted nostrils	HP:0000463	85.00%
Micrognathia	HP:0000210	84.00%
Flattened nasal bridge	HP:0000425	83.00%
Hirsutism	HP:0001007	78.00%
Fith finger clinodactyly	HP:0001158	74.00%
Weak cry	HP:0001612	74.00%
Undescended testes	HP:0000797	73.00%
Proximally placed thumbs	HP:0001170	72.00%
Short neck	HP:0000470	66.00%
Elbow contractures	HP:0002987	64.00%
Hearing loss	HP:0000365	60.00%
Male: Hypoplastic male genitalia	HP:0008721	57.00%
Myosis *or* ptosis *or* nystagmus	HP:0000545 *or* HP:0000508 *or* HP:0000639	57.00%
Cutis marmorata	HP:0000965	56.00%
Transverse palmar creases	HP:0000954	51.00%
abnormal umbilicus	HP:0001551	50.00%
Hypoplastic nipples	HP:0002557	50.00%
Hypospadias	HP:0000047	33.00%
Gastrooesophagial reflux	HP:0002020	30.00%
Phocomelia *and* Oligodactyly	HP:0002994 *and* HP:0001180	27.00%
Mental retardation	HP:0001249	main
Short sternum *and* Supernumerary ribs	HP:0000879 *and* HP:0005815	main
Dislocated radial head *or* Hypoplastic radial head	HP:0003083 *or* HP:0003997	main
Prenatal growth deficiency	HP:0001515	main
Seizures	HP:0001250	23.00%
Optic nerve coloboma	HP:0000588	occasional
Astigmatism	HP:0000483	occasional
Optic atrophy	HP:0000648	occasional
Cardiac malformation *or* Ventricular septal defect	HP:0002564 *or* HP:0001629	occasional
Hypoplastic radius	HP:0002984	occasional
Strabismus	HP:0000486	occasional
Proptosis	HP:0000520	occasional
Thrombocytopenia	HP:0001873	occasional
Low set ears	HP:0000369	occasional
Hypoplastic labia majora	HP:0000059	occasional
Hiatus hernia	HP:0002036	occasional
Diaphragmatic hernia	HP:0000776	occasional
Cleft palate	HP:0000175	occasional
Microcornea	HP:0000482	occasional
Abnormality of the esophagus	HP:0002031	occasional
Pyloric stenosis	HP:0002021	occasional
Choanal atresia	HP:0000453	occasional
Inguinal hernia	HP:0000023	occasional
Gastroesophagial obstruction *or* Duplication of internal organs *or* Malrotation of colon	HP:0002020 *or* HP:0005217 *or* HP:0004785	occasional
Inheritance: Autosomal dominant and isolated cases		

Table S15: **Cornelia de Lange Syndrome 1 [MIM 122470].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Hemisacrum (S2-S5)	HP:0009790	75.00%
Anterior sacral meningocele	HP:0007293	102/205
Chronic constipation	HP:0002241	84/205
Rectovaginal fistula	HP:0000143	frequent
Presacral teratoma	HP:0009793	frequent
Recurrent urinary tract infections	HP:0000010	frequent
Bifid sacrum	HP:0009791	22.00%
Gastrointestinal obstruction	HP:0004796	33/205
Tethered cord	HP:0002144	29/205
Meningitis	HP:0001287	23/205
Perianal abscess	HP:0009789	23/205
Vesicoureteral reflux	HP:0000076	occasional
Bicornuate uterus	HP:0000813	occasional
Inheritance: Autosomal dominant		

Table S16: **Currarino syndrome [MIM 176450].** Feature frequencies according to [12] and [13].

HPO Term	Term ID	Frequency
Distichiasis	HP:0009743	100.00%
Lymphedema, predominantly in the lower limbs	HP:0003550	66.00%
Abnormalities of the vertebrae	HP:0003468	62.00%
Epidural arachnoid cysts of the spinal canal	HP:0009745	46.00%
Cardiac malformation	HP:0002564	38.00%
Kyphosis	HP:0002808	occasional
Scoliosis	HP:0002650	occasional
Microphthalmos	HP:0000568	occasional
Ptosis	HP:0000508	occasional
Micrognathia	HP:0000210	occasional
Strabismus	HP:0000486	occasional
Ectropion	HP:0000656	occasional
Bifid uterus	HP:0000136	occasional
Cleft palate	HP:0000175	occasional
Webbed neck	HP:0000465	occasional
Epicanthal folds	HP:0000286	occasional
Bifid uvula	HP:0000193	occasional
Cryptorchidism	HP:0000028	occasional
Short stature	HP:0001509	occasional
Cleft lip	HP:0000204	4.00%
Inheritance: autosomal dominant		

Table S17: **Distichiasis Lymphedema Syndrome [MIM 153400].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Vertical talus	HP:0001838	88.00%
Congenital hip dislocation *or* Decreased hip abduction *or* Hip contractures	HP:0001374 *or* HP:0003184 *or* HP:0003273	38.00%
Calcaneovalgus deformities	HP:0001848	33.00%
knee contractures	HP:0002978	30.00%
Ulnar deviation of the hand or of fingers of the hand *and* Camptodactyly	HP:0001193 *and* HP:0001160	main
Clenched hands	HP:0001188	main
Talipes equinovarus	HP:0001762	25.00%
Adducted thumbs	HP:0001181	main
Absent distal interphalangeal creases	HP:0001032	main
Stiff shoulders	HP:0009742	17.00%
Transverse palmar creases	HP:0000954	occasional
Mild scoliosis	HP:0003303	occasional
Trismus	HP:0000211	occasional
Cryptorchidism	HP:0000028	occasional
Inheritance: Autosomal dominant		

Table S18: **Distal Arthrogryposis Syndrome Type 1 [MIM 108120].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Ectrodactyly *and* Ectrodactyly (feet) *and* Syndactyly	HP:0001171 *and* HP:0001839 *and* HP:0001159	84.00%
Cleft lip	HP:0000204	68.00%
Lacrimal duct abnormalities	HP:0000614	59.00%
Renal agenesis *and/or* Renal aplasia *and/or* Hydroureter *and/or* bladder diverticula *and/or* Duplicated collecting system *and/or* Hydronephrosis	HP:0000119 *and/or* HP:0000104 *and/or* HP:0000110 *and/or* HP:0000072 *and/or* HP:000015 *and/or* HP:000081 *and/or* HP:0000126	52.00%
Blepharitis	HP:0000498	main
Photophobia	HP:0000613	main
Malar hypoplasia	HP:0000272	main
Microdontia	HP:0000691	main
Dacryocystitis	HP:0000620	main
Carious teeth	HP:0000670	main
Fair skin *and* Thin skin	HP:0000984 *and* HP:0000963	main
Hypoplastic nipples	HP:0002557	main
Maxillary hypoplasia	HP:0000327	main
Fine, sparse, light colored hair	HP:0004538	main
Blepharophimosis	HP:0000581	main
Partial anodontia	HP:0000702	main
Blue irides	HP:0000635	main
Mild hyperkeratosis	HP:0007523	main
Nail dysplasia	HP:0002164	main
Hearing loss, conductive	HP:0000405	14.00%
Central diabetes insipidus	HP:0000863	occasional
Clinodactyly	HP:0001157	occasional
Growth hormone deficiency	HP:0000824	occasional
Telecanthus *and* Hypertelorism	HP:0000506 *and* HP:0000316	occasional
Abnormal form of ears *or* Small ears	HP:0000377 *or* HP:0000409	occasional
Female: Anal atresia *and* Rectovaginal fistula	HP:0002023 *and* HP:0000143	occasional
Polydactyly	HP:0001161	occasional
Hypogonadotropic hypogonadism	HP:0000044	occasional
Broad nasal tip	HP:0000455	occasional
Microcephaly	HP:0000252	occasional
Semilobar holoprosencephaly	HP:0002507	occasional
Choanal atresia	HP:0000453	occasional
Inguinal hernia	HP:0000023	occasional
Mental retardation	HP:0001249	7.00%
Recurrent respiratory infections	HP:0002205	6.00%
Inheritance: autosomal dominant with variable expression		

Table S19: **Ectrodactyly, ectodermal dysplasia, and cleft lip/palate syndrome (EEC1) [MIM 129900].** Feature frequencies according to [3]. Note that EEC3 is clinically identical and also has a separate OMIM entry [MIM 604292].

HPO Term	Term ID	Frequency
Hypertelorism	HP:0000316	89/100
Mild to moderate short stature	HP:0003503	86/98
Wide philtrum	HP:0000289	88/104
Fleshy earlobes	HP:0009748	85/103
Short broad hands	HP:0001174	63/77
Brachydactyly	HP:0001156	63/77
Curved linear dimple below the lower lip	HP:0002055	80/99
Maxillary hypoplasia	HP:0000327	84/104
Anteverted nostrils	HP:0000463	42/53
Shawl scrotum	HP:0000049	74/96
Widow's peak	HP:0000349	52/68
Finger joint hyperextensibility	HP:0006158	46/61
Clinodactyly	HP:0001157	57/82
Transverse palmar creases	HP:0000954	38/55
Small, short nose	HP:0003192	42/62
Broad nasal bridge	HP:0000431	50/75
Prominent umbilicus	HP:0001544	16/24
Cryptorchidism	HP:0000028	60/94
Inguinal hernia	HP:0000023	58/94
Mild syndactyly	HP:0001236	45/73
Downward slanting palpebral fissures	HP:0000494	43/81
Ptosis	HP:0000508	41/81
Short broad feet	HP:0001778	typical
Pectus excavatum	HP:0000767	34/74
Inheritance: X-linked recessive		

Table S20: **Faciogenital dysplasia (Aarskog-Scott Syndrome) [MIM 305400].** Feature frequencies according to [14].

HPO Term	Term ID	Frequency
Cryptophthalmos	HP:0001126	93.00%
partial cutaneous syndactyly	HP:0006054	57.00%
mental deficiency	HP:0001267	50.00%
Cup-shaped ears *or* External auditory canal atresia	HP:0000378 *or* HP:0000413	44.00%
Renal hypoplasia *or* Renal agenesis	HP:0000089 *or* HP:0000104	37.00%
Unusual hairline with hair growth on temples extending to lateral eyebrow	HP:0005352	34.00%
Hypoplastic notched nares	HP:0005286	main
Vaginal atresia	HP:0000148	main
Broad nose *and* Flattened nasal bridge	HP:0000445 *and* HP:0000425	main
Bicornuate uterus	HP:0000813	main
Hypospadias	HP:0000047	main
Clitoromegaly	HP:0000057	main
Cryptorchidism	HP:0000028	main
Laryngeal stenosis *or* Laryngeal atresia	HP:0005950 *or* HP:0008750	21.00%
Skull defect	HP:0001362	9.00%
Hypoplastic/absent phalanges	HP:0006056	occasional
Hypoplastic nostrils	HP:0004497	occasional
Abnormality of the anus	HP:0004378	occasional
Middle ear malformation	HP:0008609	occasional
Cardiac abnormality	HP:0001627	occasional
Wide pubic symphysis	HP:0003183	occasional
Anophthalmia	HP:0000528	occasional
Abnormal gyration	HP:0002536	occasional
Pulmonary hypoplasia	HP:0002089	occasional
Midline nasal groove	HP:0004112	occasional
Upper eyelid coloboma	HP:0000636	occasional
Abnormality of the thymus	HP:0000777	occasional
Microtia	HP:0000393	occasional
Absent eyebrows and eyelashes	HP:0002288	occasional
Absent or hypoplastic thumbs	HP:0002950	occasional
Subglottic stenosis	HP:0001607	occasional
Abnormality of the urinary tract	HP:0000079	occasional
Abnormal umbilicus	HP:0001551	occasional
Wide intermamillary distance	HP:0006610	occasional
Microcephaly	HP:0000252	occasional
White corneal opacification	HP:0007883	occasional
Aplpasia/Hypoplasia of the sternum	HP:0006714	occasional
Microphtalmia, bilateral	HP:0001585	occasional
meningomyelocele	HP:0002475	occasional
Low-set ears	HP:0000369	occasional
Hydrocephalus	HP:0000238	occasional
Facial cleft	HP:0002006	occasional
Abnormality of the small intestine	HP:0002244	occasional
Dental malocclusion *and* Dental overcrowding	HP:0000689 *and* HP:0000678	occasional
Hypoplastic superior helix	HP:0008559	occasional
choanal stenosis	HP:0000452	occasional
Encephalocele	HP:0002084	occasional
Difficulty in tongue movement	HP:0000183	6.00%
Cleft lip	HP:0000204	4.00%
Cleft palate	HP:0000175	3.00%
Inheritance: autosomal recessive		

Table S21: **Fraser Syndrome [MIM 219000].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Whistling' appearance	HP:0000346	100.00%
Ulnar deviation	HP:0001193	91.00%
Contractures of fingers	HP:0004094	88.00%
Kyphoscoliosis	HP:0002751	84.00%
Hip contractures	HP:0003273	73.00%
Knee contractures	HP:0002978	73.00%
Postnatal growth retardation	HP:0001514	62.00%
Talipes Equinovarus *and* Toe contractures	HP:0001762 *and* HP:0001860	59.00%
Microcephaly	HP:0000252	44.00%
Mental deficiency	HP:0001267	31.00%
High palate	HP:0000218	main
Telecanthus	HP:0000506	main
Hypoplastic nose	HP:0000440	main
Deep set eyes	HP:0000490	main
Long philtrum	HP:0000343	main
Strabismus	HP:0000486	main
Small tongue	HP:0000226	main
Blepharophimosis	HP:0000581	main
Prominent chin with central dimple	HP:0004648	main
Vertical talus	HP:0001838	main
Broad nasal bridge	HP:0000431	main
Undescended testes	HP:0000797	main
Hypoplastic nasal alae	HP:0000430	main
Shoulder contractures	HP:0003044	main
Adducted thumbs	HP:0001181	main
Epicanthal folds	HP:0000286	main
Inguinal hernia	HP:0000023	main
Nasal speech	HP:0001611	main
Seizures	HP:0001250	19.00%
Cerebellar atrophy *and* hypoplasia of the brainstem	HP:0001272 *and* HP:0002365	occasional
Spina bifida occulta	HP:0003298	occasional
Ptosis	HP:0000508	occasional
Short neck	HP:0000470	occasional
Dislocated hips	HP:0002827	occasional
Low birth weight	HP:0001518	occasional
Abnormal brainstem auditory evoked potentials	HP:0006923	occasional
Inheritance: autosomal dominant		

Table S22: **Freeman-Sheldon Syndrome [MIM 193700].** Feature frequencies according to [15].

HPO Term	Term ID	Frequency
Abnormality of the carpal bones	HP:0001547	typical
Atrial septum defect	HP:0001631	34/82
Hypoplastic radius	HP:0002984	31/82
Ventricular septum defect	HP:0001629	12/82
Phocomelia	HP:0002994	9/82
Pectus excavatum/carinatum	HP:0006708	Occasional
Patent ductus arteriosus	HP:0001643	Occasional
Thoracic scoliosis	HP:0002943	Occasional
Aplasia of the pectoralis major muscle	HP:0009751	Occasional
Inheritance: Autosomal dominant		

Table S23: **Holt-Oram Syndrome [MIM 142900].** Feature frequencies according to [16].

HPO Term	Term ID	Frequency
Micrognathia	HP:0000210	100%
Severe prenatal onset hydrocephalus	HP:0006882	92%
Polyhydramnios	HP:0001561	92%
Microphthalmos	HP:0000568	86%
Bifid nose	HP:0003190	86%
Postaxial polydactyly	HP:0001162	77%
Cleft in skull base	HP:0009752	76%
Stillbirth	HP:0001624	73%
Abnormal form of ears *and* low-set ears	HP:0000377 *and* HP:0000369	70%
Defective lung lobation	HP:0009753	66%
Preaxial polydactyly (feet)	HP:0001841	65%
Tracehal stenosis *and* Hypoplastic larynx	HP:0002777 *and* HP:0008749	57%
Cleft palate *and/or* Cleft lip	HP:0000175 *and/or* HP:0000204	55%
Talipes equinovarus	HP:0001762	52%
Atrioventricular canal *or* Ventricular septal defect	HP:0001674 *or* HP:0001629	48%
Duplicated halluces	HP:0001784	47%
Male: Hypospadias	HP:0000047	frequent
Female: Bifid uterus	HP:0000136	frequent
Short arms	HP:0003056	24%
Hydronephrosis	HP:0000126	16%
Inheritance: Autosomal dominant		

Table S24: **Hydrolethalus syndrome 1 [MIM 236680].** Feature frequencies according to [17].

HPO Term	Term ID	Frequency
I-III toe syndactyly	HP:0001495	90.00%
Broad halluces	HP:0001834	89.00%
CHECK THIS	HP:0001159	82.00%
Broad nasal root	HP:0000424	79.00%
Postaxial polydactyly	HP:0001162	78.00%
High forehead	HP:0000348	70.00%
Frontal bossing	HP:0000254	58.00%
Macrocephaly	HP:0000256	52.00%
Hypertelorism	HP:0000316	main
Mild mental deficiency	HP:0001256	occasional
Umbilical hernia	HP:0001537	occasional
Cardiac abnormality	HP:0001627	occasional
Downward slanting palpebral fissures	HP:0000494	occasional
Preaxial polydactyly	HP:0006046	occasional
Agenesis of corpus callosum	HP:0001274	occasional
Camptodactyly	HP:0001160	occasional
Hyperglycemia	HP:0001943	occasional
Abnormality of muscle fibers	HP:0004303	occasional
Syndactyly	HP:0001159	occasional
Accelerated skeletal maturation	HP:0005616	occasional
Delayed closure of cranial sutures	HP:0002704	occasional
Postaxial polydactyly (feet)	HP:0001830	occasional
Hirsutism	HP:0001007	occasional
Hydrocephalus	HP:0000238	occasional
Inguinal hernia	HP:0000023	occasional
Seizures	HP:0001250	occasional
Craniosynostosis	HP:0001363	occasional
Hypospadias	HP:0000047	occasional
Cryptorchidism	HP:0000028	occasional
Inheritance: Autosomal dominant		

Table S25: **Greig cephalopolysyndactyly syndrome [MIM 175700].** Feature frequencies according to [3] and [18].

HPO Term	Term ID	Frequency
Pancreatic insuffiency *and* malabsorption	HP:0002581 *and* HP:0002024	100.00%
Hypoplastic nasal alae	HP:0000430	100.00%
Sparse scalp hair *and* frontal hair upsweep	HP:0002209 *and* HP:0002236	96.00%
Hypoplastic deciduous teeth	HP:0006334	90.00%
Absent permanent teeth	HP:0006349	90.00%
Scalp aplasia cutis congenita	HP:0007568	87.00%
Hypotonia	HP:0001318	80.00%
Sensorineural deafness	HP:0000374	75.00%
Mental retardation	HP:0001249	67.00%
Prenatal growth deficiency	HP:0001515	60.00%
Mild microcephaly	HP:0001366	50.00%
Imperforate anus *or* anteriorly placed anus	HP:0001550 *or* HP:0001545	40.00%
Hypothyroidism	HP:0000821	30.00%
Female: Hydronephrosis *and* septate vagina	HP:0000126 *and* HP:0001153	25.00%
Male: Hydronephrosis *and* cryptorchidism *and* micropenis *and* hypospadias	HP:0000126 *and* HP:0000028 *and* HP:0000054 *and* HP:0000047	25.00%
Rectovaginal fistula	HP:0000143	18.00%
Transverse palmar crease	HP:0000954	occasional
Diabetes mellitus	HP:0000819	occasional
Hypoplastic nipples	HP:0002557	occasional
Skull defect	HP:0001362	occasional
Strabismus	HP:0000486	occasional
Fifth finger clinodactyly	HP:0001158	occasional
EEG abnormalities	HP:0002253	occasional
Cardiac abnormalities	HP:0001627	occasional
Abdominal situs inversus *and* situs inversus	HP:0003362 *and* HP:0001696	occasional
Cafe-au-lait-spots	HP:0000957	occasional
Inheritance: Autosomal recessive		

Table S26: **Johanson-Blizzard syndrome [MIM 243800].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Wide palpebral fissures	HP:0000637	95.00%
Eversion of lateral third of lower eyelids	HP:0007655	90.00%
Developmental delay	HP:0000754	87.00%
Persistent fetal fingertip pads	HP:0001235	82.00%
Thick, arched eyebrows	HP:0004533	79.00%
Large, prominent ears	HP:0000382	79.00%
Flat nasal tip	HP:0000437	71.00%
Short Stature	HP:0001509	64.00%
Short fifth finger	HP:0004211	62.00%
Hyperextrnsible joints	HP:0001378	52.00%
Recurrent infections	HP:0002719	48.00%
Dental abnormality	HP:0000164	48.00%
Cleft palate	HP:0000175	44.00%
High-arched palage	HP:0000156	44.00%
cardiac abnormality	HP:0001627	37.00%
Feeding difficulties	HP:0002022	35.00%
Hypotonia	HP:0001318	30.00%
Microcephaly	HP:0000252	25.00%
Genitourinary abnormality	HP:0000119	23.00%
Strabismus	HP:0000486	22.00%
Blue sclerae	HP:0000592	21.00%
Micrognathia	HP:0000210	16.00%
Congenital hip dislocations	HP:0001374	11.00%
Ptosis	HP:0000508	11.00%
Broad nasal root	HP:0000424	9.00%
Seizures	HP:0001250	8.00%
Inheritance: Autosomal dominant		

Table S27: **Kabuki Syndrome [MIM 147920].** Feature frequencies according to [19].

HPO Term	Term ID	Frequency
Small chest	HP:0001590	12/12
Short, curved femora	HP:0009749	12/12
Metaphyseal flaring	HP:0003015	12/12
Severe micromelia	HP:0003030	12/12
Short, flared ribs	HP:0009750	10/12
Malar hypoplasia	HP:0000272	8/12
Tibial bowing	HP:0002982	7/12
Radial bowing	HP:0002986	7/12
Metacarpal hypoplasia	HP:0005695	typical
Short, dumbbell-shaped humeri	HP:0005009	typical
Decreased mobility of joints	HP:0001376	6/12
Platyspondyly	HP:0000926	5/12
Horizontal acetabular roof	HP:0003171	5/12
Micrognathia	HP:0000210	4/12
Ulnar hypoplasia	HP:0003022	2/12
Talipes equinovarus	HP:0001762	2/12
Bowed ulna	HP:0003031	1/12
Inheritance: Autosomal recessive		

Table S28: **Kyphomelic Dysplasia [MIM 211350].** Feature frequencies according to [20].

HPO Term	Term ID	Frequency
Short radius *and* Short ulna	HP:0002995 *and* HP:0002998	95%
Bifid thumb	HP:0001244	95%
Preaxial polydactyly	HP:0001177	95%
Aplasia of the 1st finger *and* Absent ossification/absence of radius	HP:0009637 *and* HP:0003974	95%
2-3 finger syndactyly	HP:0001233	95%
Broad halluces	HP:0001834	95%
Bilateral digitalized thumbs	HP:0005707	95%
Triphalangeal thumb	HP:0001199	95%
Clinodactyly, 3,5 finger	HP:0006181	95%
Thenar hypoplasia	HP:0001245	95%
Hypodontia *and/or* Peg-shaped incisors *and/or* Hypoplastic dental enamel *and/or* Delayed eruption of deciduous teeth	HP:0000668 *and/or* HP:0000673 *and/or* HP:0006297 *and/or* HP:0000680	90%
Simple, cup-shaped ears *and* Hypoplastic antihelix	HP:0008531 *and* Hypoplastic antihelix	70%
Mixed hearing loss	HP:0000410	55%
Severe dental caries	HP:00006295	typical
Aplastic/hypoplastic lacrimal puncta	HP:0007892	45%
Alacrima *and* Aplastic/hypoplastic lacrimal glands	HP:0000522 *and* HP:0008038	40%
Nasolacrimal duct obstruction	HP:0000579	main
Downward slanting palpebral fissures	HP:0000494	occasional
Renal agenesis	HP:0000104	occasional
Coronal hypospadias	HP:0008743	occasional
Aplasia of the parotid gland *and* Absence of Stensen duct	HP:0009740 *and* HP:0000198	occasional
Hypertelorismus *or* Telecanthus	HP:0000316 *or* HP:0000506	occasional
Nephrosclerosis	HP:00009741	occasional
Inheritance: Autosomal dominant		

Table S29: **Lacrimoauriculodentodigital syndrome type 1 [MIM 149730].** Also known as Levy-Hollister syndrome. Feature frequencies according to [3].

HPO Term	Term ID		Frequency
Mental retardation, moderate to severe	HP:0002316		100.00%
Seizures	HP:0001250		90.00%
Microcephaly	HP:0000252		84.00%
Megacolon	HP:0002029		62.00%
Pointer chin	HP:0000307		typical
Prominent nasal tip	HP:0005274		typical
Downward slanting palpebral fissures	HP:0000494		typical
Ptosis	HP:0000508		typical
Deep-set eyes	HP:0000490		typical
Constipation	HP:0002019		typical
Short stature	HP:0001509		typical
Columella extends below the ala nasi	HP:0009766		typical
Hypertelorism	HP:0000316		typical
Wide nasal bridge	HP:0000431		typical
Fleshy upturned lobules	HP:0009764		typical
Cup-shaped ears	HP:0000378		typical
Iris coloboma	HP:0000612		typical
Impaired speech development	HP:0002116		typical
Esotropia	HP:0000565		typical
Agenesis of corpus callosum	HP:0001274		42.00%
Abdominal distension	HP:0003720		frequent
Male: Bifid scrotum *and/or* Cryptorchidism *and/or* Hypospadias	HP:0000048 HP:0000028 HP:0000047	*and/or* *and/or*	frequent
Barium enema shows transition zone between aganglionic contracted segment and dilated proximal bowel	HP:0002606		frequent
Submucous cleft palate	HP:0000176		occasional
Inheritance: Autosomal dominant			

Table S30: **Mowat-Wilson syndrome [MIM 235730].** Feature frequencies according to [21].

HPO Term	Term ID	Frequency
Scoliosis	HP:0002650	10/10
Camptodactyly (feet)	HP:0001836	11/11
Micrognathia	HP:0000210	11/11
Dysplastic patella	HP:0006446	5/5
Contractures	HP:0001371	11/11
Bilateral camptodactyly	HP:0005617	11/11
Low-set ears	HP:0000369	10/11
Short stature	HP:0001509	10/11
Ptosis	HP:0000508	9/11
Downward-slanting palpebral fissures	HP:0000494	9/11
Female: Absence of labia majora	HP:0008729	4/5
Neonatal respiratory distress	HP:0002643	8/11
Talipes equinovarus	HP:0001762	8/11
Downturned corners of mouth	HP:0002714	8/11
Kyphosis	HP:0002808	7/10
Male: Cryptorchidism	HP:0000028	2/3
Neck pterygia	HP:0009759	7/11
Popliteal pterygia	HP:0009756	6/11
Syndactyly	HP:0001159	6/11
Epicanthal folds	HP:0000286	6/11
Microstomia	HP:0000160	typical
Long philtrum	HP:0000343	5/11
Dislocated radial head	HP:0003083	3/7
Axillary pterygium	HP:0001060	4/11
Fused cervical vertebrae	HP:0002949	3/10
Anterior clefting of vertebral bodies	HP:0009761	3/10
Antecubital pterygium	HP:0009760	3/11
Hearing loss, conductive	HP:0000405	3/11
Rib fusion	HP:0000902	2/9
Intercrural pterygium	HP:0009757	2/11
Cleft palate	HP:0000175	2/11
Inheritance: Autosomal recessive		

Table S31: **Multiple pterygium syndrome, Escobar variant [MIM 265000].** Feature frequencies according to [22].

HPO Term	Term ID		Frequency
Koilonychia *and/or* Anonychia *and/or* Longitudinal ridging	HP:0001598 HP:0001798 HP:0001801	*and/or* *and/or*	117/119
Absent distal interphalangeal creases	HP:0001032		114/119
Aplasia/Hypoplasia of the patella	HP:0006498		200/237
Limited elbow extension	HP:0001377		167/240
Iliac horns	HP:0009780		34/50
Pes planus	HP:0001763		76/118
Lester's sign	HP:0009781		64/119
Increased lumbar lordosis	HP:0002941		41/87
Pectus excavatum	HP:0000767		14/39
Scoliosis	HP:0002650		8/35
Talipes equinovarus	HP:0001762		23/122
Antecubital pterygium	HP:0009760		15/123
Glaucoma	HP:0000501		8/83
Quadriceps aplasia	HP:0009788		occasional
Triceps aplasia	HP:0009785		occasional
Biceps aplasia	HP:0009783		occasional
Pectoralis minor aplasia	HP:0005255		occasional
Inheritance: Autosomal dominant			

Table S32: **Nail-Patella Syndrome [MIM 161200].** Feature frequencies according to [23].

HPO Term	Term ID	Frequency
Neurofibromas	HP:0001067	100.00%
Cafe-au-lait spots	HP:0000957	100.00%
Lisch nodules	HP:0009737	95.00%
Freckling	HP:0001480	67.00%
Macrocephaly	HP:0000256	45.00%
Short stature	HP:0001509	31.00%
Learning disability	HP:0001328	30.00%
Plexiform neurofibroma	HP:0009732	30.00%
Scoliosis	HP:0002650	5.00%
Epilepsy	HP:0001275	4.00%
Tibial pseudarthrosis	HP:0009736	4.00%
Renal artery stenosis	HP:0001920	1.5%
Spinal neurofibromas	HP:0009735	1.5%
Hypsarrhthmia	HP:0002521	1.5%
Optic glioma	HP:0009734	1.5%
Rhabdomyosarcoma	HP:0002857	1.5%
Aqueduct stenosis	HP:0002410	1.5%
Pheochromocytoma	HP:0002666	1.00%
Meningioma	HP:0002858	Very rare
Glaucoma	HP:0000501	0.7%
Inheritance: Autosomal dominant		

Table S33: **Neurofibromatosis type 1 [MIM 162200].** Feature frequencies according to [24].

HPO Term	Term ID	Frequency
Bilateral vestibular schwannoma	HP:0009589	85.00%
Juvenile posterior subcapsular lenticular opacities	HP:0007935	72.00%
Peripheral schwannoma	HP:0009593	68.00%
Meningioma	HP:0002858	45.00%
Occasional cafe-au-lait spots	HP:0005601	43.00%
Juvenile cortical cataract	HP:0007876	41.00%
Hearing loss	HP:0000365	35.00%
Occasional neurofibromas	HP:0009595	27.00%
Tinnitus	HP:0000360	10.00%
Retinal hamartoma	HP:0009594	9.00%
Ataxia	HP:0001251	8.00%
Headache	HP:0000266	occasional
Unilateral vestibular schwannoma	HP:0009590	6.00%
Astrocytoma	HP:0009592	4.00%
Ependymoma	HP:0002888	2.5%
Inheritance: Autosomal dominant		

Table S34: **Neurofibromatosis type 2 [MIM 101000].** Feature frequencies according to [25] and [26].

HPO Term	Term ID		Frequency
Mental retardation	HP:0001249		97.00%
Frontal bossing	HP:0000254		95.00%
Frontal hair upsweep	HP:0002236		91.00%
Motor retardation *and/or* muscular hypotonia	HP:0001270	*and/or*	90.00%
	HP:0001252		
Downward slanting palpebral fissures	HP:0000494		85.00%
Ocular hypertelorismus	HP:0000316		83.00%
Broad thumbs and broad great toes	HP:0005833		81.00%
Wide anterior fontanel	HP:0000260		77.00%
Macrocephaly, postnatal	HP:0005490		74.00%
Seizures	HP:0001250		70.00%
Hyperactivity *and* Attention deficit disorder	HP:0000752 *and* HP:0001577		70.00%
Constipation	HP:0002019		69.00%
Abnormalitiy of the sternum	HP:0000766		69.00%
Small, simple ears	HP:0000379		66.00%
Mild vertebral anomalies	HP:0005719		64.00%
Transverse palmar crease	HP:0000954		60.00%
Epicanthal folds	HP:0000286		56.00%
Camptodactyly	HP:0001160		55.00%
Syndactyly	HP:0001159		54.00%
Clinodactyly	HP:0001157		53.00%
Strabismus	HP:0000486		52.00%
Persistent fetal fingertip pads	HP:0001235		50.00%
Prominent lower lip	HP:0000179		44.00%
Anal stenosis *and/or* imperforate anus *and/or* anteriorly	HP:0002025	*and/or*	38.00%
placed anus	HP:0001150	*and/or*	
	HP:0001545		
Cryptorchidism	HP:0000028		36.00%
Postnatal short stature	HP:0003501		main
Sacral dimple	HP:0000960		main
Partial or complete agenesis of the corpus callosum	HP:0007090		main
Narrow palate	HP:0000189		main
Multiple joint contractures	HP:0002828		main
Facial wrinkling	HP:0009762		main
Sparse hair *and* Fine hair	HP:0008070 *and* HP:0002213		main
Cardiac abnormality	HP:0001627		occasional
High-pitched voice	HP:0001620		occasional
Sensorineural deafness	HP:0000374		occasional
Ectrodactyly	HP:0001171		occasional
Short neck	HP:0000470		occasional
Hydrocaphalus	HP:0000236		occasional
Cleft palate	HP:0000175		occasional
Pyloric stenosis	HP:0002021		occasional
Neuronal migration disorder	HP:0002269		occasional
Choanal atresia	HP:0000453		occasional
Hypospadias	HP:0000047		occasional
Intestinal malrotation	HP:0002026		occasional
Inheritance: X-linked recessive			

Table S35: **Opitz-Kaveggia Syndrome [MIM 305450].** Note that the Opitz-Kaveggia syndrome is also known as FG syndrome-1. Feature frequencies according to [3].

HPO Term	Term ID		Frequency
Cleft palate	HP:0000175		53/57
Popliteal pterygium	HP:0009756		33/57
Cleft lip	HP:0000204		33/57
Cutaneous syndactyly	HP:0005637		29/57
Lower lip pits	HP:0000196		26/57
Syngnathia	HP:0009754		23/57
Male: Scrotal haypoplastic *and/or* Bifidscrotum *and/or*	HP:0000046	*and/or*	21/57
Cryptorchidism	HP:0000048	*and/or*	
	HP:0000028		
Female: Hypoplastic uterus *and/or* Hypoplastic vagina	HP:0000013	*and/or*	21/57
and/or Hypoplastic labia majora	HP:0000726	*and/or*	
	HP:0000059		
Pyramidal skinfold extending from the base to the top of the nails	HP:0009758		19/57
Ankyloblepharon	HP:0009755		10/57
Talipes equinovarus	HP:0001762		8/57
Intercrural pterygium	HP:0009757		5/57
Spina bifida occulta	HP:0003298		occasional
Inheritance: Autosomal dominant			

Table S36: **Popliteal Pterygium syndrome [MIM 119500].** Feature frequencies according to [27].

HPO Term	Term ID	Frequency
Mental retardation	HP:0001249	100.00%
Broad great toes	HP:0003094	100.00%
Hypoplastic maxilla *and* Narrow palate	HP:000032 *and* HP:0000189	100.00%
Beaked nose	HP:0000444	90.00%
Short columella	HP:0002000	90.00%
Poor speech	HP:0002465	90.00%
Downward slanting palpebral fissures	HP.0000494	88.00%
Long eyelashes	HP:0000527	87.00%
Broad thumbs	HP:0001173	87.00%
Unsteady gait	HP:0002317	85.00%
Abnormal form of ears	HP:0000377	84.00%
Male: Cryptorchidism	HP:0000028	78.00%
Heavy eyebrows	HP:0000574	76.00%
Hirsutism	HP:0001007	75.00%
Delayed skeletal maturation	HP:0002750	74.00%
Highly arched eyebrows	HP:0001584	73.00%
Pes planus	HP:0001763	72.00%
Deviated nasal septum	HP:0004411	71.00%
Strabismus	HP:0000486	69.00%
Hypotonia	HP.0001318	67.00%
Fifth finger clinodactyly	HP:0001158	62.00%
EEG abnormality	HP:0002353	57.00%
Small opening of mouth	UPDATE	56.00%
Epicanthal folds	HP:0000286	55.00%
Spina bifida occulta	HP:0003298	47.00%
Nasolacrimal duct obstruction	HP:0000579	43.00%
Scoliosis	HP:0002650	42.00%
Low posterior hairline	HP:0002162	42.00%
Wide anterior fontanel	HP:0000260	41.00%
Hyperreflexia	HP:0001282	40.00%
Microcephaly	HP:0000252	35.00%
Frontal bossing	HP:0000254	33.00%
Atrial septal defect *or* Ventricular spetal defect *or* patent ductus arteriosus	HP:0001631 *or* HP:0001629 *or* HP:0001643	33.00%
Deep plantar crease between first and second toes	HP:0008107	33.00%
Persistent fetal fingertip pads	HP:0001135	31.00%
Small, flared iliac wings	HP:0003181	26.00%
Postnatal growth deficiency	HP:0001514	main
Capillary hemangiomas	HP:0005306	25.00%
Low frontal hairline	HP:0000294	24.00%
Delayed closure of fontanel	HP:0000270	24.00%
Seizures	HP:0001250	23.00%
Enophthalmos	HP:0000663	22.00%
Frontal hair up-sweep	HP:0002236	20.00%
Transverse palmar creases	HP:0000954	occasional
Large foramen magnum	HP:0002700	occasional
Ptosis	HP:0000508	occasional
Micrognathia	HP:0000210	occasional
Polydactyly	HP:0001161	occasional
Abnormality of the sternum	HP:0000766	occasional
Male: Shawl scrotum	HP:0000049	occasional
Syndactyly	HP:0001159	occasional
Male: Hypospadias	HP:0000047	occasional
Caf-au-lait spots	HP:0000957	occasional
Glaucoma	HP:0000501	occasional
Parietal foramina	HP:0002697	occasional
Dislocation of patella	HP:0002999	occasional
Cataract	HP:0000518	occasional
Inheritance: Autosomal dominant		

Table S37: **Rubinstein-Taybi syndrome [MIM 180849].** Feature frequencies according to [3].

HPO Term	Term ID	Frequency
Arachnodactyly	HP:0001166	34/37
Micrognathia	HP:0000210	33/37
Developmental delay	HP:0000754	32/37
Low-set, posteriorly rotated ears	HP:0000368	32/37
Downward slanting palpebral fissures	HP:0000494	31/37
Abnormality of the sternum	HP:0000766	30/37
High-arched palate	HP:0000156	30/37
Exophthalmos	HP:0000645	29/37
Dolichocephaly	HP:0000268	28/37
Hypertelorism	HP:0000316	28/37
Hypotonia	HP:0001318	26/37
Camptodactyly	HP:0001160	24/37
Scoliosis	HP:0002650	23/37
Increased mobility of joints	HP:0001382	21/37
Abnormal form of ears	HP:0000377	20/37
Inguinal hernia	HP:0000023	19/37
Craniosynostosis	HP:0001363	18/37
High, prominent forehead	HP:0000254	17/37
Strabismus	HP:0000486	17/37
Ptosis	HP:0000508	16/37
Maxillary hypoplasia	HP:0000327	16/37
Umbilical hernia	HP:0001537	13/37
Mitral valve prolapse	HP:0001634	13/37
Talipes equinovarus	HP:0001762	13/37
Hydrocephalus	HP:0000238	13/37
Abnormality of the vertebral column	HP:0000925	10/37
Reduced subcutaneous adipose tissue	HP:0003758	10/37
Osteopenia	HP:0000938	10/37
Wide anterior fontanel	HP:0000260	9/37
Feeding difficulties	HP:0002022	9/37
Shallow orbits	HP:0000586	9/37
Myopia	HP:0000545	9/39
Upturned nose	HP:0000427	9/39
Aortic dilatation	HP:0001724	8/37
Joint contractures	HP:0001372	7/37
Skin hyperelasticity	HP:0007389	7/37
Microcephaly	HP:0000252	6/37
Obstructive sleep apnea	HP:0002870	6/37
Hooked clavicles	HP:0000895	6/37
Bowing of the long bones	HP:0006487	5/37
Dislocated radial head	HP:0003083	5/37
Abdominal wall muscle weakness	HP:0009023	5/37
Supernumerary ribs	HP:0005815	5/37
Hearing loss, conductive	HP:0000405	5/37
Genu valgum	HP:0002857	4/37
Widened metaphyses	HP:0003016	4/37
Gastroesophageal reflux	HP:0002020	4/37
Cryptorchidism	HP:0000028	4/37
Inheritance: Isolated cases		

Table S38: **Shprintzen-Goldberg Craniosynostosis Syndrome [MIM 182212].** Feature frequencies according to [28].

HPO Term	Term ID		Frequency
2-3 toe syndactyly	HP:0004691		99.00%
Mental retardation	HP:0001249		156/164
Flat, broad nasal bridge	HP:0000439		hallmark
Microcephaly	HP:0000252		138/164
Failure to thrive	HP:0001508		134/164
Anteverted nostrils	HP:0000463		123/164
Ptosis	HP:0000508		115/164
Micrognathia	HP:0000210		typical
Long philtrum	HP:0000343		typical
Feeding difficulties	HP:0002022		typical
Bitemporal narrowing	HP:0000314		typical
Hypoplastic corpus callosum	HP:0002079		common
Hypoplastic thumb	HP:0009628		typical
Frontal lobe hypoplasia	HP:0002424		common
Male: Hypospadias	HP:0000047		common
Periventricular gray matter heterotopias	HP:0007165		typical
Broad alveolar ridges	HP:0000187		typical
Postaxial polydactyly (feet) *and/or* Postaxial polydactyly	HP:0001830 HP:0001162	*and/or*	79/164
Cleft palate	HP:0000175		77/164
Defective lung lobation	HP:0009753		74/164
Posteriorly rotated ears	HP:0000358		frequent
Renal agenesis	HP:0000104		frequent
Hydronephrosis	HP:0000121		frequent
Low-set ears	HP:0000369		frequent
Cataract	HP:0000518		36/164
Atrial septal defect	HP:0001631		20.00%
Patent ductus arteriosus	HP:0001643		18.00%
Pyloric stenosis	HP:0002021		23/164
Ventricular septal defect	HP:0001629		10.00%
Hypertelorism	HP:0000316		occasional
Epicanthal folds	HP:0000286		occasional
Inheritance: Autosomal recessive			

Table S39: **Smith-Lemli-Opitz Syndrome [MIM 270400].** Feature frequencies according to [29].

HPO Term	Term ID	Frequency
Ectrodactyly	HP:0001171	99/134
Aplasia the tibia	HP:0009556	79/134
Aplasia/hypoplasia of the ulna	HP:0006495	16/134
Absent fingers	HP:0004093	occasional
Metatarsus adductus	HP:0001768	occasional
Lower limb hypotrophy	HP:0007210	occasional
Preaxial polydactyly	HP:0001177	occasional
Knee contractures *and* Patellar hypoplasia	HP:0002978 *and* HP:0003065	occasional
Syndactyly	HP:0001159	occasional
Aplasia/hypoplasia of the humerus	HP:0006507	occasional
Talipes equinovarus	HP:0001762	occasional
Proximally placed thumbs	HP:0001170	occasional
Monodactyly	HP:0004058	occasional
Aplasia/hypoplasia of the radius	HP:0006501	occasional
Craniosynostosis	HP:0001363	occasional
Aplasia/hypoplasia of femur	HP:0005613	occasional
Ectrodactyly (feet)	HP:0001839	occasional
Aplastic/hypoplastic halluces	HP:0008118	8/134
Postaxial polydactyly	HP:0001162	6/134
Cup-shaped ears	HP:0000378	2/134
Inheritance: autosomal dominant with widely variable expression and frequent nonpenetrance in normal obligate carriers		

Table S40: **Split-Hand/foot Malformation with long bone deficiency 1 (SHFLD1) [MIM 119100].** Feature frequencies according to [3] and [30].

HPO Term	Term ID		Frequency
Preaxial polydactyly	HP:0001177		common
Sensorineural deafness	HP:0000374		typical
Triphalangeal thumb	HP:0001199		common
Microtia *or* Preauricular pit *or* Preauricular skin tag	HP:0000393	*and/or*	typical
	HP:0000392	*and/or*	
	HP:0000384		
Fifth toe clinodactyly	HP:0001864		common
Anal atresia	HP:0002023		31/66
Multicystic kidneys	HP:0000003		occasional
Renal failure	HP:0000083		occasional
Renal dysplasia	HP:0000110		occasional
2-3 and 3-4 finger syndactyly	HP:0006018		occasional
Renal hypoplasia	HP:0000089		occasional
Vesicoureteral reflux	HP:0000076		occasional
Inheritance: Autosomal dominant			

Table S41: **Townes-Brocks Syndrome [MIM 107480].** Feature frequencies according to [31].

HPO Term	Term ID	Frequency
Malar hypoplasia	HP:0000272	89.00%
Downward slanting palpebral fissures	HP:0000494	89.00%
Mandibular hypoplasia	HP:0000347	78.00%
Abnormal form of ears	HP:0000377	77.00%
Lower eyelid coloboma	HP:0000652	69.00%
Partial-total absence of lower eyelashes	HP:0007785	53.00%
Conductive deafness	HP:0000367	40.00%
Visual loss	HP:0000572	37.00%
auditory canal abnormality	HP:0000372	36.00%
Cleft soft palate	HP:0000185	32.00%
Cleft palate	HP:0000175	28.00%
Projection of scalp hair onto lateral cheek	HP:0009554	26.00%
Hypoplasia of the pharynx	HP:0009555	occasional
Microstomia	HP:0000160	occasional
Ptosis	HP:0000508	occasional
Abnormality of the parotid gland	HP:0000197	occasional
Upper eyelid coloboma	HP:0000636	occasional
Preauricular sinus	PH:0004467	occasional
Strabismus	HP:0000486	occasional
Cryptorchism	HP:0000028	occasional
Macrostomia	HP:0000181	occasional
Nasolacrimal duct stenosis	HP:0007678	occasional
Preauricular skin tag	HP:0000384	occasional
Microphtalmia, bilateral	HP:0001585	occasional
Choanal atresia	HP:0000453	occasional
Cardiac malformation	HP:0002564	occasional
Mental retardation	HP:0001249	5.00%
Inheritance: autosomal dominant		

Table S42: **Treacher Collins Syndrome [MIM 154500].** Feature frequencies according to [3] and [32].

HPO Term	Term ID	Frequency
Subependymal nodules	HP:0009716	95.00%
Cerebral hamartomata	HP:0009731	93.00%
Cortical tubers	HP:0000717	93.00%
Facial angiofibromas	HP:0009720	85.00%
Hypomelanotic macules	HP:0009719	82.00%
Seizures *or* Infantile spasms	HP:0001250 *or* HP:0002391	78.00%
Mental retardation	HP:0001249	53.00%
Multiple bilateral renal angiomyolipoma	HP:0006772	52.00%
Cardiac rhabdomyoma	HP:0009729	50.00%
Subcutaneous nodules	HP:0001482	typical
Retinal hamartoma	HP:0009554	50.00%
Behavioral disturbances	HP:0000715	50.00%
dental enamel pit	HP:0009722	48.00%
Subungual fibromata	HP:0009724	32.00%
Shagreen patch	HP:0009721	31.00%
Achromatic retinal patches	HP:0009727	13.00%
Subependymal giant-cell astrocytoma	HP:0009717	10.00%
Renal cysts	HP:0000107	10.00%
Renal cell carcinoma	HP:0005584	rare
Inheritance: Autosomal dominant		

Table S43: **Tuberous Sclerosis [MIM 191100].** Feature frequencies according to [5].

HPO Term	Term ID	Frequency
Cerebellar hemangioblastoma	HP:0006880	59%
Retinal capillary hemangioma	HP:0009711	59%
Pancreatic cysts	HP:0001737	40%
Multiple renal cysts	HP:0005562	28%
Renal cell carcinoma	HP:0005584	28%
Papillary cystadenoma of the epididymis	HP:0009715	26%
Spinal hemangioblastoma	HP:0009713	13%
Pheochromocytoma	HP:0002666	13%
Inheritance: autosomal dominant		

Table S44: **von Hippel Lindau Syndrome [MIM 193300].** Feature frequencies according to [24] and [33].

HPO Term	Term ID	Frequency
Cerebellar malformation	HP:0002438	100.00%
Type II lissencephaly	HP:0007260	100.00%
Retinal malformation	HP:0007901	100.00%
Congenital muscular dystrophy	HP:0003741	100.00%
Ventriculomegaly	HP:0002189	95.00%
Anterior chamber malformation	HP:0007699	91.00%
Male: Abnormalities of the genital tract	HP:0000078	65.00%
Hydrocephaly	HP:0000238	53.00%
Microphthalmos	HP:0000568	53.00%
Dandy-Walker malformation	HP:0001305	53.00%
Congenital contractures	HP:0002803	43.00%
Thick cerebral cortex	HP:0006891	main
Detached retina *and* Retinal dysplasia	HP:0000541 *and* HP:0007973	main
Agenesis of corpus callosum *or* Hypoplastic corpus callosum	HP:0001274 *or* HP:0002079	main
Absent septum pellucidum	HP:0006891	main
Occipital encephalocele	HP:0002085	24.00%
Coloboma	HP:0000589	24.00%
Microcephaly	HP:0000252	16.00%
Cleft lip/palate	HP:0000202	14.00%
External auditory canal atresia	HP:0000413	occasional
Megalocornea	HP:0000485	occasional
Imperforate anus	HP:0001550	occasional
Renal dysplasia	HP:0000110	occasional
Microtia	HP:0000393	occasional
Inheritance: Autosomal recessive		

Table S45: **Walker-Warburg syndrome [MIM 236670].** Feature frequencies according to [3].

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