**Table S1.** Table showing the complete list of included RD in the study.

| Rare Disease Name | ORPHA Code |
|---|---|
| 15q13.3 microdeletion syndrome | 199318 |
| 16p13.3 microduplication syndrome | 96078 |
| 17p11.2 microduplication syndrome | 1713 |
| 1p36 deletion síndrome | 1606 |
| 22q11.2 deletion syndrome | 567 |
| 3q29 microdeletion syndrome | 65286 |
| 4p16.3 microduplication syndrome | 96072 |
| Achondroplasia | 15 |
| Achromatopsia | 49382 |
| Acrodysostosis | 950 |
| Acromegaly | 963 |
| Acute intermittent porphyria | 79276 |
| Addison disease | 85138 |
| Adenosine monophosphate deaminase deficiency | 45 |
| ADNP syndrome | 404448 |
| Adult-onset cervical dystonia | 420492 |
| Adult-onset foveomacular vitelliform dystrophy | 99000 |
| Adult-onset Still disease | 829 |
| Aicardi syndrome | 50 |
| Alagille syndrome due to a JAG1 point mutation | 261619 |
| Alkaptonuria | 56 |
| Allan-Herndon-Dudley syndrome | 59 |
| Alopecia universalis | 701 |
| Alpha-1-antitrypsin deficiency | 60 |
| Alpha-sarcoglycan-related limb-girdle muscular dystrophy R3 | 62 |
| Alström syndrome | 64 |
| Alternating hemiplegia of childhood | 2131 |
| American trypanosomiasis | 3386 |
| Amyotrophic lateral sclerosis | 803 |
| Angelman syndrome | 72 |
| Anorectal malformation | 96346 |
| Antiphospholipid syndrome | 80 |
| Antisynthetase syndrome | 81 |
| Arachnoid cyst | 2356 |
| Arachnoiditis | 137817 |
| Arnold-Chiari malformation type I | 268882 |
| Arnold-Chiari malformation type I/Arnold-Chiari malformation type II | 268882/1136 |
| Arnold-Chiari malformation type II | 1136 |
| Arthrogryposis multiplex congenita | 1037 |
| ATTRV122I amyloidosis | 85451 |
| Autism spectrum disorder due to AUTS2 deficiency | 352490 |
| Autoimmune hepatitis | 2137 |
| Autoimmune pancreatitis | 103919 |
| Autoimmune polyendocrinopathy type 1 | 3453 |
| Autoimmune polyendocrinopathy type 2 | 3143 |
| Autosomal dominant cerebellar ataxia | 99 |
| Autosomal dominant Charcot-Marie-Tooth disease type 2K | 99944 |
| Autosomal dominant chorioretinopathy-microcephaly syndrome | 1432 |
| Autosomal dominant intellectual disability-craniofacial anomalies-cardiac defects syndrome | 457193 |
| Autosomal dominant non-syndromic intellectual disability | 178469 |
| Autosomal dominant spastic paraplegia type 3 | 100984 |
| Autosomal dominant spastic paraplegia type 4 | 100985 |
| Autosomal erythropoietic protoporphyria | 79278 |
| Autosomal recessive cerebellar ataxia | 1172 |
| Autosomal recessive cerebelloparenchymal disorder type 3 | 1170 |
| Autosomal recessive congenital ichthyosis | 281097 |
| Autosomal recessive spastic paraplegia type 76 | 488594 |
| Bardet-Biedl syndrome | 110 |
| Becker muscular dystrophy | 98895 |
| Behçet disease | 117 |
| Benign concentric annular macular dystrophy | 251287 |
| Bernard-Soulier syndrome | 274 |
| Best vitelliform macular dystrophy | 1243 |
| Bilateral generalized polymicrogyria | 208447 |
| Bilateral striopallidodentate calcinosis | 1980 |
| Bipartite talus | 364198 |
| Blackfan-Diamond anemia | 124 |
| Bohring-Opitz syndrome | 97297 |

| | |
|---|---|
| Borjeson-Forssman-Lehmann syndrome | 127 |
| Brittle cornea syndrome | 90354 |
| Bronchiolitis obliterans with obstructive pulmonary disease | 1303 |
| Brown-Vialetto-van Laere syndrome type II | 97229 |
| Brugada syndrome | 130 |
| Bullous pemphigoid | 703 |
| Calpain-3-related limb-girdle muscular dystrophy R1 | 267 |
| Cardiofaciocutaneous syndrome | 1340 |
| Carnitine palmitoyltransferase II deficiency | 157 |
| Caroli disease | 53035 |
| Catecholaminergic polymorphic ventricular tachycardia | 3286 |
| Caudal regression sequence | 3027 |
| Central areolar choroidal dystrophy | 75377 |
| Central diabetes insipidus | 178029 |
| Cerebral autosomal dominant arteriopathy-subcortical infarcts-leukoencephalopathy | 136 |
| Charcot-Marie-Tooth disease type 1A | 101081 |
| Charcot-Marie-Tooth disease/Hereditary motor and sensory neuropathy | 166 |
| CHD3-related developmental delay-speech delay-intellectual disability-abnormalities of vision-facial dysmorphism syndrome | 599082 |
| Childhood disintegrative disorder | 168782 |
| Cholesteryl ester storage disease | 75234 |
| Choroideremia | 180 |
| Chronic inflammatory demyelinating polyneuropathy | 2932 |
| Clark-Baraitser syndrome | 600731 |
| Classic Bartter syndrome | 93605 |
| Classic galactosemia | 79239 |
| Classic glucose transporter type 1 deficiency syndrome | 71277 |
| Classic mycosis fungoides | 2584 |
| Clippers | 284448 |
| Coffin-Siris syndrome | 1465 |
| Cogan syndrome | 1467 |
| Cohen syndrome | 193 |
| Combined dystonia | 98203 |
| Combined oxidative phosphorylation defect type 23 | 444013 |
| Combined pituitary hormone deficiencies, genetic forms | 95494 |
| Common variable immunodeficiency | 1572 |
| Complex regional pain syndrome type 1 | 99995 |
| Complex regional pain syndrome type 2 | 99994 |
| Cone rod dystrophy | 1872 |
| Congenital erythropoietic porphyria | 79277 |
| Congenital factor VII deficiency | 327 |
| Congenital factor XI deficiency | 329 |
| Congenital fiber-type disproportion myopathy | 2020 |
| Congenital fibrosis of extraocular muscles | 45358 |
| Congenital glaucoma | 98976 |
| Congenital hypothyroidism | 442 |
| Congenital limbs-face contractures-hypotonia-developmental delay syndrome | 562528 |
| Congenital pulmonary lymphangiectasia | 2414 |
| Constitutional megaloblastic anemia due to vitamin B12 metabolism disorder | 98396 |
| Cornelia de Lange syndrome | 199 |
| Cowden syndrome | 201 |
| CREST syndrome | 90290 |
| Crisponi syndrome | 1545 |
| Cushing disease | 96253 |
| Cutaneous mastocytosis | 66646 |
| Cystic fibrosis | 586 |
| Dent disease | 1652 |
| Dermatomyositis | 221 |
| Desmoid tumor | 873 |
| Diffuse cutaneous mastocytosis | 79456 |
| Diffuse neonatal hemangiomatosis | 2123 |
| Disorder of fructose metabolism | 308463 |
| Disorder of urea cycle metabolism and ammonia detoxification | 79167 |
| Distal monosomy 12p | 280325 |
| Distal myotilinopathy | 98911 |
| Distal renal tubular acidosis | 18 |
| Distal spinal muscular atrophy | 53739 |
| Dravet síndrome | 33069 |
| Duane retraction syndrome | 233 |
| Duchenne muscular dystrophy | 98896 |
| Dural sinus malformation | 97339 |
| Dystrophic epidermolysis bullosa | 303 |
| Early infantile epileptic encephalopathy | 1934 |
| Early-onset generalized limb-onset dystonia | 256 |
| Early-onset non-syndromic cataract | 91492 |
| Ectrodactyly with and without other manifestations | 498477 |
| Ehlers-Danlos syndrome | 98249 |
| Eosinophilic esophagitis | 73247 |

| | |
|---|---|
| Eosinophilic fasciitis | 3165 |
| Eosinophilic gastroenteritis | 2070 |
| Eosinophilic granulomatosis with polyangiitis | 183 |
| Epidermolysis bullosa simplex | 304 |
| Epithelioid hemangioendothelioma | 157791 |
| Esophageal atresia | 1199 |
| Essential iris atrophy | 98981 |
| Essential thrombocythemia | 3318 |
| F12-related hereditary angioedema with normal C1Inh | 100054 |
| Fabry disease | 324 |
| Facioscapulohumeral dystrophy | 269 |
| Familial drusen | 75376 |
| Familial exudative vitreoretinopathy | 891 |
| Familial Mediterranean fever | 342 |
| Familial paroxysmal ataxia | 97 |
| Febrile infection-related epilepsy syndrome | 163703 |
| Female restricted epilepsy with intellectual disability | 101039 |
| Fibrodysplasia ossificans progressiva | 337 |
| Focal, segmental or multifocal dystonia | 1866 |
| FOXG1 syndrome | 561854 |
| Fragile X syndrome | 908 |
| Friedreich ataxia | 95 |
| Gastrointestinal stromal tumor | 44890 |
| Gaucher disease type 1 | 77259 |
| Gitelman syndrome | 358 |
| Global developmental delay-neuro-ophthalmological abnormalities-seizures-intellectual disability syndrome | 488613 |
| Glutaryl-CoA dehydrogenase deficiency | 25 |
| Glycogen storage disease due to muscle glycogen phosphorylase deficiency | 368 |
| GNAO1-related developmental delay-seizures-movement disorder spectrum | 592564 |
| Goldenhar syndrome | 374 |
| Gorlin syndrome | 377 |
| Granulomatosis with polyangiitis | 900 |
| GRIN2B-related developmental delay, intellectual disability and autism spectrum disorder | 589547 |
| Gyrate atrophy of choroid and retina | 414 |
| Hemolytic anemia due to red cell pyruvate kinase deficiency | 766 |
| Hereditary angioedema type 1 | 100050 |
| Hereditary angioedema type 2 | 100051 |
| Hereditary fructose intolerance | 469 |
| Hereditary hemorrhagic telangiectasia | 774 |
| Hereditary motor and sensory neuropathy type 5 | 64751 |
| Hereditary neuropathy with liability to pressure palsies | 640 |
| Hereditary spastic paraplegia | 320335 |
| Hidrotic ectodermal dysplasia | 189 |
| Hinman syndrome | 84085 |
| Hirschsprung disease | 388 |
| Holt-Oram syndrome | 392 |
| Horizontal gaze palsy with progressive scoliosis | 2744 |
| Huntington disease | 399 |
| Hyperlipoproteinemia type 1 | 411 |
| Hypermobile Ehlers-Danlos syndrome | 285 |
| Hypohidrotic ectodermal dysplasia | 238468 |
| Hypoxanthine guanine phosphoribosyltransferase partial deficiency | 79233 |
| Ichthyosis | 79354 |
| Idiopathic achalasia | 930 |
| Idiopathic hypersomnia | 33208 |
| Idiopathic intracranial hypertension | 238624 |
| Idiopathic multicentric Castleman disease | 570431 |
| Idiopathic pleuroparenchymal fibroelastosis | 494428 |
| Idiopathic pulmonary arterial hypertension | 275766 |
| Idiopathic pulmonary fibrosis | 2032 |
| IgG4-related retroperitoneal fibrosis | 49041 |
| Immune thrombocytopenia | 3002 |
| Inclusion body myopathy with Paget disease of bone and frontotemporal dementia | 52430 |
| Indolent systemic mastocytosis | 98848 |
| Intellectual disability syndrome due to a DYRK1A point mutation | 464311 |
| Intellectual disability-cataracts-calcified pinnae-myopathy syndrome | 3042 |
| Intellectual disability-craniofacial dysmorphism-cryptorchidism syndrome | 329224 |
| Intellectual disability-expressive aphasia-facial dysmorphism syndrome | 436151 |
| Intellectual disability-facial dysmorphism syndrome due to SETD5 haploinsufficiency | 404440 |
| Intellectual disability-macrocephaly-hypotonia-behavioral abnormalities syndrome | 457279 |
| Interstitial cistitis | 37202 |
| Inverted duplicated chromosome 15 syndrome | 3306 |

| | |
|---|---|
| IRF2BPL-related regressive neurodevelopmental disorder-dystonia-seizures syndrome | 597623 |
| Isolated aniridia | 250923 |
| Isolated biliary atresia | 30391 |
| Isolated complex I deficiency | 2609 |
| Isolated complex III deficiency | 1460 |
| Isolated congenital hypogonadotropic hypogonadism | 238666 |
| Isolated corpus callosum agenesis | 200 |
| Isolated cytochrome C oxidase deficiency | 254905 |
| Isolated Klippel-Feil syndrome | 2345 |
| Isolated optic neuritis | 499096 |
| Isolated scaphocephaly | 35093 |
| Juvenile dermatomyositis | 93672 |
| Juvenile overlap myositis | 329894 |
| Juvenile xanthogranuloma | 158000 |
| Kabuki syndrome | 2322 |
| KBG syndrome | 2332 |
| KCNQ2-related epileptic encephalopathy | 439218 |
| Kennedy disease | 481 |
| Kleine-Levin syndrome | 33543 |
| Klippel-Trénaunay syndrome | 90308 |
| Koolen-De Vries syndrome | 96169 |
| Lamb-Shaffer syndrome | 530983 |
| Laminin subunit alpha 2-related congenital muscular dystrophy | 258 |
| Langerhans cell histiocytosis | 389 |
| Larsen syndrome | 503 |
| Leber congenital amaurosis | 65 |
| Leber hereditary optic neuropathy | 104 |
| Legg-Calvé-Perthes disease | 2380 |
| Leigh syndrome | 506 |
| Limb-girdle muscular dystrophy | 263 |
| Localized dystrophic epidermolysis bullosa, acral form | 158673 |
| Localized scleroderma | 90289 |
| Lymphangioleiomyomatosis | 538 |
| Lynch syndrome | 144 |
| Marfan syndrome | 558 |
| McLeod neuroacanthocytosis syndrome | 59306 |
| Medium chain acyl-CoA dehydrogenase deficiency | 42 |
| Megalencephalic leukoencephalopathy with subcortical cysts | 2478 |
| Megalencephaly | 2477 |
| Megalencephaly-capillary malformation-polymicrogyria syndrome | 60040 |
| Melkersson-Rosenthal syndrome | 2483 |
| Melorheostosis | 2485 |
| Menke-Hennekam syndrome | 592574 |
| Mesial temporal lobe epilepsy with hippocampal sclerosis | 99701 |
| Metaphyseal chondrodysplasia, Jansen type | 33067 |
| Methylmalonic acidemia with homocystinuria, type cblC | 79282 |
| Microcornea-posterior megalolenticonus-persistent fetal vasculature-coloboma syndrome | 231736 |
| Mitochondrial myopathy | 206966 |
| Mitochondrial myopathy-lactic acidosis-deafness syndrome | 2597 |
| Mixed connective tissue disease | 809 |
| Monoclonal mast cell activation syndrome | 529468 |
| Monomelic amyotrophy | 65684 |
| Monosomy 18p | 1598 |
| Monosomy 22q13.3 | 48652 |
| Monosomy 5p | 281 |
| Monosomy 9p | 261112 |
| Motor neuron disease | 98503 |
| Mucopolysaccharidosis type 2 | 580 |
| Mucopolysaccharidosis type 3 | 581 |
| Multiminicore myopathy | 598 |
| Multiple endocrine neoplasia type 2[a] | 247698 |
| Multiple endocrine neoplasia type 2B | 247709 |
| Multiple myeloma | 29073 |
| Multiple osteochondromas | 321 |
| Muscular dystrophy | 98473 |
| Myasthenia gravis | 589 |
| Myelomeningocele | 93969 |
| Myhre syndrome | 2588 |
| Myoclonus-dystonia syndrome | 36899 |
| Myopic macular degeneration | 178493 |
| Narcolepsy type 1 | 2073 |
| Narcolepsy type 1 | 2073 |
| Narcolepsy type 2 | 83465 |
| Neuralgic amyotrophy | 2901 |
| Neuroacanthocytosis | 263440 |
| Neurofibromatosis type 1 | 636 |
| Neurofibromatosis type 2 | 637 |
| Neuromyelitis optica spectrum disorder | 71211 |
| Nicolaides-Baraitser syndrome | 3051 |

| | |
|---|---|
| Niemann-Pick disease type B | 77293 |
| Non-acquired panhypopituitarism | 90695 |
| Non-specific early-onset epileptic encephalopathy | 442835 |
| Noonan syndrome | 648 |
| Noonan syndrome with multiple lentigines | 500 |
| Noonan syndrome-like disorder with loose anagen hair | 2701 |
| NRXN1-related severe neurodevelopmental disorder-motor stereotypies-chronic constipation-sleep-wake cycle disturbance | 600663 |
| Oculopharyngeal muscular dystrophy | 270 |
| Oligodontia | 99798 |
| Ollier disease | 296 |
| Opsoclonus-myoclonus syndrome | 1183 |
| Oromandibular dystonia | 93958 |
| Osteochondritis dissecans | 2764 |
| Osteogenesis imperfecta | 666 |
| Osteogenesis imperfecta type 4 | 216820 |
| Overlapping connective tissue disease | 251312 |
| Paroxysmal nocturnal hemoglobinuria | 447 |
| Partial deletion of the long arm of chromosome 18 | 262146 |
| Partial deletion of the long arm of chromosome 2 | 262010 |
| Partial trisomy/tetrasomy of the short arm of chromosome 12 | 262658 |
| Pelizaeus-Merzbacher disease | 702 |
| Pemphigus vulgaris | 704 |
| Perineural cyst | 65250 |
| Peroxisome biogenesis disorder | 79189 |
| Peutz-Jeghers syndrome | 2869 |
| Phenylketonuria | 716 |
| Pigmented villonodular synovitis | 66627 |
| Pitt-Hopkins syndrome | 2896 |
| PMM2-CDG | 79318 |
| Poland syndrome | 2911 |
| Polyarteritis nodosa | 767 |
| Polycythemia vera | 729 |
| Porphyria variegata | 79473 |
| Postpoliomyelitis syndrome | 2942 |
| Postural orthostatic tachycardia syndrome due to NET deficiency | 443236 |
| Potocki-Shaffer syndrome | 52022 |
| Prader-Willi syndrome | 739 |
| Primary ciliary dyskinesia, Kartagener type | 98861 |
| Primary erythromelalgia | 90026 |
| Primary hypereosinophilic syndrome | 314950 |
| Primary progressive aphasia | 95432 |
| Progressive cone dystrophy | 1871 |
| Progressive hemifacial atrophy | 1214 |
| Prolidase deficiency | 742 |
| Proximal 16p11.2 microdeletion syndrome | 261197 |
| Pseudoachondroplasia | 750 |
| Pseudohypoparathyroidism | 97593 |
| Pseudohypoparathyroidism type 1A | 79443 |
| Pseudoxanthoma elasticum | 758 |
| Pudendal neuralgia | 60039 |
| Pulmonary alveolar microlithiasis | 60025 |
| Pulmonary arterial hypertension associated with another disease | 275791 |
| Punctate palmoplantar keratoderma | 307967 |
| Radial hemimelia | 93321 |
| Rapid-onset dystonia-parkinsonism | 71517 |
| Rare dystonia | 68363 |
| Rare genetic dystonia | 391799 |
| Rare hereditary ataxia | 183518 |
| Rare inflammatory bowel disease | 104012 |
| Rare pulmonary hypertension | 71198 |
| Recessive X-linked ichthyosis | 461 |
| Renal nutcracker syndrome | 71273 |
| Reticular dysgenesis | 335 |
| Retinitis pigmentosa | 791 |
| Retinoblastoma | 790 |
| Rett syndrome | 778 |
| Rheumatoid factor-negative polyarticular juvenile idiopathic arthritis | 85408 |
| Rubinstein-Taybi syndrome | 783 |
| SAPHO syndrome | 793 |
| Sarcoidosis | 797 |
| Selective IgM deficiency | 331235 |
| Semicircular canal dehiscence syndrome | 420402 |
| Serpiginous choroiditis | 35686 |
| Severe intellectual disability and progressive spastic paraplegia | 280763 |
| Severe intellectual disability-poor language-strabismus-grimacing face-long fingers syndrome | 363686 |
| Severe intellectual disability-progressive spastic diplegia syndrome | 404473 |
| Shwachman-Diamond syndrome | 811 |
| Sjögren-Larsson syndrome | 816 |

| | |
|---|---|
| Smith-Magenis syndrome | 819 |
| Sotos syndrome | 821 |
| Spinocerebellar ataxia type 3 | 98757 |
| Spinocerebellar ataxia type 38 | 423296 |
| Sporadic adult-onset ataxia of unknown etiology | 247234 |
| Sprengel deformity | 3181 |
| Stargardt disease | 827 |
| Steinert myotonic dystrophy | 273 |
| Steroid-responsive encephalopathy associated with autoimmune thyroiditis | 83601 |
| Stevens-Johnson syndrome | 36426 |
| Stiff person spectrum disorder | 3198 |
| Stromal corneal dystrophy | 98626 |
| Stromal corneal dystrophy | 98676 |
| Sturge-Weber syndrome | 3205 |
| STXBP1-related encephalopathy | 599373 |
| Succinic semialdehyde dehydrogenase deficiency | 22 |
| Sympathetic ophthalmia | 79098 |
| Syndrome with corpus callosum agenesis/dysgenesis as a major feature | 199639 |
| Syndromic genetic keratoconus/Syndromic keratoconus | 522564/ 98623 |
| SYNGAP1-related developmental and epileptic encephalopathy | 544254 |
| Syringomyelia | 3280 |
| Systemic capillary leak syndrome | 188 |
| Systemic lupus erythematosus | 536 |
| Systemic mastocytosis | 2467 |
| Systemic sclerosis | 90291 |
| Systemic-onset juvenile idiopathic arthritis | 85414 |
| Tetrasomy 9p | 3310 |
| Thalidomide embryopathy | 3312 |
| Thomsen and Becker disease | 614 |
| Thoracic outlet syndrome | 97330 |
| Toxic oil syndrome | 227972 |
| Treacher-Collins syndrome | 861 |
| Trigeminal neuralgia | 221091 |
| Trisomy 18 | 3380 |
| Trisomy X | 3375 |
| Tuberous sclerosis complex | 805 |
| Tumor necrosis factor receptor 1 associated periodic syndrome | 32960 |
| Turner syndrome | 881 |
| Unclassified autoinflammatory síndrome | 324936 |
| Usher syndrome | 886 |
| Usher syndrome type 1 | 231169 |
| Usher syndrome type 2 | 231178 |
| Uveal melanoma | 39044 |
| VACTERL/VATER association | 887 |
| Vascular Ehlers-Danlos syndrome | 286 |
| Vestibular schwannoma | 252175 |
| Von Willebrand disease type 1 | 166078 |
| WAGR syndrome | 893 |
| Walker-Warburg syndrome | 899 |
| White matter hypoplasia-corpus callosum agenesis-intellectual disability syndrome | 3207 |
| Williams syndrome | 904 |
| Wilson disease | 905 |
| Wolf-Hirschhorn syndrome | 280 |
| X-linked adrenoleukodystrophy | 43 |
| X-linked Charcot-Marie-Tooth disease | 64747 |
| X-linked creatine transporter deficiency | 52503 |
| X-linked non-syndromic intellectual disability | 777 |
| Xeroderma pigmentosum | 910 |