Genetics (alphabetic), associated disease, laboratory and clinical picture, together with special features of inherited platelet defects
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Defect	Abbreviation, Synonym	Disease	Inheritance	Gene OMIM #	Phenotype OMIM#	Gene location	#	Size	BT	S	P	Special features (Background, Laboratory, Clinic)
ABCG5	ATP-BINDING CASSETTE, SUBFAMILY G, MEMBER 5; STEROLIN 1	Sitosterolemia with macrothrombocytopenia	AR	605459	618666	2p21	r	l	/	S	/	Sitosterolemia, also known as phytosterolemia, is an autosomal recessive metabolic condition characterized by unrestricted intestinal absorption of both cholesterol and plant-derived cholesterol-like molecules, such as sitosterol. Patients with this disorder have very high levels of plant sterols in the plasma and develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease.
ABCG8	ATP-BINDING CASSETTE, SUBFAMILY G, MEMBER 8; STEROLIN 2	Sitosterolemia with macrothrombocytopenia	AR	605460	210250	2p21	r	l	/	S	/	Sitosterolemia, also known as phytosterolemia, is an autosomal recessive metabolic condition characterized by unrestricted intestinal absorption of both cholesterol and plant-derived cholesterol-like molecules, such as sitosterol. Patients with this disorder have very high levels of plant sterols in the plasma and develop tendon and tuberous xanthomas, accelerated atherosclerosis, and premature coronary artery disease.
ACTB	BETA-ACTIN	Baraitser-Winter syndrome 1 with macrothrombocytopenia	AD	102630	243310	7p22.1	r	l	/	S	/	BRWS is a rare developmental phenotype characterized by the combination of hypertelorism, broad nose with large tip and prominent root, congenital nonmyopathic ptosis, ridged metopic suture, arched eyebrows, iris or retinal coloboma, sensorineural deafness, shoulder girdle muscle bulk and progressive joint stiffness, and pachygyria with anteroposterior severity gradient, rarely lissencephaly or neuronal heterotopia.
ACTN1	ALPHA-1 ACTININ	ACTN1-RELATED THROMBOCYTOPENIA; Bleeding disorder, platelet-type, 15; BDPLT15	AD	102575	615193	14q24.1	r/n	l	n/mi	/	/	ACTN1 mutations lead to a benign form of platelet macrocytosis not always associated with thrombocytopenia. Platelet-type bleeding disorder-15 is an autosomal dominant form of macrothrombocytopenia. Affected individuals usually have no or only mild bleeding tendency, such as epistaxis. Laboratory studies show reduced numbers of large platelets and anisocytosis, but the platelets show no in vitro functional abnormalities.
ADAMTS13	A DISINTEGRIN-LIKE AND METALLOPROTEASE WITH THROMBOSPONDIN TYPE 1 MOTIF, 13	Thrombotic thrombocytopenic purpura, familial; TTP; Moschcowitz disease	AR	604134	274150	9q34.2	r	n	n	S	/	TTP is an aggressive and life-threatening form of thrombotic microangiopathy characterized by hemolytic anemia with fragmentation of erythrocytes, thrombocytopenia, diffuse and nonfocal neurologic findings, decreased renal function, heart and brain dysfunction, fever, weakness, shortness of breath, confusion, and headache. Purpura and petechiae are the most common bleeding manifestations.
ANKRD26	ANKYRIN REPEAT DOMAIN-CONTAINING PROTEIN 26	ANKRD26-Related Thrombocytopenia 2; THROMBOCYTOPENIA 2; THC2	AD	610855	18800	10p12.1	r	n/l	n/mi	/	P	Lifelong mild-to-moderate thrombocytopenia. Most individuals have normal hemostasis or a mild bleeding phenotype and do not develop severe spontaneous bleeding. No syndromic associations. About 8% of patients acquire myeloid malignancies. Normal platelet size. Some patients have increased levels of hemoglobin and/or leukocytes. Reduced alpha granules in some patients.
ANO6	ANOCTAMIN 6; TRANSMEMBRANE PROTEIN 16F; TMEM16F	SCOTT SYNDROME	AR	608663	262890	12q12	n	n	mi/mo	S	/	Scott syndrome is a mild to moderate platelet-type bleeding disorder characterized by impaired surface exposure of procoagulant phosphatidylserine (PS) on platelets and other blood cells, following activation with Ca(2+)-elevating agents. Normal platelet count. Defective thrombin generation. Missing Annexin-A5 binding to activated platelets in flow cytometry.
AP3B1	ADAPTOR-RELATED PROTEIN COMPLEX 3, BETA-1 SUBUNIT; AP3B1	HERMANSKY-PUDLAK SYNDROME 2; HPS2	AR	603401	608233	5q14.1	r/n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive mutli-system disorder characterized by platelet defects and oculocutaneous albinism. HPS2 differs from the other forms of HPS in that it includes immunodeficiency, and patients with HPS2 have an increased susceptibility to infections due to congenital neutropenia. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.

AP3D1	ADAPTOR-RELATED PROTEIN COMPLEX 3, DELTA-1 SUBUNIT; AP3D1	HERMANSKY-PUDLAK SYNDROME 10; HPS10	AR	607246	617050	19p13.3	r/n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive mutli-system disorder characterized by platelet defects and oculocutaneous albinism. HPS2 differs from the other forms of HPS in that it includes immunodeficiency, and patients with HPS2 have an increased susceptibility to infections due to congenital neutropenia. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
ARPC1B	ACTIN-RELATED PROTEIN 2/3 COMPLEX, SUBUNIT 1B	Platelet abnormalities with eosinophilia and immune-mediated inflammatory disease; PLTEID	AR	604223	617718	7q22.1	r/n	s/n	mi	/	/	PLTEID is an autosomal recessive immune-mediated inflammatory disease with highly variable manifestations. More severely affected individuals have recurrent infections, vasculitis, and thrombocytopenia, whereas other patients have mild vasculitis and normal numbers of small platelets without severe infections. Laboratory studies show platelets with abnormal shape, decreased dense granules, and impaired spreading ability, as well as immune dysregulation with increased eosinophils, B cells, IgA and IgE, and autoantibodies.
BLOC1S3	BIOGENESIS OF LYSOSOME-RELATED ORGANELLES COMPLEX 1, SUBUNIT 3	BLOC1S3 Defiency; HERMANSKY-PUDLAK SYNDROME 8; HPS8	AR	609762	614077	19q13.32	n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive mutli-system disorder characterized by platelet defects and oculocutaneous albinism. Affected individuals display features of incomplete oculocutaneous albinism and platelet dysfunction; several have easy bruising, prolonged or excessive bleeding from wounds, and menorrhagia. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release; oculocutaneous albinism.
BLOC1S6	BIOGENESIS OF LYSOSOME-RELATED ORGANELLES COMPLEX 1, SUBUNIT 6	BLOC1S6 Defiency; HERMANSKY-PUDLAK SYNDROME 9; HPS9	AR	604310	614171	15q21.1	n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive mutli-system disorder characterized by platelet defects and oculocutaneous albinism. The 'pallid' mouse mutant represents a platelet storage pool deficiency manifesting with prolonged bleeding time, pigment dilution, and other features of the Hermansky-Pudlak Syndrome. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release; oculocutaneous albinism.
CDC42	CELL DIVISION CYCLE 42; CDC42; GTP-BINDING PROTEIN, 25-KD; G25K	Takenouchi-Kosaki syndrome with macrothrombocytopenia	AD	116952	616737	1p36.12	r	l	n/mi	S	/	Takenouchi-Kosaki syndrome is a highly heterogeneous autosomal dominant complex congenital developmental disorder affecting multiple organ systems. The core phenotype includes delayed psychomotor development with variable intellectual disability, dysmorphic facial features, and cardiac, genitourinary, and hematologic or lymphatic defects, including thrombocytopenia and lymphedema.
CD36	CD36 ANTIGEN; LEUKOCYTE DIFFERENTIATION ANTIGEN CD36 PLATELET GLYCOPROTEIN IV; GP4	Platelet glycoprotein IV deficiency; BLEEDING DISORDER, PLATELET-TYPE, 10; BDPLT10; CD36 DEFICIENCY	AR	173510	608404	7q21.11	r/n	g	n/mi	/	/	Platelet glycoprotein IV deficiency is a disorder characterized by macrothrombocytopenia with variable bleeding tendency. Platelet glycoprotein IV deficiency can be divided into 2 subgroups. The type I phenotype is characterized by platelets and monocytes/macrophages exhibiting complete CD36 deficiency. The type II phenotype lacks the surface expression of CD36 in platelets, but expression in monocytes/macrophages is near normal. Giant platelets, no neutrophil inclusions, low-to normal platelet count. Variable bleeding tendency, thrombocytopenia, prolonged bleeding times.
CYCS	CYTOCHROME C	CYCS-related thrombocytopenia; Thrombocytopenia 4, THC4	AD	123970	612004	7p15.3	r/n	n	n	/	/	Clinical manifestations of thrombocytopenia are absent or mild. Affected individuals have normal longevity, fertility, and fitness with no evidence of neurodegenerative, muscular, eye, or kidney disease, or diabetes. Peripheral blood smear show normal platelet size and morphology. No bleeding abnormalities or hematologic or extra-hematologic defects associated with the thrombocytopenia.
DIAPH1	DIAPHANOUS-RELATED FORMIN 1; DIAPHANOUS, DROSOPHILA, HOMOLOG OF, 1 DIA1	Deafness, autosomal dominant 1, DFNA1 KONIGSMARK SYNDROME DEAFNESS, AUTOSOMAL DOMINANT 1, WITH OR WITHOUT THROMBOCYTOPENIA	AD	602121	124900	5q31.3	r/n	l	n	S	/	DFNA1 is an autosomal dominant form of progressive hearing loss with onset in the first decade. Most of these individuals do not have significant bleeding tendencies. Some patients may have mild thrombocytopenia, mild transient leukopenia and enlarged platelets.
DTNBP1	DYSTROBREVIN-BINDING PROTEIN 1; DYSBINDIN SANDY, MOUSE, HOMOLOG OF; SDY HPS7 GENE; HPS7 BIOGENESIS OF LYSOSOME-RELATED ORGANELLES COMPLEX 1, SUBUNIT 8; BLOC1S8; BLOC1, SUBUNIT 8; BLOS8	HERMANSKY-PUDLAK SYNDROME 7; HPS7	AR	607145	614076	6p22.3	n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive mutli-system disorder characterized by platelet defects and oculocutaneous albinism. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release; oculocutaneous albinism.

ENG	ENDOGLIN; CD105	TELANGIECTASIA, HEREDITARY HEMORRHAGIC, TYPE 1; HHT1; Osler–Weber–Rendu syndrome	AD	131195	187300	9q34.11	n/i	n	mi/s	/	/	HTT1 is an autosomal dominant vascular dysplasia leading to telangiectases and arteriovenous malformations of skin, mucosa, and viscera. Epistaxis and gastrointestinal bleeding are frequent complications of mucosal involvement. Visceral involvement includes that of the lung, liver, and brain. Anemia with evidence of iron deficiency is common. In people with HHT, iron deficiency is associated with marginal increases in platelet counts, as seen in the general population. Iron deficiency is also associated with elevated factor VIII levels and a shortened aPTT.
ETV6	ETS VARIANT GENE 6	ETV6-related thrombcytopenia; ETV6-RT	AD	616216	616216	12p13.2	r/n	n/l	n/mo	/	P	Thrombocytopenia-5 is an autosomal dominant disorder characterized by a decreased number of platelets and a bleeding tendency. About 25% of patients aquire acute lymphoblastic leukemia and other hematological malignancies. Thrombocytopenia is usually apparent in early childhood, whereas the development of malignancy can occur throughout life. Maturation of megakaryocytes defective, impaired proplatelet formation, platelets have reduced ability to spread on fibrinogen.
FERMT3	FERMITIN FAMILY, MEMBER 3; UNC112-RELATED PROTEIN 2, URP2; KINDLIN 3; KIND3; MIG2B	LEUKOCYTE ADHESION DEFICIENCY, TYPE III; LEUKOCYTE ADHESION DEFICIENCY 3, LAD3; LEUKOCYTE ADHESION DEFICIENCY 1 VARIANT, LAD1V; INTEGRIN ACTIVATION DEFICIENCY DISEASE, IADD	AR	607901	612840	11q13.1	r/n	n	s	/	/	Leukocyte adhesion deficiency-3 (LAD3) is an autosomal recessive disorder characterized by LAD1 (116920)-like immune deficiency and Glanzmann thrombasthenia (GT; 273800)-like bleeding problems. Severe bacterial infections, poor wound healing and severe bleeding disorder. Leukocytosis with neutrophilia. No platelet aggregation to collagen, normal aggregation to ristocetin.
FLI1	FRIEND LEUKEMIA VIRUS INTEGRATION 1	BLEEDING DISORDER, PLATELET-TYPE, 21; BDPLT21	AD,AR	193067	617443	11q24.3	r/n	n/l	mi/mo	/	/	BDPLT21 is a hematologic disorder characterized by increased risk of bleeding resulting from a functional platelet defect. Some patients may have mild to moderate macrothrombocytopenia. Platelets have decreased or even absent dense bodies and abnormally enlarged and fused alpha-granules, and they show defective secretion and aggregation responses to agonists. Platelets are usually enlarged.
FLNA	FILAMIN A	FLNA-related thrombocytopenia; FLAR-RT; Filaminopathies A	XLD	300017	n.a.	Xq28	r	l	mi/mo	S	/	X-linked dominant form of periventricular nodular heterotopia (FLNA-PVNH) and the otopalatodigital syndrome spectrum of disorders. Hemorrhage and coagulopathy. Abnormal platelet morphology.
FYB	FYN-BINDING PROTEIN; ADHESION AND DEGRANULATION ADAPTOR PROTEIN; ADAP	FYB-related thrombocytopenia; Thrombocytopenia 3	AR	602731	273900	5p13.1	r	s/n	mi/mo	/	/	Thrombocytopenia-3 is an autosomal recessive hematologic disorder characterized by onset of small-platelet thrombocytopenia in infancy. Patients may show variable bleeding tendency, manifest as petechiae, epistaxis, or heavy menstrual bleeding. Mild iron deficiency anemia. Reduction of megakaryocytes in bone marrow. Normal WBCs count. Low mean platelet volume.
GALE	UDP-GALACTOSE-4-EPIMERASE	Inherited thrombocytopenia	n.k.	606953	n.a.	1p36.11	r	n/l	mi/s	S	/	Severe thrombocytopenia, characterized by dysplastic megakaryocytes and intracranial bleeding. Some patients have mild anemia and febrile neutropenia. Galactosemia, hypotenia, seizures, jaundice, galactosuria, and hepatomegaly. Large and pale platelets.
GATA1	GATA-BINDING PROTEIN 1; ERYTHROID TRANSCRIPTION FACTOR 1; ERYF1 GLOBIN TRANSCRIPTION FACTOR 1; GF1	THROMBOCYTOPENIA, X-LINKED, WITH OR WITHOUT DYSERYTHROPOIETIC ANEMIA; XLTDA	XLR	305371	300367	Xp11.23	r	n/l	mi/s	/	/	The GATA1 gene encodes a zinc finger DNA-binding transcription factor that plays a critical role in the normal development of hematopoietic cell lineages. XLTDA is characterized by variable severity of thrombocytopenia and abnormal platelet morphology and function due to defective platelet maturation. Some patients have a variable severity of dyserythropoietic anemia. Predisposition for myelodysplasia. Macrothrombocytopenia. Less alpha-granula.
GATA1	GATA-BINDING PROTEIN 1; ERYTHROID TRANSCRIPTION FACTOR 1; ERYF1 GLOBIN TRANSCRIPTION FACTOR 1; GF1	THROMBOCYTOPENIA WITH BETA-THALASSEMIA, X-LINKED; XLTT	XLR	305371	314050	Xp11.23	r	n/l	mi/s	/	/	Hemolytic anemia with laboratory abnormalities resembling macrothrombocytopenia, beta-thalassemia, splenomegaly, and dyserythropoietic anemia. Congenital erythropoietic porphyria. Decreased alpha-granules.
GFI1B	GROWTH FACTOR-INDEPENDENT 1B	GFI1b-related thrombocytopenia; BLEEDING DISORDER, PLATELET-TYPE, 17; BDPLT17; Gray Platelet-like syndrome	AD,AR	604383	187900	9q34.13	r/n	l	mo/s	S	/	BDPLT17 is characterized by increased bleeding tendency due to abnormal platelet function. It is a type of 'gray platelet syndrome' because the platelets appear abnormal on light microscopy.Moderate macrothrombocytopenia. Electron microscopy shows decreased or absent alpha-granules within platelets, and bone marrow biopsy shows increased numbers of abnormal megakaryocytes, suggesting a defect in megakaryopoiesis and platelet production. Red cell anisopoikilocytosis. The bleeding severity is variable. No aggregation towards agonists.
GNE	UDP-N-ACETYLGLUCOSAMINE 2-EPIMERASE/N-ACETYLMANNOSAMINE KINASE	Nonaka myopathy associated with thrombocytopenia	AR	603824	605820	9p13.3	r	n	n	/	/	GNE myopathy is a rare autosomal recessive distal myopathy characterized by early adult-onset, slowly to moderately progressive distal muscle weakness that preferentially affects the tibialis anterior muscle and that usually spares the quadriceps femoris. Muscle biopsy reveals presence of rimmed vacuoles.

GP1BA	GLYCOPROTEIN Ib, PLATELET, ALPHA POLYPEPTIDE	PSEUDO-VON WILLEBRAND DISEASE; BLEEDING DISORDER, PLATELET-TYPE, 3; BDPLT3; VON WILLEBRAND DISEASE, PLATELET-TYPE; PTvWD	AD	606672	177820	17p13.2	r	n/l	n/mi	/	/	Spontaneous platelet aggregation in vitro and increased platelet agglutination according to ristocetin. VWF multimeres / VWF:AG reduced. Platelet count is normal in most patients but may decrease greatly under stressful conditions (pregnancy, surgery, infection). *Important:* Distinction to vW Syndrome 2B!
GP1BA	GLYCOPROTEIN Ib, PLATELET, ALPHA POLYPEPTIDE	Bernard-Soulier syndrome, type A1 (recessive; biallelic)	AR	606672	231200	17p13.2	r	l/g	s	S	/	Bernard-Soulier syndrome is a mild to severe bleeding disorder due to abscence or dysfunction of the platelet glycoprotein receptor Ib/V/IX complex with mild to moderate thrombocytopenia. Platelets are large. Abnormal platelet function with absent or markedly reduced aggregation response to ristocetin.
GP1BA	GLYCOPROTEIN Ib, PLATELET, ALPHA POLYPEPTIDE	Bernard-Soulier syndrome, type A2 (dominant)	AD	606672	153670	17p13.2	r/n	l	mi/n	S	/	Autosomal dominant (mono-allelic) form of BBS with mild thrombocytopenia, variable larg platelets, and mild or no bleeding tendency.
GP1BB	GLYCOPROTEIN Ib, PLATELET, BETA POLYPEPTIDE	Bernard-Soulier syndrome; type B	AR	138720	231200	22q11.21	r	l/g	s	S	/	Bernard-Soulier syndrome is a mild to severe bleeding disorder due to abscence or dysfunction of the platelet glycoprotein receptor Ib/V/IX complex with mild to moderate thrombocytopenia. Platelets are large. Abnormal platelet function with absent or markedly reduced aggregation response to ristocetin.
GP6	PLATELET GLYCOPROTEIN VI	Bleeding disorder, platelet-type, 11	AR	605546	614201	19q13.42	n	n	mi/mo	/	/	Glycoprotein VI (GP6) is a 58-kD platelet membrane glycoprotein that plays a crucial role in the collagen-induced activation and aggregation of platelets. Platelet-type bleeding disorder-11 is an autosomal recessive mild to moderate bleeding disorder caused by defective platelet activation and aggregation in response to collagen. Defective platelet activation and aggregation in response to collagen.
GP9	PLATELET GLYCOPROTEIN IX	Bernard-Soulier syndrome, type C (monoallelic)	AR	173515	231200	3q21.3	r/n	l	n/mi	S	/	Autosomal dominant (mono-allelic) form of BBS with mild thrombocytopenia, variable larg platelets, and mild or no bleeding tendency. No ristocetin-mediated agglutination.
HOXA11	HOMEBOX A11	Radioulnar synostosis with amegakaryocytic thrombocytopenia 1; RUSAT1	AD	142958	605432	7p15.2	r	n/l	s	S	/	Radioulnar synostosis with amegakaryocytic thrombocytopenia (RUSAT) is characterized by thrombocytopenia that progresses to pancytopenia, in association with congenital proximal fusion of the radius and ulna that results in extremely limited pronation and supination of the forearm. Cardiac and renal malformations. Hearing loss. B-cell deficiency. Reduced/absent megakaryocytes in bone marrow.
HPS1	Hermansky-Pudlak syndrome 1	Hermansky-Pudlak syndrome 1	AR	604982	203300	10q24.2	n	n	mi/mo	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disorder in which oculocutaneous albinism, bleeding, and lysosomal ceroid storage result from defects of multiple cytoplasmic organelles: melanosomes, platelet-dense granules, and lysosomes. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
HPS2	Hermansky-Pudlak syndrome 2	Hermansky-Pudlak syndrome 2	AR	603401	608233	5q14.1	n	n	mi/mo	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disorder in which oculocutaneous albinism, bleeding, and lysosomal ceroid storage. HPS2 differs from the other forms of HPS in that it includes immunodeficiency, and patients with HPS2 have an increased susceptibility to infections due to congenital neutropenia. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
HPS3	Hermansky-Pudlak syndrome 3	Hermansky-Pudlak syndrome 3	AR	606118	614072	3q24	n	n	mi	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disorder in which oculocutaneous albinism, bleeding, and lysosomal ceroid storage. HPS3 is associated with milder bleeding symptoms and minimal hypopigmentation. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
HPS4	Hermansky-Pudlak syndrome 4	Hermansky-Pudlak syndrome 4	AR	606682	614073	22q12.1	n	n	mi/mo	S	/	Hermansky-Pudlak syndrome (HPS) is a rare autosomal recessive disorder in which oculocutaneous albinism, bleeding, and lysosomal ceroid storage. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
HPS5	Hermansky-Pudlak syndrome 5	Hermansky-Pudlak syndrome 5	AR	607521	614074	11p15.1	r/n	n	mi/mo	S	/	Hermansky-Pudlak syndrome-5 (HPS5) is characterized by oculocutaneous albinism, a bleeding diathesis, and lack of platelet dense bodies. HPS5 appears to be a milder form of the syndrome because the complications present in other forms of HPS, such as pulmonary fibrosis, granulomatous colitis, and neutropenia, have not been reported in HPS5 patients. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.

HPS6	Hermansky-Pudlak syndrome 6	Hermansky-Pudlak syndrome 6	AR	607522	614075	10q24.32	n	n	mi	S	/	Huizing et al. (2009) identified homozygous or compound heterozygous mutations in the HPS6 gene in 4 unrelated patients with Hermansky-Pudlak syndrome. All mutations except 1 resulted in a truncated protein. The phenotype was characterized by early-onset nystagmus, oculocutaneous albinism, and a mild bleeding diathesis, but no pulmonary fibrosis, granulomatous colitis, or renal involvement. However, 2 patients had gastrointestinal symptoms. Giant granula; reduced or absent d-granula; Luminometry: reduced or absent ATP release.
ITGA2	INTEGRIN, ALPHA-2	BLEEDING DISORDER, PLATELET-TYPE 9; BDPLT9; GLYCOPROTEIN Ia DEFICIENCY	AD	192974	614200	5q11.2	r/n	n	mi	/	/	The ITGA2 gene encodes alpha-2 integrin, a membrane glycoprotein known as GP Ia, which is expressed in a variety of cell types, including megakaryocytes and platelets. In platelets, GP Ia forms a complex with GP IIa (ITGB1; 135630) and represents one of the collagen receptors on the cell surface. BDPLT19 is an inherited blood coagulation disease characterized by mild thrombocytopenia, mild alpha-granue deficiency, defective platelet adhesion. Defective GPIIb/IIIa (CD41a, CD41b, CD61). Homozygous: defective platelet aggregation to all agonists, except ristocetin. Heterzoygous: mostly symptom-free; proof via flow cytometry.
ITGA2B	INTEGRIN, ALPHA-2B; PLATELET GLYCOPROTEIN IIb; GP2B	ITGA2B-related thrombocytopenia; BLEEDING DISORDER, PLATELET-TYPE, 16; BDPLT16	AD	607759	187800	17q21.31	r	l	n/mi	/	/	BDPLT16 is an autosomal dominant form of congenital macrothrombocytopenia associated with platelet anisocytosis. It is a disorder of platelet production. Affected individuals may have no or only mildly increased bleeding tendency. In vitro studies show mild platelet functional abnormalities.
ITGA2B	INTEGRIN, ALPHA-2B; PLATELET GLYCOPROTEIN IIb; GP2B	Glanzmann Thrombastenia	AR	607759	273800	17q21.31	n	n	mi/s	/	/	Glanzmann thrombasthenia is mild to severe bleeding disorder characterized by failure of platelet aggregation and by absent or diminished clot retraction. The abnormalities are related to quantitative or qualitative abnormalities of the GPIIb/IIIa platelet surface fibrinogen receptor complex resulting from mutations in either the GPIIb or GPIIIa genes. No platelet aggregation to any agonist.
ITGB3	INTEGRIN, BETA-3, PLATELET GLYCOPROTEIN IIIa; GP3A	ITGB3-related thrombocytopenia; BLEEDING DISORDER, PLATELET-TYPE, 16; BDPLT16	AD	173470	187800	17q21.31	n	l	mi/mo	/	/	BDPLT16 is an autosomal dominant form of congenital macrothrombocytopenia associated with platelet anisocytosis. It is a disorder of platelet production. Affected individuals may have no or only mildly increased bleeding tendency. In vitro studies show mild platelet functional abnormalities.
ITGB3	INTEGRIN, BETA-3, PLATELET GLYCOPROTEIN IIIa; GP3A	Glanzmann thrombasthenia	AR	173470	273800	17q21.31	n	n	mi/s	/	/	Glanzmann thrombasthenia is an autosomal recessive bleeding disorder characterized by failure of platelet aggregation and by absent or diminished clot retraction. The abnormalities are related to quantitative or qualitative abnormalities of the GPIIb/IIIa platelet surface fibrinogen receptor complex resulting from mutations in either the GPIIb or GPIIIa genes. No platelet aggregation to any agonist.
JAK2	JANUS KINASE 2	THROMBOCYTHEMIA 3; THCYT13; THROMBOCYTOSIS 3	AD	147796	614521	9p24.1	i	n	n	/	/	Thrombocythemia-3 is an autosomal dominant hematologic disorder characterized by increased platelet production resulting in increased numbers of circulating platelets. Thrombocythemia can be associated with thrombotic episodes, such as cerebrovascular events or myocardial infarction.
JBS	JACOBSEN SYNDROME	JACOBSEN SYNDROME; CHROMOSOME 11q DELETION SYNDROME	AD	147791	147791	Deletion von 11q23-24	r	n/l	mo/s	S	/	Cardiac and facial anomaly. Mental retardation. Giant a-granula. Favier et al. (1993) reported the cases of a 30-year-old woman and her 1-year-old son with chronic thrombocytopenia associated with mild hemorrhagic complications. The platelets contained giant, red-staining granules, and in the bone marrow megakaryocytes were increased with many micromegakaryocytes. Using electron microscopy to examine the platelets of an infant with an 11q23.3-qter deletion and clinical features of Jacobsen syndrome (147791), Krishnamurti et al. (2001) identified giant alpha-granules identical to those described in Paris-Trousseau syndrome. They suggested that TCPT may be a variant of Jacobsen syndrome and that the thrombocytopenia in all cases of 11q23.3 deletion is due to dysmegakaryopoiesis, with formation of giant alpha-granules during prolonged residence in the bone marrow.
KDSR	3-KETODIHYDROSPHINGOSINE REDUCTASE; FOLLICULAR LYMPHOMA VARIANT TRANSLOCATION 1; FVT1	Thrombocytopenia and erythrokeraderma; Erythrokeratodermia variabilis et progressiva 4	AR	136440	617526	18q21.33	r	n	mi/n	S	/	Erythrokeratodermia variabilis et progressiva-4 is characterized by severe lesions of thick scaly skin on the face and genitals, as well as thickened, red, and scaly skin on the hands and feet.

LYST	LYSOSOMAL TRAFFICKING REGULATOR	Chediak-Higashi syndrome 1; CHS	AR	606897	214500	1q42.3	r/n	n	mi	S	/	Multisystem disorder. Immunodefficiency. The features of Chediak-Higashi syndrome are decreased pigmentation of hair and eyes (partial albinism), photophobia, nystagmus, large eosinophilic, peroxidase-positive inclusion bodies in the myeloblasts and promyelocytes of the bone marrow, neutropenia, following cerebral hemorrhage (probably secondary to thrombocytopenia caused by hypersplenism), anormal susceptibility to infection, and peculiar malignant lymphoma. Death often occurs before the age of 7 years. following cerebral hemorrhage (probably secondary to thrombocytopenia caused by hypersplenism). Giant inclusions in neutrophiles. Reduced or irregular d-granula.
MASTL	MICROTUBULE-ASSOCIATED SERINE/THREONINE KINASE-LIKE;	Autosomal dominant thrombocytopenia	AD	608221	n.a.	10p12.1	r	n	n/mi	/	/	Mild thrombocytopenia.
MECOM	MDS1 AND EVI1 COMPLEX LOCUS	RADIOULNAR SYNOSTOSIS WITH AMEGAKARYOCYTIC THROMBOCYTOPENIA 2; RUSAT2	AD	165215	616738	3q26.2	r	n/l	s	S	/	Radioulnar synostosis with amegakaryocytic thrombocytopenia (RUSAT) is characterized by thrombocytopenia that progresses to pancytopenia, in association with congenital proximal fusion of the radius and ulna that results in extremely limited pronation and supination of the forearm. Possible progression to bone marrow aplasia.
MPIG6B	MEGAKARYOCYTE AND PLATELET INHIBITORY RECEPTOR G6B	Thrombocytopenia, anemia and myelofibrosis; THAMY	AR	606520	617441	6p21.33	r	g	mi/mo	/	/	An autosomal recessive disorder characterized by thrombocytopenia, giant platelets, and anemia manifesting in early childhood. Bone marrow biopsy shows increased number of megakaryocytes and reticular fibrosis consistent with myelofibrosis.
MPL	MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE; THROMBOPOIETIN RECEPTOR; TPOR	AMEGAKARYOCYTIC THROMBOCYTOPENIA, CONGENITAL; CAMT	AR	159530	604498	1p34.2	r	s/n	s	/	/	The MPL gene encodes the receptor for thrombopoietin (THPO; 600044), a hematopoietic growth factor that regulates the production of multipotent hematopoietic progenitor cells and platelets. Congenital amegakaryocytic thrombocytopenia (CAMT) is a rare disorder expressed in infancy and characterized by isolated severe thrombocytopenia and megakaryocytopenia. Evolution to severe bone marrow aplasia in infancy in all patients. Absence or reduced numbers of megakaryocytes in bone marrow.
MPL	MYELOPROLIFERATIVE LEUKEMIA VIRUS ONCOGENE; THROMBOPOIETIN RECEPTOR; TPOR	THROMBOCYTHEMIA 2; THCYT2; Essential thrombocythemie; ET	AD	159530	601977	1p34.2	i	n	n	/	/	The MPL gene encodes the receptor for thrombopoietin (THPO; 600044), a hematopoietic growth factor that regulates the production of multipotent hematopoietic progenitor cells and platelets. Thrombocythemia is a myeloproliferative disorder characterized by excessive platelet production resulting in increased numbers of circulating platelets. Thrombocythemia can be associated with thrombotic or hemorrhagic episodes and occasional leukemic transformation.
MYH9	MYOSIN, HEAVY CHAIN 9, NONMUSCLE	BLEEDING DISORDER, PLATELET-TYPE 6; BDPLT6; MAY-HEGGLIN ANOMALY; MHA; MACROTHROMBOCYTOPENIA WITH LEUKOCYTE INCLUSIONS; GIANT PLATELET SYNDROME WITH THROMBOCYTOPENIA; SEBASTIAN SYNDROME; SBS; EPSTEIN SYNDROME; EPSTNS; MACROTHROMBOCYTOPENIA, NEPHRITIS, AND DEAFNESS; FECHTNER SYNDROME; FTNS; MACROTHROMBOCYTOPENIA AND PROGRESSIVE SENSORINEURAL DEAFNESS; ALPORT SYNDROME WITH MACROTHROMBOCYTOPENIA; APSM	AD	160775	155100	22q12.3	r	l/g	n/mi	S	/	Macrothrombocytopenia with or without granulocyte inclusions, nephritis, or sensorineural hearing loss was previously thought to be comprised of 4 distinct entities with overlapping features: Fechtner syndrome, May-Hegglin anomaly, Epstein syndrome, and Sebastian syndrome. Fechtner syndrome was characterized by the triad of thrombocytopenia, giant platelets, and Dohle body-like inclusions in peripheral blood leukocytes, with the additional Alport syndrome (301050)-like features of nephritis, hearing loss, and eye abnormalities, predominantly cataracts. May-Hegglin anomaly was characterized by the triad of thrombocytopenia, giant platelets, and Dohle body-like inclusions in peripheral blood leukocytes. Epstein syndrome was characterized by thrombocytopenia, deafness, and nephritis, and lacked leukocyte inclusion bodies on classic staining of peripheral blood smears. Sebastian syndrome was similar to May-Hegglin anomaly, but had a different ultrastructural appearance of the leukocyte inclusions. Seri et al. (2003) suggested that these 4 disorders were not distinct entities, but rather represented a single disorder with a continuous clinical spectrum because variable phenotypic expression is observed not only between families but also within families having the same MYH9 mutation.
NBEA	NEUROBEACHIN	Autism with platelet dense granule defect	AD	604889	n.a.	13q13.3	n	n	n/mi	/	/	Autism with platelet dense granule defect.

NBEAL2	NEUROBEACHIN-LIKE 2	Gray platelet syndrome; GPS	AR	614169	139090	3p21.31	r	l	mi/mo	S	/	The gray platelet syndrome (GPS) is a rare inherited disorder characterized by mild to moderate bleeding tendency, moderate thrombocytopenia, and a marked decrease or absence of platelet alpha-granules and of the proteins contained in alpha-granules. The platelets are enlarged, but not giant, and have a gray appearance on light microscopy of Wright-stained peripheral blood smears due to decreased granules. Abnormalities in megakaryocyte development. Many patients with gray platelet syndrome develop a stable myelofibrosis and splenomegaly. Elevated serum vitamin B12 levels.
ORAI1	ORAI CALCIUM RELEASE-ACTIVATED CALCIUM MODULATOR ; CALCIUM RELEASE-ACTIVATED CALCIUM MODULATOR 1; CRACM1	Myopathy, tubular aggregate, 2	AD	610277	615883	12q24.31	n	n	n/mi	/	/	ORAI1 is CRAC channel expressed in human platelets. CRAC channelopathy. Severe combined immunodeficiency, autoimmunity, muscular hypotonia, and ectodermal dysplasia. ORAI1 deficient mice show pulmonary thromboembolism, arterial thrombosis, ischemic brain infarction, but only mild bleeding time prolongation. Platelets show impaired activation and thrombus formation.
P2RX1	PURINERGIC RECEPTOR P2X1	n.k.	n.k.	600845	n.a.	17p13.2	n.k.	n.k.	n.k.	n.k.	n.k.	Mahaut-Smith et al. (2004) reviewed evidence that P2RX1 alone and in synergy with other receptor pathways, such as P2Y1, P2Y12 (P2RY12; 600515), and GP6 (605546), generates significant platelet and megakaryocyte responses, particularly under conditions of shear stress, such as arterial thrombosis.
P2RY1	PURINERGIC RECEPTOR P2Y1	n.k.	n.k.	601167	n.a.	3q25.2	n	n	n	/	/	Leon et al. (1999) generated P2Y1-null mice to define the physiologic role of the P2Y1 receptor. These mice were viable with no apparent abnormalities affecting their development, survival, reproduction, or morphology of platelets, and the platelet count in these animals was identical to that of wildtype mice. However, platelets from P2Y1-deficient mice were unable to aggregate in response to usual concentrations of ADP and displayed impaired aggregation to other agonists, while high concentrations of ADP induced platelet aggregation without shape change. In addition, ADP-induced inhibition of adenylyl cyclase still occurred, demonstrating the existence of an ADP receptor distinct from P2Y1. P2Y1-null mice had no spontaneous bleeding tendency but were resistant to thromboembolism induced by intravenous injection of ADP or collagen and adrenaline. Hence, the P2Y1 receptor plays an essential role in thrombotic states and represents a potential target for antithrombotic drugs.
P2RY12	PURINORECEPTOR P2Y12;PLATELET ADP RECEPTOR	Bleeding disorder, platelet-type, 8; BLEEDING DISORDER DUE TO P2RY12 DEFECT	AR	600515	609821	3q25.1	n	n	mi/mo	/	/	Platelet-type bleeding disorder-8 is an autosomal recessive condition characterized by mild to moderate bleeding diathesis with easy bruising, mucosal bleedings, and excessive post-operative hemorrhage. Congenital disorder. The defect is due to the inability of ADP to induce platelet aggregation. Platelet aggregation: anormal reaction to ADP.
PLA2G4A	Phospholipase A2, GROUP IVA	Gastrointestinal ulceration, recurrent, with dysfunctional platelets	AR	600522	618372	1q31.1	n	n	mi/mo	/	/	An autosomal recessive disorder characterized by recurrent gastrointestinal mucosal ulcers, gastrointestinal bleeding, chronic anemia, iron deficiency, and abdominal pain. Disease features also include platelet dysfunction, and globally decreased eicosanoid synthesis. No ADP-induced dense granule release.
PLA2G7	Phospholipase A2, GROUP VII; PLATELET-ACTIVATING FACTOR ACETYLHYDROLASE; PAFAH; PAF Acetylhydrolase	Platelet-activating factor acetylhydrolase deficiency; PAFAD	AR	601690	614278	6p12.3	n	n	n	S	/	Deficiency of plasma platelet-activating factor acetylhydrolase results in increased levels of PAF, a chemotactic lipid that activates inflammatory cells, bronchoconstriction, and airway hyperresponsiveness, and can moderate the release of inflammatory agonists. It can be associated with several disease states including inflammatory gastrointestinal disorders, asthma, schizophrenia and atopy. Asthmatic individuals with PAFAD may manifest aggravated respiratory symptoms.
PLAU	Urinary plasminogen activator; Urokinase, URK	Quebec platelet disorder; Quebec platelet syndrome; QPS	AD	191840	601709	10q22.2	r	n	mo/s	/	/	Quebec platelet disorder is a bleeding disorder due to a gain-of-function defect in fibrinolysis. Although affected individuals do not exhibit systemic fibrinolysis, they show delayed onset bleeding after challenge, such as surgery. The disease is characterized by moderate to severe bleeding after trauma, surgery or obstetric interventions, frequent ecchymoses, mucocutaneous bleeding and muscle and joint bleeds. The hallmark of the disorder is markedly increased PLAU levels within platelets, which causes intraplatelet plasmin generation and secondary degradation of alpha-granule proteins. The disorder shows a favorable therapeutic response to fibrinolytic inhibitors. Variable thrombocytopenia; anormal urokinase levels in platelets; rebleeding type.

PRKACG	PROTEIN KINASE, cAMP-DEPENDENT, CATALYTIC, GAMMA	PRKACG-related thrombocytopenia; BLEEDING DISORDER, PLATELET-TYPE, 19; BDPLT19	AR	176893	616176	9q21.11	r	l/g	mo/s	/	/	A disorder characterized by moderate-severe bleeding tendency due to platelet dysfunction.Clinical features include epistaxis, hematomas, bleeding after tooth extraction, and menorrhagia. Severe macrothrombocytopenia due to defects in megakaryocyte proplatelet formation, platelet activation and cytoskeleton reorganization.
PTP2C	PROTEIN-TYROSINE PHOSPHATASE 2C; TYROSINE PHOSPHATASE SHP2; SHP2	NOONAN SYNDROME 1; MALE TURNER SYNDROME; FEMALE PSEUDO-TURNER SYNDROME; TURNER PHENOTYPE WITH NORMAL KARYOTYPE	AD	176876	163950	12q24.13	r/n	n	mi/s	S	/	Noonan syndrome (NS) is an autosomal dominant disorder characterized by short stature, facial dysmorphism, and a wide spectrum of congenital heart defects. The distinctive facial features consist of a broad forehead, hypertelorism, downslanting palpebral fissures, a high-arched palate, and low-set, posteriorly rotated ears. Cardiac involvement is present in up to 90% of patients. Pulmonic stenosis and hypertrophic cardiomyopathy are the most common forms of cardiac disease. Additional relatively frequent features include multiple skeletal defects (chest and spine deformities), webbed neck, mental retardation, and cryptorchidism. NS is associated with bleeding diathesis and a number of hematological abnormalities including clotting factor deficiencies, von Willebrand disease and abnormal platelet count/function.
PTPRJ	PROTEIN-TYROSINE PHOSPHATASE, RECEPTOR-TYPE, J	Inherited thrombocytopenia	n.k.	600925	n.a.	11p11.2	r	s	s	S	/	Syndromic thromboccytopenia characterized by spontaneous bleeding, small-sized platelets. Impaired platelet function.
RAB27A	RAS-ASSOCIATED PROTEIN RAB27A; RAS-RELATED GENE FROM MEGAKARYOCYTE; RAM	GRISCELLI SYNDROME, TYPE 2; GS2	AR	603868	607624	15q21.3	r	n	mi	S	/	The Griscelli syndrome type 2 (GS2) is characterized by hypomelanosis without neurologic impairment (type 1). Haemophagocytic lymphohistocytosis. Similar to the Chediak-Higashi Syndrom (CHS; 214500). Partial albinism; often pyogenic infections; acute fevers; neutropenia; anemia; reduced platelet aggregation. Abscence of giant granules in nucleated cells can eliminate CHS as disease.
RASGRP2	RAS GUANYL NUCLEOTIDE-RELEASING PROTEIN 2; CALCIUM AND DIACYLGLYCEROL-REGULATED GUANINE NUCLEOTIDE EXCHANGE FACTOR I; CALDAG-GEFI; CDC25-LIKE GENE; CDC25L;	BLEEDING DISORDER, PLATELET-TYPE, 18; BDPLT18	AR	605577	615888	11q13.1	n	n	mi	/	/	Mild bleeding disorder. Features include epistaxis, hematomas, bleeding after tooth extraction, and menorrhagia. Bleeding times are increased. Platelets show reduced aggregation in response to ADP or epinephrine.
RBM8A	RNA-BINDING MOTIF PROTEIN 8	THROMBOCYTOPENIA-ABSENT RADIUS SYNDROME; TAR; TAR SYNDROME; CHROMOSOME 1q21.1 DELETION SYNDROME, 200-KB	AR	605313	274000	1q21.1	r/n	s/n	s	S	/	The thrombocytopenia-absent radius syndrome (TAR) is characterized by reduction in the number of platelets and absence of the radius; preservation of the thumb distinguishes TAR from other syndromes that combine blood abnormalities with absence of the radius, such as Fanconi anemia (see 227650). The severity of skeletal anomalies varies from absence of radii to virtual absence of upper limbs, with or without lower limb defects such as malformations of the hip and knee. Skeletal, urogenital, kindney, and heart defects. Individuals with TAR have low numbers of megakaryocytes. Reduced numbers of platelets. Elevated hemoglobin level in patients with 5′UTR SNP. Normal WBCs count and some patients have leukocytosis and eosinophilia. Anemia.
RNU4ATAC	RNA, U4ATAC SMALL NUCLEAR	Roifman Syndrome	AR	601428	616651	2q14.2	r	n	mi/n	S	/	Roifman syndrome is a rare autosomal recessive disorder characterized by growth retardation, spondyloepiphyseal dysplasia, cognitive delay, facial dysmorphism, and antibody deficiency
RUNX1	RUNT-RELATED TRANSCRIPTION FACTOR 1; ACUTE MYELOID LEUKEMIA 1 GENE; AML1	PLATELET DISORDER, FAMILIAL, WITH ASSOCIATED MYELOID MALIGNANCY; FPDMM; PLATELET DISORDER, ASPIRIN-LIKE; THROMBOCYTOPENIA, FAMILIAL, WITH PROPENSITY TO ACUTE MYELOGENOUS LEUKEMIA; FPD/AML	AD	151385	601399	21q22.12	r/n	n/l	n/mo	/	P	Germline RUNX1 mutations lead to thrombocytopenia and platelet dysfunction. Multiple aspects of platelet function are impaired in these patients, associated with altered expression of genes (e.g. MYL9 in megakaryocytes) regulated by RUNX1. Over 40% of patients acquire acute myelogenous leukemia or myelodysplastic syndromes. Mild to moderate thrmbocytopenia. Qualitative platelet defects. Reduced platelet aggregation and ATP secretion.
SLFN14	SCHLAFEN FAMILY, MEMBER 14	SLFN14-related thrombocytopenia; SLFN14-RT; Bleeding disorder, platelet-type, 20	AD	614958	616913	17q12	r/n	l	mi/s	/	/	Impaired platelet function. Giant platelets. Decreaed ATP secretion. Reduced number of dense granules.
SRC	V-SRC AVIAN SARCOMA (SCHMIDT-RUPPIN A-2) VIRAL ONCOGENE	SRC-related thrombocytopenia; SRC-RT; THROMBOCYTOPENIA 6; THC6; THROMBOCYTOPENIA, AUTOSOMAL DOMINANT, 6	AD	190090	616937	20q11.23	r	l	mo/s	S	/	A dominant gain-of-function mutation in universal tyrosine kinase SRC causes thrombocytopenia, myelofibrosis, bleeding, and bone pathologies. Thrombocytopenia-6 is an autosomal dominant hematologic disorder characterized by increased bleeding episodes due to reduced platelet count and anormal platelet morphology (hypogranular or agranular; abundant vacuoles) resulting from defective megakaryopoiesis. Patients may also have bone abnormalities, including congenital facial dysmorphism, severe osteoporosis or tooth loss, as well as an increased risk for myelofibrosis and splenomegaly.

STIM1	STROMAL INTERACTION MOLECULE 1	STORMORKEN SYNDROME; STRMK	AD	605921	185070	11p15.4	r	n	mi	S	/	Stormorken syndrome is an autosomal dominant disorder characterized by mild bleeding tendency due to platelet dysfunction, thrombocytopenia, anemia, asplenia, tubular aggregate myopathy, congenital miosis, and ichthyosis. Additional features may include headache or recurrent stroke-like episodes. Low numbers of platelets. Reduced aggregation to ADP and collagen.
STIM1	STROMAL INTERACTION MOLECULE 1	YORK PLATELET SYNDROME; YPS; MYOPATHY, TUBULAR AGGREGATE; TAM; TUBULAR AGGREGATE MYOPATHY	AD	605921	160565	11p15.4	r/n	n/l	mi	S	/	York Platelet Syndrome (YPS) is a calcium channelopathy caused by gain of function in STIM1, a gene which acts as a calcium sensor. It is a multisystem disorder characterized by mild bleeding tendency due to platelet dysfunction, thrombocytopenia, anemia, asplenia, tubular aggregate myopathy, congenital miosis, and ichthyosis, with variable headache or recurrent stroke-like episodes. Platelet ultrastructural abnormalities, such as moderately decreased alpha granules, increased vacuoles, and giant electron dense and targeted-like bodies.
STXBP2	SYNTAXIN-BINDING PROTEIN 2	Familial hemophagocytic lymphohistiocytosis; FHL5	AR	601717	613101	19p13.2	n	n	n	/	/	A rare disorder characterized by immune dysregulation with hypercytokinemia, defective function of natural killer cell, and massive infiltration of several organs by activated lymphocytes and macrophages. The clinical features of the disease include fever, hepatosplenomegaly, cytopenia, and less frequently neurological abnormalities ranging from irritability and hypotonia to seizures, cranial nerve deficits and ataxia.
TBX1	T-BOX1	Velocardiofacial Syndrome; CHROMOSOME 22q11.2 DELETION SYNDROME; VCF SYNDROME; VCFS; SHPRINTZEN VCF SYNDROME	AD	602054	192430	22q11.21	r/n	l	n	S	/	Highly variable phenotype. Cardiac, cognitive and facial anomalies. Cleft palate. Hypoparathyroidism. Learning disabilities. Less frequent features: microcephaly, mental retardation, short stature, slender hands and digits, minor auricular anomalies, and inguinal hernia. Macrothrombocytopenia is increasingly being considered a feature of the broad spectrum of 22q11DS and may potentially be a clinical marker for the syndrome.
TBX1	T-BOX1	DiGeorge Syndrome; CHROMOSOME 22q11.2 DELETION SYNDROME; HYPOPLASIA OF THYMUS AND PARATHYROIDS; THIRD AND FOURTH PHARYNGEAL POUCH SYNDROME	AD	602054	188400	22q11.21	r	l	n	S	/	Neonatal hypocalcemia arising from parathyroid hypoplasia, thymic hyploplasia, and outflow tract defects of the heart. Susceptibility to infections due to a deficit of T cells. Cardiac and facial malformations. Micrognathia may be present. Short stature and variable mild to moderate learning difficulties are common. Macrothrombocytopenia is increasingly being considered a feature of the broad spectrum of 22q11DS and may potentially be a clinical marker for the syndrome.
TBXA2R	THROMBOXANE A2 RECEPTOR	BLEEDING DISORDER, PLATELET-TYPE, 13; BDPLT13	AD	188070	614009	19p13.3	n	n	mi/mo	/	/	TBXA2R plays an essential role in hemostasis by interacting with thromboxane A2 (TXA2) to induce platelet aggregation. Thromboxane A2 is an arachidonate metabolite that is a potent stimulator of platelet aggregation and a constrictor of vascular and respiratory smooth muscles. TXA2 has been implicated as a mediator in diseases such as myocardial infarction, stroke, and bronchial asthma. Mild to moderate mucocutaneous bleeding. Platalet aggregation: anormal reaction to arachidonic acid. Defective second phase platelet aggregation in response to epinephrine or ADP.
TBXAS1	THROMBOXANE A SYNTHASE 1	BLEEDING DISORDER, PLATELET-TYPE, 14; BDPLT14; THROMBOXANE SYNTHETASE DEFICIENCY; GHOSAL SYNDROME	AD	274180	614158	7q34	r/n	n	mi/mo	S	/	Thromboxane synthase catalyzes the conversion of the prostaglandin endoperoxide into thromboxane A2, a potent vasoconstrictor and inducer of platelet aggregation. In concert with prostacyclin, thromboxane A2 plays a pivotal role in the maintenance of hemostasis. Thromboxane synthase deficiency is characterized by mucocutaneous, gastrointestinal, or surgical bleeding. Defective second phase platelet aggregation to ADP, impaired aggregation to collagen, thrombin, epinephrin and absent aggregation to arachidonic acid using platelet aggregometry.
TCPT	THROMBOCYTOPENIA, PARIS-TROUSSEAU TYPE	Paris-Trousseau Type Thrombocytopenia; TCPT; CHROMOSOME 11q23 DELETION SYNDROME	AD	188025	188025	Deletion of 11q23-24; Hemizygous deletion of FLI1 (11q24.1-q24.3)	r	n/l	mi/mo	S	/	TCPT is a contiguous gene syndrome characterized by mild bleeding tendency, variable thrombocytopenia, dysmorphic facies, cardiac anomalies, mental retardation, abnormal giant alpha-granules in platelets and dysmegakaryopoiesis.

THPO	THROMBOPOIETIN	Megakaryocyte growth and development factor; MGDF; THROMBOCYTHEMIA 1; THCYT1; THROMBOCYTOSIS 1; Inherited thrombocytopenia from monoallelic THPO mutation	AD	600044	187950	3q27.1	i	n/l	n	/	/	Thrombopoietin (THPO) is a cytokine involved in the production of platelets by stimulating the differentiation and maturation of megakaryocyte progenitors. It acts as a ligand for MPL receptor, a member of the hematopoietic cytokine receptor superfamily and is essential for megakaryocyte maturation. Thrombocythemia, or thrombocytosis, is a myeloproliferative disorder characterized by excessive platelet production resulting in increased numbers of circulating platelets. Thrombocythemia can be associated with thrombotic or hemorrhagic episodes and occasional leukemic transformation. The drugs Hydroxyurea and Aspirin have been mentioned in the context of this disorder. Affiliated tissues include bone marrow, myeloid and skin, and related phenotypes are hypertension and splenomegaly.
TPM4	TROPOMYOSIN 4	TPM4-related thrombocytopenia; TPM4-RT	AD	600317	n.a.	19p13.12-p13.11	r	l	mi	/	/	Macrothrombocytopaenia. All other blood cell counts are normal. Mild effect on platelet function.
TRPM7	TRANSIENT RECEPTOR POTENTIAL CATION CHANNEL, SUBFAMILY M, MEMBER 7	TRPM7-related thrombocytopenia; TRPM7-RT	AD	605692	105500	15q21.2	r	l	n/mi	/	/	Macrothrombocytopaenia. Abberant distribution of granules, increased number and anarchic organization of microtubules.
TUBB1	TUBULIN, BETA-1	TUBB1-related Macrothrombocytopenia, autosomal dominant	AD	612901	613112	20q13.32	r	l/g	n/mo	/	/	Microtubules are involved in a wide variety of cellular processes, including mitosis, morphogenesis, platelet formation, and mobility of cilia and flagella. Circulating platelets carry a single marginal microtubule coil that is wound in 8 to 12 turns and is responsible for platelet shape. TUBB1 is the major beta-tubulin expressed in platelets and megakaryocytes and is required for optimal platelet assembly. Kunishima et al. (2009) reported a Japanese boy who was incidentally found to have thrombocytopenia (40-60 x 10(9) platelets). Peripheral blood smears showed prominent giant platelets. Platelet aggregation function was normal, and bone marrow biopsy showed normal megakaryocyte number and morphology. The mother of the patient also had macrothrombocytopenia. Cultured mature megakaryocytes from the proband showed large and irregular bleb protrusions, suggesting impaired megakaryocyte fragmentation and release of large platelets. Further studies indicated that the thrombocytopenia resulted from peripheral destruction, not platelet underproduction.
UNC13D	UNC13 HOMOLOG D; MUNC13-4	HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS, FAMILIAL, 3; FHL3	n.k.	608897	608898	17q25.1	r/n	n	n/mi	/	P	FHL is a hyperinflammatory disorder characterized by unremitting fever, hepatosplenomegaly, hyperferritinemia, cytopenia, and sometimes hemophagocytosis. The brain may also be affected in familial hemophagocytic lymphohistiocytosis. As a result, affected individuals may experience irritability, delayed closure of the bones of the skull in infants, neck stiffness, abnormal muscle tone, impaired muscle coordination, paralysis, blindness, seizures, and coma. In addition to neurological problems, FHL can cause abnormalities of the heart, kidneys, and other organs and tissues. Affected individuals also have an increased risk of developing cancers of blood-forming cells (leukemia and lymphoma).
VIPAS39	VPS33B-INTERACTING PROTEIN, APICAL-BASOLATERAL POLARITY REGULATOR, SPE39 HOMOLOG	Arthrogryposis, renal dysfunction, and cholestasis 2	AR	613401	613404	14q24.3	n	n/l	n/mi	/	/	A multisystem disorder, characterized by neurogenic arthrogryposis multiplex congenita, renal tubular dysfunction and neonatal cholestasis with bile duct hypoplasia and low gamma glutamyl transpeptidase activity. Platelet dysfunction is common.
VPS33B	VACUOLAR PROTEIN SORTING 33	Arthrogryposis, renal dysfunction, and cholestasis 1; ARC SYNDROME; ARCS; Autosomal recessive keratoderma-ichthyosis-deafness syndrome; ARKID	AR	608552	208085	15q26.1	r	l	mi	S	/	Autosomal recessive keratoderma-ichthyosis-deafness (ARKID) syndrome is a rare multisystem disorder caused by biallelic mutations in VPS33B. ARKID syndrome is allelic to arthrogryposis-renal dysfunction-cholestasis (ARC) syndrome, a severe disorder with early lethality whose phenotypic characteristics also include ichthyosis, hearing loss, severe failure to thrive, platelet dysfunction and osteopenia. Secondary infection and cardivascular anomalies. Abnormal platelet count and function. Grey platelets. No a-granula.

VWF	VON WILLEBRAND FACTOR	von Willebrand disease, type 1	AD	613160	193400	12p13.31	n	n	mi	/	/	VWD type 1 is a quantitative partial deficiency of circulating VWF. In this type of VWD, there is a normal ratio of functional VWF activity (VWF:RCo, ristocetin cofactor activity) relative to VWF antigen level (VWF:Ag). Mannucci (2004) stated that type 1 VWD accounts for 60 to 80% of all VWD cases and is characterized by mild to moderate quantitative deficiencies of VWF and factor VIII, which are coordinately reduced to 5 to 30% of normal plasma levels (pathogenic levels of 5 to 30 IU/dL). The bleeding anomalies are generally characterized by mucocutaneous hemorrhage (menorrhagia, epistaxis, or prolonged bleeding after trauma or a surgical intervention).
VWF	VON WILLEBRAND FACTOR	von Willebrand disease, types 2A, 2B, 2M, and 2N	AD,AR	613160	613554	12p13.31	n	n	mi/mo	/	/	VWD type 2 accounts for 10 to 30% of cases and is characterized by qualitative abnormalities of VWF; it is further divided into subtypes 2A, 2B, 2M, and 2N. The mutant VWF protein in types 2A, 2B, and 2M are defective in their platelet-dependent function, whereas the mutant protein in type 2N is defective in its ability to bind F8. Symptoms are mild to moderate.
VWF	VON WILLEBRAND FACTOR	von Willibrand disease, type 3	AR	613160	277480	12p13.31	n	n	s	/	/	VWD type 3 accounts for 1 to 5% of cases, and is characterized by a severe quantitative defect of VWF in plasma (less than 1% of normal plasma levels), with low but usually detectable levels of factor VIII (1 to 10% of normal plasma levels). In the rare type 3 disease (1 in 1 million people), symptoms are more frequent and severe and include spontaneous bleeding episodes, often into joints and muscles.
WAS	WAS Gene	Wiskott-Aldrich syndrome	XLR	300392	301000	Xp11.23	r	s/n	s	S	/	Severe immunodeficiency leading to early death. Eczema. Increased risk of malignancies and autoimmunity. Decreased aggregation and secretion. Decreased or absent WAS protein in flow cytometry. Hyporeactivity towards many agonists in flow cytometry.
WAS	WAS Gene	X-linked thrombocytopenia; XLT; THROMBOCYTOPENIA 1; THC1	XLR	300392	313900	Xp11.23	r	s/n	mi/mo	S	/	Mild immunodeficiency. Mild transient eczema. Increased risk of malignancies and autoimmunity. Nonsyndromic patients with only thrombocytopenia are decribed. Defective WAS protein.
WIPF1	WAS/WASL-INTERACTING PROTEIN FAMILY, MEMBER 1; WISKOTT-ALDRICH SYNDROME PROTEIN-INTERACTING PROTEIN; WASPIP WASP-INTERACTING PROTEIN; WIP	Wiskott-Aldrich syndrome 2; wipf1 deficiency	n.k.	602357	614493	2q31.1	r	n	mi/mo	S	/	An immunodeficiency disorder characterized by eczema, thrombocytopenia, recurrent infections, defective T-cell proliferation, and impaired natural killer cell function.

Legend:
bold: genes recognized as causal for platelet disorders by the International Society on Thrombosis and Hemostasis (ISTH)
AD = Autosomal dominant; AR = Autosomal recessive; XLR = X-linked recessive ; n.k. = not known; n.a. = not available; # = platelet number (reduced (r), normal (n), increaed (i)); Size = platelet size under the light microscope (small (s), normal (n), large (l), giant (g)); BT = most likely/ suspected bleeding tendency (no (n), mild (mi), moderate (mo), severe (s)); S = Syndromic; P = Predisposition to secondary disease; / = not applicable

Sources: www.orpha.net; www.omim.org; www.isth.org; www.malacards.org; www.uniprot.org