Fibrin(ogen) in human disease: both friend and foe

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 doi:10.3324/haematol.2019.236901

Received: September 19, 2019.

Accepted: November 21, 2019.

Pre-published: January 16, 2020.

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Supplementary data

Fibrinogen molecule	Chain	Nascent variant	Mature variant	Affected process(es)	Reported phenotype(s)	References
Dusart (Paris V)/ Chapel Hill III	Aα	p.Arg573Cys	p.Arg554Cys	• Plasminogen binding to (abnormal) fibrin and activation • Fibrinolysis	• Pulmonary embolism • Deep vein thrombosis • Superficial thrombosis • Cerebral vein thrombosis • Hepatic portal system thromboses	(1-4)
Caracas V	Aα	p.Ser551Cys	p.Ser532Cys	• Plasminogen binding to (abnormal) fibrin and activation • Fibrinolysis	• Arterial thrombosis • Deep and superficial venous thrombosis • Pulmonary embolism	(5)
Ijmuiden/ Christchurch II/ London VIII/ St-Germain III/ Vicenza III	Bβ	p.Arg44Cys	p.Arg14Cys	• N.I.	• Deep vein thrombosis • Pulmonary embolism (spontaneous abortion) • Superficial thrombophlebitis • Thrombotic stroke • Venous and arterial thrombosis	(6-10)
New York I	Bβ	p.Gly39_Leu102del (exon 2 deletion)	p.Gly9_Leu72del (exon 2 deletion)	• Thrombin binding to (abnormal) fibrin • Fibrinolysis	• Pulmonary embolism • Venous thrombosis	(11, 12)
Nijmegen	Bβ	p.Arg74Cys	p.Arg44Cys	• Plasminogen activation • Fibrinolysis	• Venous thrombosis	(6, 13)
Naples/Milano II at homozygous state	Bβ	p.Ala98Thr	p.Ala68Thr	• Thrombin binding to (abnormal) fibrin • Fibrinolysis	• Deep vein thrombosis • Severe arterial and venous thrombosis • Stroke	(14, 15)
Melun	γ	p.Asp390Val	p.Asp364Val	N.I.	• Arterial thrombosis • Deep and superficial venous thrombosis	(16)

Table S1

Nascent Aα chain variant	Mature Aα chain variant	Type	Reference
p.Glu543Lys	p.Glu524Lys	Missense	Rowczenio et al. (17)
p.Glu545Lys	p.Glu526Lys	Missense	Rowczenio et al. (17)
p.Glu545Val	p.Glu526Val	Missense	Uemichi et al. (18)
p.Thr557Lysd	p.Thr538Lys	Missense	Gillmore et al. (19)
p.Glu559Val	p.Glu540Val	Missense	Gillmore et al. (19)
p.Pro571His	p.Pro552His	Missense	Gillmore et al. (19)
p.Ser572Leu	p.Ser553Leu	Missense	Zhen et al. (20)
p.Arg573Leu	p.Arg554Leu	Missense	Benson et al. (21)
p.Gly574Phe	p.Gly555Phe	Missense	Rowczenio et al. (17)
p.Thr555Val	p.Thr536Val	Missense	Zhen et al. (20)
p.Met536GlnfsTer28	p.Met517GlnfsTer28	Frameshift	Kang et al. (22)*
p.Gly538GlufsTer30	p.Gly519GlufsTer30	Frameshift	Rowczenio et al. (17)
p.Phe540LeufsTer28	p.Phe521LeufsTer28	Frameshift	Garnier et al. (23)
p.Phe540SerfsTer27	p.Phe521SerfsTer27	Frameshift	Rowczenio et al. (17)
p.Val541AlafsTer27	p.Val522AlafsTer27	Frameshift	Hamidi Asl et al. (24)
p.Ser542ArgfsTer25	p.Ser523ArgfsTer25	Frameshift	Yazaki et al. (25)
p.Thr544LeufsTer24	p.Thr525LeufsTer24	Frameshift	Uemichi et al. (26)**
p.Glu545SerfsTer23	p.Glu526SerfsTer23	Frameshift	Gillmore et al. (19)***

(*), (**), (***), These mutations were originally described as p.517_522delinsQSfsX548, p.Glu524GlufsX25, and p.Thr525ThrfsX24 respectively

Table S2

Table S1 – Mutations known to significantly increase the risk for thrombosis, therefore predisposing carriers to thrombotic events. For this reason, according to the Factor XIII and Fibrinogen Scientific and Standardization Committee (SSC) of the International Society on Thrombosis and Haemostasis (ISTH), their identification validates the diagnosis of congenital fibrinogen disorders and facilitates family screening (27). This table was adapted from (28) Abbreviations: N.I., not identified.

Table S2 – Fibrinogen mutations in *FGA* associated with amyloidosis (29).

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