Inherited metabolic disorder	Gene symbol	Vascular	Ichthyosis	Papulonodular	Abnormal pigmentation	Photosensitivity	Cutis laxa	Hair shaft involvement	Nail abnormalities	Other	Diagnostic laboratory markers	Specific treatment	Representative references (PMID or DOI)
DISORDERS OF NITROGEN-CONTAINING COMPOUNDS													
Disorders of nucleotide metabolism													
Repair exonuclease 1 deficiency (Aicardi-Goutières syndrome type 1)	***TREX1***	**Chilblain**								Panniculitis	ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 lysophosphatidylcholine	JAK inhibitors (baricitinib, ruxolitinib)	17440703, 30673078, 30282666, 25604658
Ribonuclease H2 subunit B deficiency (Aicardi-Goutières syndrome type 2)	***RNASEH2B***	**Chilblain**									ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 fatty acids (P)	JAK inhibitors	25604658
Ribonuclease H2 subunit C deficiency (Aicardi-Goutières syndrome type 3)	***RNASEH2C***	**Chilblain**									ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 fatty acids (P)	JAK inhibitors	25604658
Ribonuclease H2 subunit A deficiency (Aicardi-Goutières syndrome type 4)	***RNASEH2A***	**Chilblain**									ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 fatty acids (P)	JAK inhibitors	25604658
SAMHD1 deficiency (Aicardi-Goutières syndrome type 5)	***SAMHD1***	**Chilblain**								Panniculitis	ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 fatty acids (P)	JAK inhibitors	25604658, 21204240
RNA-specific adenosine deaminase deficiency (Aicardi-Goutières syndrome type 6)	***ADAR***	Chilblain			**Dyschromatosis**					Systemic lupus erythematosus	ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF)	JAK inhibitors	25604658, 12916015
MDA5 superactivity (Aicardi-Goutières syndrome type 7)	*IFIH1*	Chilblain								Systemic lupus erythematosus; psoriasis-like	ASAT/ALAT (P), Blood count (B), Interferon-alpha (B), Pterins (CSF), C26:0 fatty acids (P)	JAK inhibitors	25604658
STING superactivity (SAVI: STING-Associated Vasculopathy with onset in Infancy)	*TMEM173*	Chilblain								Ulcerative lesions with infarcts and gangrene; nasal septum perforation; malar rash	CRP (P); Interferon-stimulated genes or interferon signature (PBMC); Erythrocyte sedimentation rate; IgG (S)	JAK inhibitors (tofacitinib)	27566796, 25029335
ABCC6 deficiency	***ABCC6***			**Pseudoxanthoma**							DNA		26361562
Ectonucleotide pyrophosphatase/phosphodiesterase 1 deficiency	*ENPP1*			Pseudoxanthoma							ALP (P); Calcium (P); Phosphate (P)		22229486, 22209248, 33005041
Ectonucleotide pyrophosphatase/phosphodiesterase 1 dimerization deficiency (Cole disease)	***ENPP1***			**Keratotic papules (palms, soles)**	**Hypopigmented macules**						Phosphate (P,U)		24075184, 28964717
Equilibrative nucleoside transporter 3 deficiency	***SLC29A3***				**Hyperpigmentation**			**Hypertrichosis**			Erythrocyte sedimentation rate; IgG (S)		19336477, 18940313, 28554179
RIG-I superactivity (Singleton-Merten syndrome type 2)	*DDX58*									Psoriasis-like	Interferon-stimulated genes or interferon signature (PBMC)		25620203, 30574673
Disorders of ammonia detoxification													
Carbamoylphosphate synthetase I deficiency	*CPS1*									Acrodermatitis	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline, liver transplant	7234771
Ornithine transcarbamylase deficiency	*OTC*									Acrodermatitis	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline, liver transplant	12063505, 17845164
Argininosuccinate synthetase deficiency	*ASS1*									Acrodermatitis	Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline, liver transplant	3950131
Argininosuccinate lyase deficiency	*ASL*							Trichorrhexis nodosa			Ammonia (B), ASAT/ALAT (P), Urea (P), Amino acids (P), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline, liver transplant	17300644
Disorders of amino acid transport													
Hartnup disorder	***SLC6A19***					**X**					Amino acids (U)	Niacin	13358233
Lysinuric protein intolerance	*SLC7A7*							Sparse, fine			Amino acids (P, U), Ammonia (P), Ferritin (S), Lipid panel (S), Orotic acid (U)	Protein restriction, ammonia scavengers, citrulline	1155480
Disorders of monoamine metabolism													
Monoamine oxidase A deficiency	*MAOA*	Flushing									Biogenic amines (U)	Serotonin reuptake inhibitors	25807999, 11700166
Disorders of phenylalanine and tetrahydrobiopterin metabolism													
Phenylalanine hydroxylase deficiency	*PAH*				Hypopigmentation			Hyopigmentation		Sclerodermatous, atrophic lesions	Amino acids (P)	Phe-restricted diet, sapropterin, pegvaliase	13823434, 12894120, 1569253, 4164666, 677922, 2279504
6-Pyruvoyl-tetrahydropterin synthase deficiency	*PTS*							Hyopigmentation		Rash, eczematous	Amino acids (P); Pterins (DBS,U); Biogenic amines (CSF)	Low Phe/BH4 supplementation, L-dopa, 5-hydr	21880449
Dihydropteridine reductase deficiency	*QDPR*							Hyopigmentation		Rash, eczematous	Amino acids (P); Pterins (DBS,U); DHPR activity (DBS); Biogenic amines (CSF), 5-methyl-THF (CSF)	Low Phe, L-dopa, 5-hydroxytryptophan, folinic a	30221392
Disorders of tyrosine metabolism													
Tyrosinase deficiency	*TYR*				Hypopigmentation						DNA		20301345
Tyrosine aminotransferase deficiency	***TAT***									Palmoplantar keratosis; skin blisters	Amino acids (P); Organic acids (U)	Tyr-restricted diet	28255985, 4120698
Homogentisate 1,2-dioxygenase deficiency	***HGD***				**Bluish-black pigmentation**						Homogentisate (U)	NTBC	10971492, 11264498, 12359141, 32904992
Disorders of sulfur amino acid and sulfide metabolism													
Cystathionine beta-synthase deficiency	*CBS*	Malar flush, cutis marmorata						Thin hair			Amino acids (P); SAM/SAH (P); Homocysteine (P)	Met-restricted diet, betaine, pyridoxine	28473367, 18797062, 20213008
Mitochondrial sulfur dioxygenase deficiency	***ETHE1***	**Acrocyanosis**									Organic acid (U), Acylcarnitines (P), Thiosulphate (P), Lactate (B)	Liver transplant	doi.org/10.1007/978-3-540-29676-8_24
Disorders of branched-chain amino acid metabolism													
Maple syrup urine disease	*BCKDHA, BCKDHB, DBT*									Acrodermatitis	Amino acids (P), Organic acids (U)	Low BCAA diet, valine/isoleucine supplementation	19419460, 27334242, 8942030, 8362810
Propionic acidemia	*PCCA, PCCB*									Acrodermatitis	Amino acids (P), Organic acids (U), Acylcarnitines (DBS, P)	Low protein diet, carnitine	19419460, 8120711, 8043426
Methylmalonic aciduria due to methylmalonyl-CoA mutase deficiency	*MMUT*									Acrodermatitis	Amino acids (P), Organic acids (U), MMA (S), Acylcarnitines (DBS, P)	Low protein diet, carnitine, hydroxycobalamin	19419460, 8120711, 8043426
Disorders of lysine metabolism													
Glutaryl-CoA dehydrogenase deficiency (glutaric acidemia type 1)	*GCDH*									Acrodermatitis	Organic acids (U); Acylcarnitines (DBS, P)		11358733, 23330977
Disorders of proline and ornithine metabolism													
Pyrroline-5-carboxylate synthetase deficiency	***ALDH18A1***						**X**	Sparse			Amino acids (P), Ammonia (P)		21739576, 24913064, 26320891, 26026163
Pyrroline-5-carboxylate reductase 1 deficiency	***PYCR1***						**X**				DNA		19576563, 19648921
Prolidase deficiency	***PEPD***	Telangiectasia		X				Premature graying		**Skin ulceration**; eczematous lesions; malar rash	Amino acids (U)		
Ornithine decarboxylase 1 superactivity	***ODC1***							**Alopecia**			N-Acetylputrescine (P)		30239107, 30475435
Spermidine/spermine N(1)-acetyltransferase superactivity	***SAT1***									Keratosis follicularis spinulosa decalvans	Putrescine (F)		12215835
Disorder of glutamine metabolism													
Glutamine synthetase deficiency	***GLUL***									**Necrolytic migratory erythema**	Amino acids (P, CSF); Ammonia (B)		16267323, 21353613
Glutaminase 1 superactivity	*GLS*			Nodules						Perivascular and periglandular lymphohistiocytic infiltrates of the dermis	Amino acids (U, CSF)		30239721
Disorder of serine metabolism													
3-phosphoglycerate dehydrogenase deficiency	***PHGDH***		**X**								Amino acids (P, CSF)		25152457
Phosphoserine aminotransferase deficiency	***PSAT1***		**X**								Amino acids (P, CSF)		25152457
Phosphoserine phosphatase deficiency	***PSPH***		**X**								Amino acids (P, CSF)		25152457
DISORDERS OF VITAMINS, COFACTORS, METALS AND MINERALS													
Disorders of cobalamin metabolism													
Methylmalonic aciduria and homocystinuria, cblF type					Hyperpigmentation						Organic acids (U), Acylcarnitines (DBS, P)	Hydroxycobalamin, betaine	32875039
Methylmalonic aciduria and homocystinuria, cblJ type					Hyperpigmentation						Organic acids (U), Acylcarnitines (DBS, P)	Hydroxycobalamin, betaine	25234635
Methylmalonic aciduria and homocystinuria, cblC type										Desquamative/erosive dermatitis	Organic acids (U), Acylcarnitines (DBS, P)	Hydroxycobalamin, betaine	9420542, 29379858, 29098535
Disorders of biotin metabolism													
Biotinidase deficiency	***BTD***							**Alopecia**		**Desquamative and/or erythematous dermatitis**	Organic acids (U), Acylcarnitines (DBS, P)	Biotin	10849128, 32972606

Inherited metabolic disorder	Gene symbol	Vascular	Ichthyosis	Papulonodular	Abnormal pigmentation	Photosensitivity	Cutis laxa	Hair shaft involvement	Nail abnormalities	Other	Diagnostic laboratory markers	Specific treatment	Representative references (PMID or DOI)
Holocarboxylase synthetase deficiency	***HLCS***			x				**Alopecia**		**Desquamative and/or erythematous dermatitis**	Organic acids (U), Acylcarnitines (DBS, P), Lactate (P)	Biotin	24094765, 8006369, 16650223, 32358368, 29701239, 21615476, 15165201
Disorders of niacin and NAD metabolism													
NAD(P)HX epimerase deficiency	***NAXE***									**Bullous/erosive dermatitis (acral/intertriginous)**	Cyclic NADHX (F)		27616477
NAD(P)HX dehydratase deficiency	***NAXD***									**Bullous/erosive dermatitis (acral/intertriginous)**	DNA		30576410
Nicotinamide nucleotide transhydrogenase deficiency	*NNT*				Hyperpigmentation						Steroids (P); Glucose (P)		22634753, 25879317, 26070314
Disorders of pantothenate metabolism													
Phosphopantothenoylcysteine synthetase deficiency	*PPCS*						X				DNA		29754768
Disorder of vitamin C metabolism													
GLUT10 deficiency	*SLC2A10*						X				DNA		29323665
Disorders of vitamin A metabolism													
β-carotene 15,15'-dioxygenase deficiency	*BCO1*				Yellow/orange skin						Vitamin A (P)		17951468
Plasma retinol-binding protein deficiency	*RBP4*			Comedones						Follicular keratosis	DNA		9888420
9-cis-retinoic acid-metabolizing cytochrome deficiency	***CYP26C1***									**Focal facial dermal dysplasia**	DNA		23161670
Disorders of vitamin D metabolism													
Vitamin D receptor deficiency	***VDR***							**Alopecia**			ALP (P); Calcium (P); Phosphate (P)	Calcitriol, calcium, cinacalcet	30555810
Disorder of vitamin E metabolism													
Alpha-tocopherol transfer protein deficiency	*TTPA*			Xanthomas							Cholesterol (S); Triglyceride (S); Vitamin E (P)		4000224
Disorder of vitamin K metabolism													
γ-glutamyl carboxylase deficiency	***GGCX***						**X**			**Pseudoxanthoma elasticum**	Coagulation factors (Blood)		17110937, 33000479, 19519828
Disorders of copper metabolism													
Menkes disease	***ATP7A***						**X**	**Pili torti, monilethrix, trichorrhexis nodosa**			Copper (S), Ceruloplasmin (S)		19888294, 27748070
Wilson disease	*ATB7B*				Hyperpigmentation				Azure lunulae	Dry skin	Copper (S, U), Ceruloplasmin (S)		23546359, 19400828, 5467055
MEDNIK syndrome	***AP1S1***		**X**							**Erythrokeratodermia variabilis, palmoplantar keratoderma, pale skin**	AST/ALT (P), Copper (S, U), Ceruloplasmin (S), VLCFA (P)		15668823, 19057675
MEDNIK-like syndrome	***AP1B1***		**X**							**Erythroderma, palmoplantar keratoderma**	Copper (S), Ceruloplasmin (S), VLCFA (P)		31630791, 31630788
Disorders of iron metabolism													
Hereditary hemochromatosis type 1	***HFE***				Hyperpigmentation			Sparse hair			Iron (S), Ferritin (S), Transferrin (S)		5822351, 29743178
Hemojuvelin deficiency	***HFE2***				**Hyperpigmentation**						Iron (S), Ferritin (S), Transferrin (S)		29743178
Hepcidin deficiency	***HAMP***				**Hyperpigmentation**						Iron (S), Ferritin (S), Transferrin (S)		29743178
Transferrin receptor 2 deficiency	*TFR2*				Hyperpigmentation						Iron (S), Ferritin (S), Transferrin (S)		29743178
Ferroportin disease	*SLC40A1*				Hyperpigmentation						Iron (S), Ferritin (S), Transferrin (S)		21199650
Hephaestin-like protein 1 deficiency	***HEPHL1***							**Pili torti; trichorrhexis nodosa; alopecia**					31125343
Disorders of zinc metabolism													
Acrodermatitis enteropathica	***SLC39A4***							**Alopecia**		**Acrodermatitis**	Zinc (S); ALP (P)		12068297, 32428274
Transient neonatal zinc deficiency	***SLC30A2***							**Alopecia**		**Acrodermatitis**	Zinc (S)		22733820, 17065149
Spondylocheirodysplastic Ehlers-Danlos syndrome	*SLC39A13*						X			Velvety, smooth skin	DNA		18513683
Hyperzincemia with hypercalprotectinemia	***PSTPIP1***									**Pyoderma gangrenosum; ulcers**	DNA		31789267
DISORDERS OF CARBOHYDRATES													
Disorders of the pentose phosphate pathway and polyol metabolism													
Ribose-5-phosphate isomerase deficiency	*RPIA*				Hyperpigmentation						Polyols (U, P, CSF)		28801340
Transaldolase deficiency	***TALDO1***	Hemangiomas			Knuckle pigmentation		**X**	Hypertrichosis			ASAT/ALAT (P), ALP (S), GGT (S), Glucose (S), Total/direct bilirubin (S), Ferritin (S), Polyol (U)		30740741, 26238251
Glycogen storage diseases													
HOIL1 deficiency	*RBCK1*									Desquamative erythroderma	CK (P); DNA		23104095
HOIP deficiency	*RNF31*									Eczematous dermatitis	DNA		30936877
Disorders of glycolysis													
Lactate dehydrogenase A deficiency	***LDHA***									**Erythematosquamous dermatitis**	Lactate (P); CK (P); Myoglobin (U)		1999544, 3789777
MITOCHONDRIAL DISORDERS OF ENERGY METABOLISM													
Disorders associated with single large-scale mtDNA deletions													
Pearson syndrome	*Multiple*				Reticulate hyperpigmentation						DNA		9925836
Kearns-Sayre syndrome	*Multiple*				Hypomelanosis					Anhidrosis	DNA		10532933, 1648309
Disorders of mtDNA-encoded tRNA and rRNA													
MELAS	*Multiple*							Brittle hair			DNA		9925836
Disorders of mitochondrial carriers													
Mitochondrial ATP-Mg/phosphate transporter deficiency	***SLC25A24***						**X**	**Hypertrichosis**			DNA		29100093, 29100094
Disorders of complex I subunits													
NADH dehydrogenase β subcomplex subunit 11 deficiency	***NDUFB11***									**Linear skin defects**	Lactate (P,CSF)		25772934
Disorders of complex I assembly													
NADH dehydrogenase α subcomplex assembly factor 5 deficiency	*NDUFAF5*							Unusual hair patterning			Lactate (P,CSF)		18940309
Disorders of complex III subunits													
UQCRFS1 deficiency	***UQCRFS1***							**Alopecia**			DNA		31883641
Disorders of complex III assembly													
BCS1L deficiency	***BCS1L***							**Pili torti**			DNA		
Disorders of complex IV subunits													
Cytochrome c oxidase subunit 7B deficiency	***COX7B***									**Linear skin defects**	Lactate (P)		23122588
Disorders of complex IV assembly and ancillary proteins													
SURF1 deficiency	***SURF1***							**Hypertrichosis**			Lactate (P)		23829769
LRPPRC deficiency	***LRPPRC***							**Hirsutism**			Lactate (P)		21266382
Disorders of mitochondrial cytochrome synthesis and incorporation													
Holocytochrome c synthase deficiency	***HCCS***									**Linear skin defects**	Lactate (P)		24735900
Disorders of mitochondrial tRNA													
Mitochondrial tRNA(Lys) deficiency	***MT-TK***			**Lipomas**							DNA		30873109, 31912494
Mitochondrial tRNA(Leu) 1 deficiency	*MT-TL1*			Lipomas							DNA		23273904, 11815527, 14757294
Mitochondrial tRNA(Ser) 1 deficiency	***MT-TS1***									**Palmoplantar keratoderma**	DNA		11069477, 9450881
Disorders of mitochondrial fusion													
MSTO1 deficiency	*MSTO1*			Lipomas							DNA		28554942
Mitofusin 2 deficiency	***MFN2***			**Lipomas**							DNA		30158064
Disorders of mitochondrial protein quality control													
HSPA9 deficiency	*HSPA9*							Sparse hair			DNA		26598328
Other disorders of mitochondrial homeostasis													
Mitochondrial thioredoxin reductase 2 deficiency	***TXNRD2***				**Hyperpigmentation**						Steroids (P)		24601690
DISORDERS OF LIPIDS													

Inherited metabolic disorder	Gene symbol	Vascular	Ichthyosis	Papulonodular	Abnormal pigmentation	Photosensitivity	Cutis laxa	Hair shaft involvement	Nail abnormalities	Other	Diagnostic laboratory markers	Specific treatment	Representative references (PMID or DOI)
Disorders of fatty acid oxidation and transport													
Fatty acid transport protein 4 deficiency (ichthyosis prematurity syndrome)	***SLC27A4***		X		Hyperpigmentation					Thick caseous, desquamative skin; follicular hyperkeratosis	DNA		27224495
Disorders of fatty acid synthesis and elongation													
Very long-chain fatty acid elongase 1 deficiency	***ELOVL1***		X		Hyper- and hypopigmentation				Thick split fingernails		DNA		29496980, 30487246
Very long-chain fatty acid elongase 4 deficiency, neurologic phenotype	***ELOVL4***		X							Xerotic skin; erythema of palmoplantar surfaces, folds, neck, and face	DNA		22100072
Disorder of fatty aldehyde metabolism													
Fatty aldehyde dehydrogenase deficiency (Sjogren-Larsson syndrome)	***ALDH3A2***		X								DNA		6179662
Disorders of cytoplasmic triglyceride metabolism													
Lysophosphatidic acid acyltransferase deficiency	*AGPAT2*							Hirsutism			AST/ALT (P); Triglyceride (S); Insulin (S)		20301391
Seipin deficiency	*BSCL2*							Hirsutism			AST/ALT (P); Triglyceride (S); Insulin (S)		15181077
Lipin 2 deficiency	***LPIN2***									**Neutrophilic dermatosis**	DNA		2809904, 15994876
Chanarin-Dorfman syndrome	***ABHD5***		X								AST/ALT (P)		18339307, 23756328, 21981352
Lipase N deficiency	***LIPN***		X								DNA		21439540
Disorders of cytoplasmic triglyceride metabolism													
Choline kinase β deficiency	***CHKB***		X								CK (P)		21665002
Phosphatidylserine synthase 1 superactivity (Lenz-Majewski syndrome)	***PTDSS1***						X	Scant pubic/axillary hair	Hyperconvex		DNA		10946362
Disorders of non-lysosomal sphingolipid metabolism													
3-Ketodihydrosphingosine reductase deficiency	***KDSR***									**Erythrokeratodermia variabilis et progressiva**	DNA		28575652
Sphingosine-1-phosphate lyase deficiency	***SGPL1***		X		**Hyperpigmentation**						ACTH (P); Glucose (P); Triglycerides (S); Albumin (U)		28165343
CYP4F22 omega hydroxylase deficiency	***CYP4F22***		X								DNA		16436457
Ceramide synthase 3 deficiency	***CERS3***		X								DNA		23754960
Acylceramide transacylase deficiency	***PNPLA1***		X								DNA		22246504
UDP-glucose ceramide glucosyltransferase deficiency	***UGCG***		X								DNA		29417556
ATP-binding cassette transporter superfamily A12	***ABCA12***		X								DNA		15756637, 12915478, 20672373
Arachinodate 12R-lipoxygenase deficiency	***ALOX12B***		X								DNA		16116617, 11773004
Arachidonate lipoxygenase 3 deficiency	***ALOXE3***		X								DNA		16116617, 11773004
Short-chain dehydrogenase/reductase family 9C member 7 deficiency	***SDR9C7***		X								DNA		28173123, 28369735
Disorders of non-mitochondrial phospholipid metabolism													
Lipase H deficiency	***LIPH***							**Hypotrichosis; wooly hair**			DNA		17095700, 18830268
Lysophosphatidic acid receptor 6 deficiency	***LPAR6***							**Hypotrichosis; wooly hair**			DNA		21426374
Disorders of eicosanoid metabolism													
15-hydroxy-prostaglandin dehydrogenase deficiency	*HPGD*									Thickened skin; hyperhidrosis; seborrhea	Prostaglandin E2 (U)		21426412
Prostaglandin transporter deficiency	*SLCO2A1*									Thickened skin; hyperhidrosis; seborrhea; cutis gyrata	DNA		22197487
Disorders of phosphoinositide metabolism													
Phosphatidylinositol 3,5-bisphosphate-5-phosphatase deficiency	***FIG4***							Sparse scalp hair, eyebrows and eyelashes	**Anonychia**		DNA		22044576, 20932945, 7496176
Phosphatidylinositol 4,5-bisphosphate-5-phosphatase deficiency	*OCRL*			Epidermal cysts							Amino acids (U); Cholesterol (S); Phosphate (U)		27178641, 28516463, 21165217, 14871328, 17621522
Phosphatidylinositol 3,4,5-trisphosphate 3-phosphatase deficiency	*PTEN*			**Papillomas; facial trichilemmomas;** lipomas						Acral keratosis	DNA		18781191
Phosphatidylinositol 4,5-bisphosphate phospholipase C γ2 deficiency	***PLCG2***						X			Recurrent skin blisters	IgE (S)		23000145, 30619256
Phosphatidylinositol 4,5-bisphosphate phospholipase C δ1 deficiency	***PLCD1***								**Leukonychia**		DNA		21665001
Phosphatidylinositol 4-kinase type 2-alpha deficiency	***PI4K2A***						X				ASAT/ALAT (P); GGT (P); Amino acids (P); Lactate (P,U)		32418222
Inositol 1,4,5-triphosphate receptor type 2 deficiency	***ITPR2***									**Anhidrosis**	DNA		25329695
Disorders of lipoprotein metabolism													
Familial hypercholesterolemia (LDLR)	***LDLR***			**Tendon, tuberous and interdigital xanthomas; xanthelasmas**							Lipid panel (S), Apo B (P)	Statins, ezetimibe, PCSK9 inhibitors	32489792, 10750084
Autosomal recessive hypercholesterolemia	***LDLRAP1***			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S), Apo B (P)	Statins, ezetimibe, PCSK9 inhibitors	32636080
Familial defective apolipoprotein B (APOB)	***APOB***			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S), Apo B (P)	Statins, PCSK9 inhibitors	10984082
PCSK9 superactivity	***PCSK9***			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S), Apo B (P)	PCSK9 inhibitors	26374825
Sitosterolemia due to ABCG5 deficiency	***ABCG5***			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S)		32713907, 28696550
Sitosterolemia due to ABCG8 deficiency	***ABCG8***			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S)		28739549
Apolipoprotein E deficiency	***APOE***			**Palmar crease xanthomas;** tuberous xanthomas							Lipid panel (S)		27603268, 12506591
Lipoprotein lipase deficiency	***LPL***			**Eruptive xanthomas**							Lipid panel (S)		28529016, 28695157
Apolipoprotein C-II deficiency	***APOC2***			**Eruptive xanthomas**							Lipid panel (S)		3944267
GPIHBP1 deficiency	*GPIHBP1*			Eruptive xanthomas							Triglycerides (S)		22008945
Apolipoprotein A5 deficiency	*APOA5*			Eruptive xanthomas							Triglycerides (S)		18324930, 15591215
Apolipoprotein A1 deficiency	*APOA1*			**Tendon and tuberous xanthomas; xanthelasmas**							Lipid panel (S), Apolipoprotein A-I		29396262,
Disorders of cholesterol biosynthesis													
Mevalonate kinase deficiency	***MVK***									**Maculopapular rash (AR); porokeratosis (AD)**	DNA		21708801, 27142780, 26202976
Phosphomevalonate kinase deficiency	***PMVK***									**Porokeratosis**	DNA		26202976, 30942823
Mevalonate pyrophosphate decarboxylase deficiency	***MVD***									**Porokeratosis**	DNA		26202976, 30942823
Farnesylpyrophosphate synthetase deficiency	***FDPS***									**Porokeratosis**	DNA		26202976
Lanosterol demethylase deficiency	*CYP51A1*				Hypopigmentation					Persistent cheek erythema	DNA		doi.org/10.1007/978-3-642-40337-8_36
Lanosterol synthase deficiency	***LSS***							**Hypotrichosis**			DNA		30401459
SC4MOL deficiency	***MSMO1***		X								Sterols (P)		21285510
CHILD syndrome	***NSDHL***		X	**Verruciform xanthoma**					**Onychodystrophy**		Sterols (P)		10710235, 32886633, 31365666, 33272544, 25845514
Conradi-Hünermann-Happle syndrome	***EBP***		X					**Alopecia**	Split nails	Follicular atrophoderma	Sterols (P)		535904
Smith-Lemli-Opitz syndrome	***DHCR7***					X					ASAT/ALAT (P), Lipid panel (S), 7/8-Dehydrocholesterol (P)		16869869, 10583043, 9666840, 10411425

Inherited metabolic disorder	Gene symbol	Vascular	Ichthyosis	Papulonodular	Abnormal pigmentation	Photosensitivity	Cutis laxa	Hair shaft involvement	Nail abnormalities	Other	Diagnostic laboratory markers	Specific treatment	Representative references (PMID or DOI)
Disorders of steroid metabolism													
ACTH receptor/melanocortin-2 receptor deficiency	***MC2R***				**Hyperpigmentation**						ACTH, Steroids (P); Glucose (P)		7627261
Melanocortin-2 receptor accessory protein deficiency	***MRAP***				**Hyperpigmentation**						ACTH, Steroids (P); Glucose (P)		21951701
Hydroxysteroid sulfotransferase deficiency	***SULT2B1***		**X**								DNA		28575648
Steroid sulfatase deficiency	*STS*		**X**								DNA		29672931
Disorders of bile acid synthesis													
Sterol 27-hydroxylase deficiency	***CYP27A1***			**Tendon xanthomas**							Lipid panel (S); Sterols (P); Cholestane pentol glucuronide (U); 25-Hydroxy-Vitamin D (P)	Chenodeoxycholic acid	
DISORDERS OF TETRAPYRROLES													
Disorders of heme metabolism													
X-linked dominant protoporphyria	***ALAS2***					**X**					Free and zinc-bound protorphyrin (RBC)		18760763
Uroporphyrinogen III synthase deficiency (congenital erythropoietic porphyria)	***UROS***					**X**		**Hypertrichosis**		**Skin blisters / fragility / scarring**	Porphyrins (U, RBC, stools)	Bone marrow transplant	24261722
Uroporphyrinogen decarboxylase deficiency (porphyria cutanea tarda type 2)	***UROD***				**Hyperpigmentation**	**X**		**Hypertrichosis**		**Skin blisters / fragility / thickening**	Porphyrins (U, P)	Phlebotomy; hydroxychloroquine	24261722
Coproporphyrinogen oxidase deficiency (hereditary coproporphyria)	***CPOX***				**Hyperpigmentation**	**X**		**Hypertrichosis**		**Skin blisters / fragility / thickening**	PBG (U); Porphyrins (U, stools)	Hemin	24261722
Protoporphyrinogen oxidase deficiency (variegate porphyria)	***PPOX***				**Hyperpigmentation**	**X**		**Hypertrichosis**		**Skin blisters / fragility / thickening**	PBG (U); Porphyrins (U, stools); Fluorescence scanning (P)	Hemin	24261722
Ferrochelatase deficiency (erythropoietic protoporphyria)	***FECH***					**X**				Seasonal palmoplantar keratoderma	Free protorphyrin (RBC); Fluorescence scanning (P)	Afamelanotide	19744342, 18787536
Mitochondrial porphyrin transporter deficiency	***ABCB6***				**Dyschromatosis**						DNA		23519333, 24224009
Erythropoietic protoporphyria type 2	***CLPX***					**X**					Protoorphyrin (RBC)		28874591
Heme oxygenase 1 deficiency	*HMOX1*									Generalized erythematous rash	DNA		9884342
STORAGE DISORDERS													
Disorders of autophagy													
EPG5 deficiency (Vici syndrome)	***EPG5***				**Hypopigmentation**					Intermittent maculopapular rash	DNA		26917586
Sphingolipidoses													
Glucocerebrosidase deficiency (Gaucher disease)	***GBA***		**X (type 2)**		Hyperpigmentation (type 1)					Blueberry muffin lesions	Enzyme activity (WBC)		10685993, 8469493, 15967693, 7641780, 26646163, 6477829
Acid sphingomyelinase deficiency	*SMPD1*			Facial papules							Enzyme activity (WBC)		7857847
GM1 gangliosidosis	*GLB1*	Angiokeratoma, telangiectasia			**Extensive dermal melanocytosis**						Oligosaccharide (U), Enzyme activity (WBC)		3930682, 2504516, 30271472, 26337817, 26765271, 25332452
Sandhoff disease	*HEXB*				Extensive dermal melanocytosis						Enzyme activity (WBC)		24134161, 30061129
Multiple sulfatase deficiency	***SUMF1***		**X**								Sulfatide (U), Glycosaminoglycans (U)		21224894, 25885655, 32749716
Fabry disease	***GLA***	**Angiokeratoma,** telangiectasia								Hypohydrosis, hyperhydrosis, lymphedema	Globotriaosylsphingosine, Globotriaosylceramide, Proteins (U)	Enzyme replacement therapy	21290701, 23448454, doi.org/10.1177/2326409816661353
Acid ceramidase deficiency (Farber disease)	***ASAH1***			**Nodules**							DNA		29048419
Oligosaccharidoses													
Neuraminidase deficiency (sialidosis)	*NEU1*	Telangiectasia								Erythematous macular rash	Enzyme activity (WBC), Oligosaccharides (U)		11195014, 19568825, 25223955
Cathepsin A deficiency (galactosialidosis)	***CTSA***	**Angiokeratoma**									Enzyme activity (WBC), Oligosaccharides (U)		6435542, 9693187
β-mannosidase deficiency	***MANBA***	**Angiokeratoma**									Enzyme activity (DBS,WBC), Oligosaccharides (U)		17420068, 8859034, 15729869
Alpha-N-acetylgalactosaminidase deficiency (Schindler disease)	***NAGA***	**Angiokeratoma**									Enzyme activity (DBS,WBC), Oligosaccharides (U)		7897017, 11251574, 8466216
Alpha-L-fucosidase deficiency (fucosidosis)	***FUCA1***	**Angiokeratoma**, acrocyanosis							Purple bands	Anhidrosis	Enzyme activity (DBS,WBC), Fucose (U)	Bone marrow transplant	2012122, 7837199, 9155966, 16008696
Aspartylglucosaminidase deficiency	*AGA*	Angiokeratoma		Piezogenic papules, facial angiofibromas						Facial rosacea	Enzyme activity (DBS,WBC), Aspartylglucosamine (U)		27906067, 6788730, 12366426, 10353787
Mucopolysaccharidoses													
Mucolipidosis	*GNPTAB*				Extensive dermal melanocytosis						Oligosaccharide (U), Glycosaminoglycans, Enzyme activity (S)		20465702
Mucopolysaccharidoses													
Hurler syndrome	***IDUA***			Papules	**Extensive dermal melanocytosis**			Hypertrichosis		Thick skin	Total GAGs (U), Dermatan sulfate (U), Heparan sulfate (U), Enzyme activity (WBC)	Enzyme replacement therapy; bone marrow transplant	16458829, 12873889, 16648922, 8912609
Hunter syndrome	***IDS***			**Pebbling**	Extensive dermal melanocytosis			Hypertrichosis		Thick skin	Total GAGs (U), Dermatan sulfate (U), Heparan sulfate (U), Enzyme activity (WBC)	Enzyme replacement therapy	9796587, 404968, 21995841, 28217482, 9843019, 17714129
Maroteaux-Lamy syndrome	*ARSB*				Extensive dermal melanocytosis						Total GAGs (U), Dermatan sulfate (U), Enzyme activity (WBC)	Enzyme replacement therapy	24134161
Disorders of lysosomal transport													
Cystinosis	*CTNS*			Facial papules	Hypopigmentation						Cystine (WBC, PMN)	Cysteamine	22649030, 9807999, 31022388, 26398166
Disorders of lysosomal protein degradation													
Cathepsin C deficiency	***CTSC***								**Atrophic nails**	**Palmoplantar keratoderma**	DNA		10581027, 12637913
Cathepsin B superactivity	***CTSB***									**Palmoplantar erythema; centrifugal epidermal peeling; hyperhidrosis**	DNA		28457472
DISORDERS OF PEROXISOMES AND OXALATE													
Disorders of plasmalogen synthesis													
Rhizomelic chondrodysplasia punctata type 1	*PEX7*		X								Plasmalogens (RBC)		12687664
Rhizomelic chondrodysplasia punctata type 5	*PEX5*									Palmoplantar keratoderma	Plasmalogens (RBC)		26220973
Disorders of peroxisomal β-oxidation													
X-linked adrenoleukodystrophy	***ABCD1***		Ichthyosis (mild)		**Hyperpigmentation**			Alopecia			VLCFA (P)		8305751, 10828629, 31269232
Refsum disease (classic, adult)	***PHYH***		**X**								Pipecolic acid (P, U), Phytanic acid (S, U), Protein (CSF)		1719201, 2433405, 11948235
Disorders of oxalate metabolism													
Glyoxylate reductase/hydroxypyruvate reductase deficiency	*GRHPR*			Calcified nodules							Oxalic acid (U, P), Glyceric acid (U), Creatinine (P), Urea (P)		26542998
Alanine-glyoxylate aminotransferase deficiency	***AGXT***	**Livedo** reticularis or racemosa, acrocyanosis		Calcified nodules						Cutaneous necrosis/ulcers	Oxalic acid (U, P), Glycolic acid (P, U), Creatinine (P), Urea (P)		20921818, 31397396, 14512927, 7611799, 8607646
CONGENITAL DISORDERS OF GLYCOSYLATION													
Disorders of N-linked glycosylation													
PMM2-CDG	***PMM2***									**Orange peel skin**	ASAT/ALAT (P), Lipid panel (S), Sialotransferrins (S), Albumin (S), Factor XI (B),		24554337, 9835963
ALG12-CDG	*ALG12*								Hypoplastic nails		ASAT/ALAT (P), Glucose (S), Lipid panel (S), Sialotransferrins (S), IGF (P)		17506107
ALG8-CDG	*ALG8*						X				CK (P), Sialotransferrins (S), Albumin (S), Factor IX and XII (B), Antithrombin III (P)		24555185
MOGS-CDG	*MOGS*							Hirsutism, trichomegaly			AST/ALT (P), Oligosaccharide (U), Sialotransferins (S)		29235540
MAN1B1-CDG	*MAN1B1*						X				AST/ALT (P), Sialotransferins (S)		24348268
SSR4-CDG	*SSR4*						X				Sialotransferins (S)		33300232

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FUT8-CDG	*FUT8*							Hirsutism			Glucose (P); Blood count		29304374
Disorders of O-xylosylation and glycosaminoglycan synthesis													
B4GALT7-CDG	*B4GALT7*						X				DNA		23956117
CHST14-CDG	***CHST14***						**X**			**Skin fragility**	DNA		26373698
DSE-CDG	***DSE***						**X**			**Skin fragility**	DNA		25703627
Disorders of O-GalNAcylation													
GALTNT3-CDG	***GALNT3***			**Calcified nodules**							Phosphate (P)		
Disorders of O-GlcNAcylation													
EOGT-CDG	***EOGT***								**Absent or hypoplastic**	**Aplasia cutis**	DNA		23522784
Disorder of O-glucosylation													
POGLUT1-CDG	***POGLUT1***			**Dark papules**	**Reticulate pigmentation**						DNA		24387993
Disorders of O-fucosylation													
POFUT1-CDG	***POFUT1***			**Dark papules**	**Reticulate pigmentation**						DNA		23684010
Disorders of glycosylphosphatidylinositol biosynthesis													
PIGA-CDG	*PIGA*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		30054924
PIGL-CDG	***PIGL***		**X**						Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		6192719, 4037840, 22444671, 30054924
PIGV-CDG	***PIGV***								**Hypoplastic**		ALP (P), GPI-anchored proteins (WBC, F)		29310717, 30054924
PIGN-CDG	*PIGN*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		30054924
PIGB-CDG	*PIGB*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		31256876
PIGO-CDG	*PIGO*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		30054924
PGAP3-CDG	*PGAP3*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		30054924
PGAP2-CDG	*PGAP2*								Hypoplastic		ALP (P), GPI-anchored proteins (WBC, F)		30054924
Disorders of glycolipid glycosylation													
ST3GAL5-CDG	***ST3GAL5***				**Hyper/ hypopigmentation**						GM3 (P)		24026681, 23436467
Disorders of dolichol metabolism													
SRD5A3-CDG	***SRD5A3***		**X**							Dry skin	Sialotransferins (S), ASAT/ALAT (P)		20637498
DOLK-CDG	***DOLK***		**X**								ASAT/ALAT (P), CK (P), Sialotransferrins (S)		17273964, 22242004
MPDU1-CDG	***MPDU1***		**X**								Sialotransferins (S)		29721919
Disorders of monosaccharide synthesis and interconversion													
Glucose-6-phosphatase catalytic subunit 3 deficiency	*G6PC3*						X	Sparse hair			Blood count; DNA		22050868, 20717171
Disorders of vesicular trafficking													
COG5-CDG	COG5									Dry, scaly skin	Sialotransferins (S)		23228021
COG6-CDG	*COG6*									**Palmoplantar hyperkeratosis; hypohidrosis;** orange peel skin	AST/ALT (P), CK (P), Lactate (P), Sialotransferins (S), Vitamins A, D, E, K (S)		26260076, 23606727
COG7-CDG	*COG7*						X				AST/ALT (P), CK (P), Glucose (S), Total/direct bilirubin (S), Sialotransferins (S)		16151902, 17356545
SCYL1-binding protein deficiency (geroderma osteodysplasticum)	***GORAB***						**X**				DNA		18348262
p34 deficiency	***AAGAB***									**Punctate palmoplantar keratoderma**	DNA		23000146, 23064416
Disorders of Golgi homeostasis													
ATP6V0A2-CDG	***ATP6V0A2***						**X**				Sialotransferins (S), ASAT/ALAT (P)		18157129
ATP6V1A-CDG	***ATP6V1A***						**X**				Lipid panel (S), Sialotransferrins (S)		28065471, 24459010, 32763190
ATP6V1E1-CDG	***ATP6V1E1***						**X**				Lipid panel (S), Sialotransferrins (S)		32763190
ATP6AP1-CDG	***ATP6AP1***						**X**				Sialotransferrins (S); Ceruloplasmin (S); Copper (S); IgG (S)		29396028, 29192153, 32216104
ATP6AP2-CDG	***ATP6AP2***						**X**				Sialotransferins (S), ASAT/ALAT (P); IgG (S); Factor XI (B)		29127204
OTHER													
Disorders of non-mitochondrial tRNA metabolism													
Familial dysautonomia	*ELP1*									Hyperhydrosis	DNA		14742604
Cysteinyl-tRNA synthetase 1 deficiency	***CARS1***							**Brittle hair**	**Brittle nails**		DNA		30824121
Threonyl-tRNA synthetase 1 deficiency	***TARS1***							**Brittle, tiger-tail hair**			DNA		31374204
Disorders of ribosomal biogenesis													
Cartilage-hair hypoplasia	***RMRP***							**Sparse hair; alopecia**			DNA		22420014
Anauxetic dysplasia type 2	*POP1*							Sparse hair			DNA		28067412
BMS1-related aplasia cutis congenita	***BMS1***									**Aplasia cutis congenita**	DNA		23785305
Cytosolic large ribosomal subunit 21 deficiency	***RPL21***							**Hypotrichosis**			DNA		21412954
Cytosolic small ribosomal subunit 23 deficiency	***RPS23***							**Trichomegaly; brittle hair**	Brittle nails		Glucose (P)		28257692, 26982655
Poly(A)-specific ribonuclease deficiency	***PARN***				**Reticulate pigmentation**			**Sparse hair**	**Nail dystrophy**		DNA		25893599
Disorders of lysosome-related organelle biogenesis													
Arthrogryposis, renal dysfunction, and cholestasis 1	***VPS33B***		**X**								DNA		16354257, 16492441
Hermansky-Pudlak syndrome type 1	***HPS1***				**Hypopigmentation**			Hypopigmented			DNA		9497254
Hermansky-Pudlak syndrome type 2	***AP3B1***				**Hypopigmentation**			Hypopigmented			DNA		11809908
Hermansky-Pudlak syndrome type 3	***HPS3***				**Hypopigmentation**			Hypopigmented			DNA		11455388
Hermansky-Pudlak syndrome type 4	***HPS4***				**Hypopigmentation**			Hypopigmented			DNA		12664304
Hermansky-Pudlak syndrome type 5	***HPS5***				**Hypopigmentation**			Hypopigmented			DNA		15296495
Hermansky-Pudlak syndrome type 6	***HPS6***				**Hypopigmentation**			Hypopigmented			DNA		19843503
Hermansky-Pudlak syndrome type 7	***DTNBP1***				**Hypopigmentation**			Hypopigmented			DNA		28259707
Hermansky-Pudlak syndrome type 8	***BLOC1S3***				**Hypopigmentation**			Hypopigmented			DNA		16385460
Hermansky-Pudlak syndrome type 9	***BLOC1S6***				**Hypopigmentation**			Hypopigmented			DNA		22461475
Hermansky-Pudlak syndrome type 10	***AP3D1***				**Hypopigmentation**			Hypopigmented			DNA		26744459
Chediak-Higashi syndrome	***LYST***				**Hypopigmentation**			**Silvery hair, pigment clumping**			DNA		20301751
Griscelli syndrome type 1	***MYO5A***				**Hypopigmentation**			**Silvery hair, pigment clumping**			DNA		19318926
Griscelli syndrome type 2	***RAB27A***				**Hypopigmentation**			**Silvery hair, pigment clumping**			DNA		10835631
Griscelli syndrome type 3	***MLPH***				**Hypopigmentation**			**Silvery hair, pigment clumping**			DNA		12148598, 12897212
Disorders of the synaptic vesicle cycle													
CEDNIK syndrome	***SNAP29***		**X**							**Palmoplantar keratoderma**	DNA		21073448, 29051910