Suppl. Table I: Selected patients with missense mutations illustrating the large biological and genetic variability in type II Glanzmann thrombasthenia

Patient (Origin/sex)	Bleeding Severity	Residual αIIbβ3 Fg or PAC-1 binding	Clot Retraction/ Platelet Fg/Adhesion	Mutation(s)/ Expression studies	References
Patients with ITGA2B gene defects					
2 Families (Germany/F: Spain/F)	Moderate. In the 2nd family a brother died from post-traumatic hemorrhage when young	1st family: 7-12% αIIbβ3 (FC) + 10-15% αIIb & β3 in WB. 2nd family 25% αIIbβ3 in FC & WB	Partial clot retraction. No platelet Fg (2nd family)	Homozygous p.R327H Expressed in COS-7 and CHO cells	27, 28
1 Case (USA/M)	Severe with GI bleeding/multiple transfusions. Destructive changes in ankle joints	Around 5% αIIbβ3 (FC). 25% αIIb and 35% β3 (WB). No PAC-1 binding	Clot retraction not reported. 5% platelet Fg. No platelet adhesion on Fg	Homozygous p.L183P Expressed in CHO cells	29
Four Families (Japan/F)	Moderate or not reported	14-22% αIIbβ3 (FC) – homozygote (3 cases) 4-8% αIIbβ3 compound heterozygote (1 case)	Near normal clot retraction. 50% platelet adhesion on Fg (homozygous patients)	Homozygous p.Q747P Compound heterozygous p.Q747P + exon 18 skipping Q747P expressed in CHO cells	30,31
1 Case (Spain/F)	Bleeding but severity not detailed	10% αIIb & β3 (FC and WB).	Clot retraction very reduced and 25% platelet Fg	Compound heterozygous p. C674R + IVS5(+2)C>A C674R expressed in CHO cells;	32, 33
3Families (USA/F+M; Dutch/M; Chinese/M)	Mostly severe with transfusions (GI bleeding + hematuria for 1 case). Mild bleeding in 1 male in the Mennonite family	Homozygous: 10%-30% FC & WB, PAC-1 failed to bind. Heterozygous: 5% or lower FC but distinct bands in WB.	Clot retraction not reported. Platelet Fg much reduced (1 case).	Homozygous p.P145L Heterozygous p.P145L with IVS15(-1)Gdel or not detected. P145L expressed in COS-1 and CHO cells	34
Osaka-12 (Japan/F)	Moderate	36%-41% αIIb & β3 but 13% αIIbβ3 (FC). No Fg or PAC-1 binding	Subnormal clot retraction. Some binding of 293 cells to immobilized Fg	Heterozygous p.R143H + null allele. Expression in 293 cells	52
1 Case (Afghanistan /F)	Severe	24% αIIbβ3 (FC & CIE). No Fg or PAC-1 binding	Clot retraction 10%. No platelet Fg. Much reduced platelet adhesion on Fg	Homozygous p.T176I Expressed in Cos-7 cells	44
1 Case (China/F)	Moderate	Residual αIIbβ3 (<10%) by FC & WB that bound	Clot retraction not reported. Platelet Fg content normal.	Heterozygous p.R553* + p.P912L Expressed in CHO cells	37

		Fg on platelet activation			
Patients with ITGB3 gene defects					
1 Case (China/F)	Severe + platelet transfusion	6%-14% αIIbβ3 (FC). 10% -35% αIIb & β3 (WB)	No clot retraction, 36% platelet Fg. Transfected cells adhered to Fg	Homozygous p.C374Y Expressed in CHO cells	40
1 Case (Caucasian/M)	Lifelong bleeding	Up to 30 % αIIb & β3 (FC & WB); <5% with MoAb to αIIbβ3 (FC).	Clot retraction normal.	Homozygous p.S162L Expressed in Cos-7 cells	51
3 Families (Japan/2M + 1F)	All with lifelong bleeding	19,9%, 7.5% and 15.4% αIIbβ3 respectively (FC)	Clot retraction normal	Homozygous H280P Heterozygous H280P with G579S or C460F Expressed in CHO cells	41
1 Case (USA/F)	Mild/moderate bleeding. Mother with VWD	Residual αIIbβ3 but no Fg binding (FC); 10% αIIb & β3 (WB).	Clot retraction normal but transfected cells failed to adhere to Fg	Heterozygous p.L262P + c.867 to 868del + fs + stop Expression in COS-7 and HEK293 cells	42
2 Families (France F/M)	Mild/moderate	15% and 8% αIIbβ3, No Fg or PAC-1 binding. αvβ3 also affected.	Clot retraction normal. 50% or more platelet Fg. Normal adhesion of transfected cells to Fg	Homozygous p.L196P (p.L222P) Heterozygous L196P + p.C598Y Expressed in CHO cells	17,45
1 Case (India/M)	Moderate bleeding	Trace αIIbβ3 with complex-dependent MoAbs (FC). 10%-30% αIIb and β3 (WB)	Clot retraction not reported. <20% platelet Fg	Homozygous p.C506Y β3 migrated as a dimer	43

F, female ; M, male; Fg, fibrinogen; FC, flow cytometry; WB, western blot; CIE, crossed immunelectrophoresis; GI, gastro-intestinal; VWD, von Willebrand disease. Each of the above patients has featured in a full case report