Inherited platelet diseases with normal platelet count: phenotypes, genotypes and diagnostic strategy

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Supplemental Table I: Inherited thrombocytopenia associated with function defects and/or granule abnormalities

Disease, (protein)	Platelet volume	Gene, transmission	Function defects	α- and/or dense granules	References
Bernard-Soulier syndrome (GPIb-IX-V)	MTP	*GPIBA, GPIBB, GP9* AR (biallelic)	Defect of platelet adhesion to VWF. Decreased aggregation with thrombin	Normal	1
Glanzman thrombasthenia – like syndrome with MTP (αIIbβ3)	MTP	*ITGA2B, ITGB3* AD (monoallelic)	Decreased aggregation	Sometimes giant α-granules	2-3
FLNA-RD (FLNA1 – filamin A)	MTP	*FLNA* X-linked	Loss-of-function but rare cases with gain-of-function mutations Adhesion and aggregation to collagen	Presence of giant α-granules	4-5
Paris-Trousseau syndrome (FLI1 with ETS-binding domain)	MTP	*FLI1* AD with hemizygosity for deletions at 11q23.3ter or AR	Platelet aggregation and secretion reduced for homozygous defect	Giant fused α-granules	6-7
GATA1 (gene repressor; in complex with FOG)	MTP	*GATA1* X-linked.	Reduced function to ristocetin and/or collagen. Heterogeneity between patients	Absence of α-granules and/or dense granules Heterogeneity between patients	8
GFI1B (gene repressor)	MTP	*GFI1B* AD	Reduced function Much heterogeneity between patients	Absence of α-granules and/or dense granules Variability between patients	9
RUNX1, (Runt family member)	Normal	*RUNX1* AD	Decreased aggregation in response to AA, epinephrine and collagen, absent second wave ADP	Dense granule and signaling defects	10
ETV6, (ETS family member; TEL oncogene)	Normal	*ETV6* AD	Abnormal platelet spreading on Fg surfaces and abnormal clot retraction, inconsistent abnormal aggregation	Normal	11
IKZF5	Normal	*IKZF5(PEGASUS gene)* AD	Inconstant defect of aggregation	Fewer α- and dense granules.	12
Gray platelet syndrome (NBEAL2)	MTP	*NBEAL2* AR	Variably decreased responses to collagen and thrombin	Lack of α-granules.	13,14
Wiskott-Aldrich syndrome, (WASp, an adaptor and signaling protein)	Small platelets	*WAS* X-linked	Decreased aggregation in response to AA, epinephrine and collagen, absence second wave ADP	Possibly fewer granules	15

(PTPRJ or CD148, a tyrosine phosphatase)	Small platelets	*PTPRJ* AR	Decreased aggregation to collagen and to a lesser extent, TRAP. Impaired secretion.	No reports	16
(Src, a tyrosine kinase)	MTP	*SRC* -gain-of-function missense mutation leading to upregulated tyrosine kinase activity. AD	Delayed aggregation with collagen. Variable other defects	Possibly decreased α-granules	17
CARST. (ADAP or SLAP-130, an adaptor protein)	Small platelets	*FYB* AR	Increased basal expression of P-selectin and reduced activation. Decreased adhesion	. No reports	18
(G6b-B, regulator of platelet activation)	MTP	*G6B (MPIG6B* *A*R	Normal or minor aggregation defects. Normal adhesion	No reports	19
SLFN14 (endoribonuclease)	MTP	*SLFN14* AD	Decreased aggregation and secretion with ADP, collagen, TRAP, but normal with AA	Reduced α- and dense granules	20
Stormorken or York platelet syndrome (STIM1; Ca^{2+}-sensor)	MTP	*STIM1* AD	Reduced thrombus formation, Abnormal PS expression and thrombin generation	No reports	21
(Protein kinase A catalytic subunit)	MTP	*PRKACG* AR	Defect of platelet activation	No reports	22
THC2 (ANKRD26)	Normal volume	*ANKRD26* AD	Limited defects	Reduced platelet α-granules	23

RD, related-disease; AR, autosomal recessive; AD, autosomal dominant; MTP, macrothrombocytopenia; ADP, adenosine diphosphate; CARST, congenital autosomal recessive small platelet thrombocytopenia; AA, arachidonic acid; TRAP, thrombin receptor activating peptide.

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