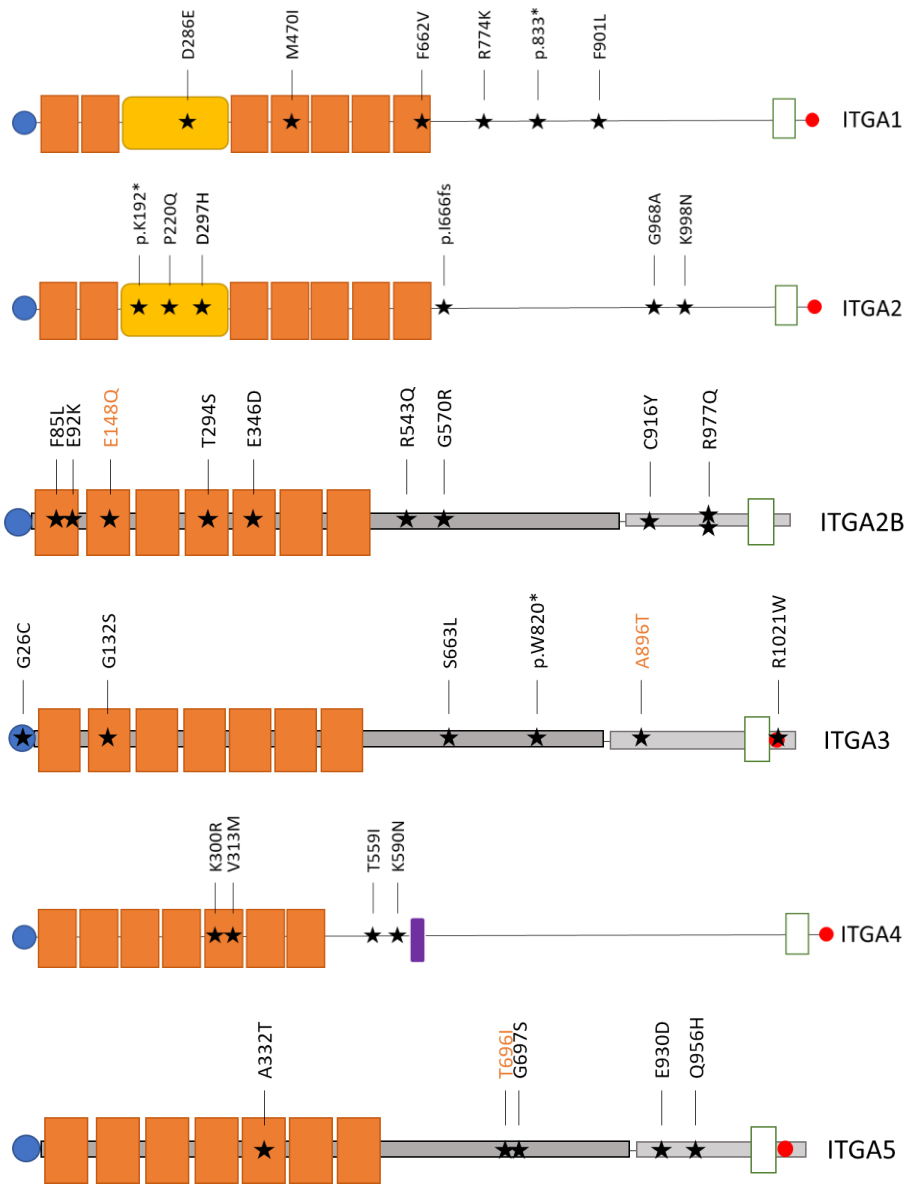
Figure S1: Visual representation of protein domains and structure of all ECM molecules. Information on protein domains was obtained from the UniProt knowledgebase (https://www.uniprot.org/). Locations of patient mutations found in the MMRF (black) and our dataset (orange) are marked with stars. Mutations within the same protein detected in the same patient are marked with grey stars. Images were created using PowerPoint.

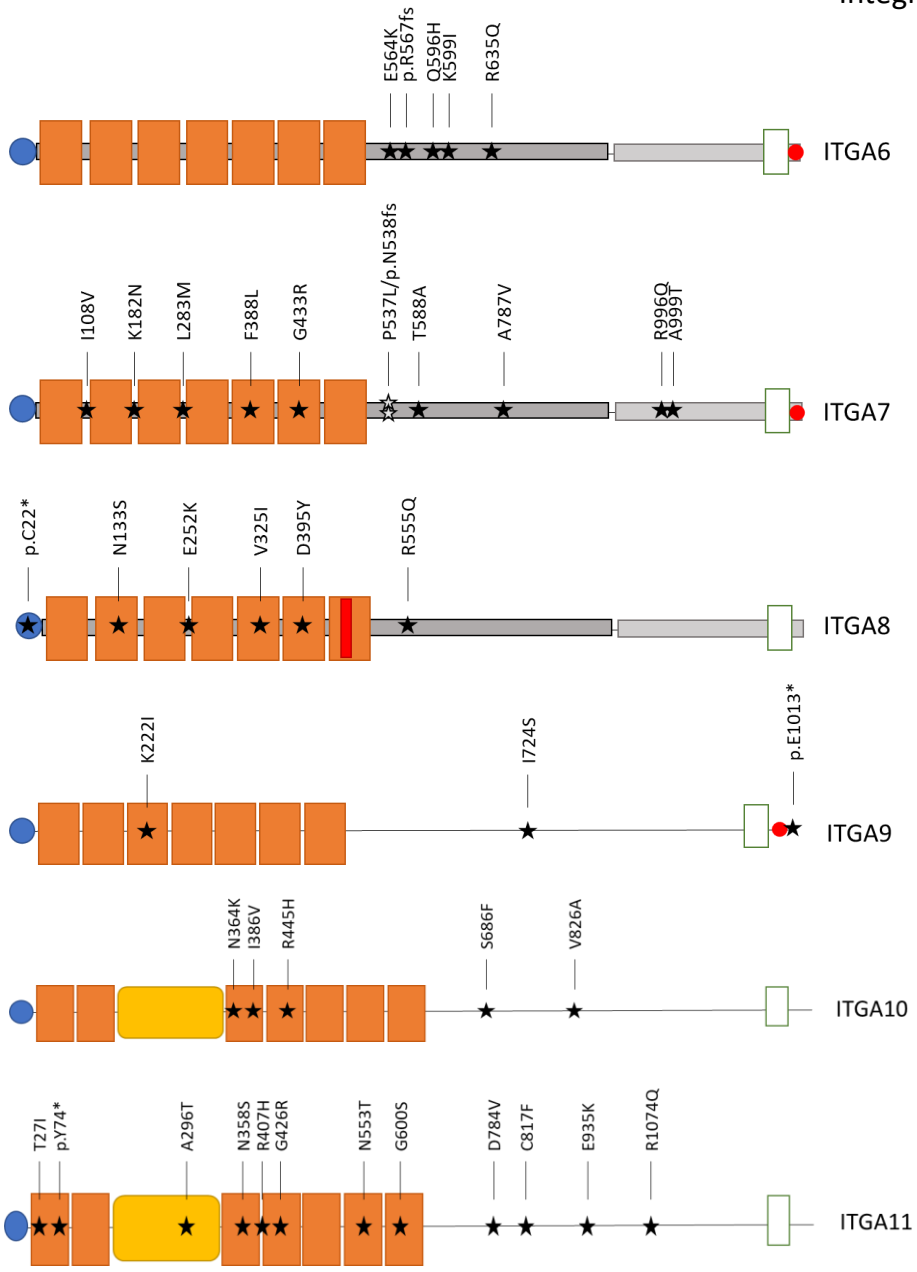
Integrins

Integrin α subunits

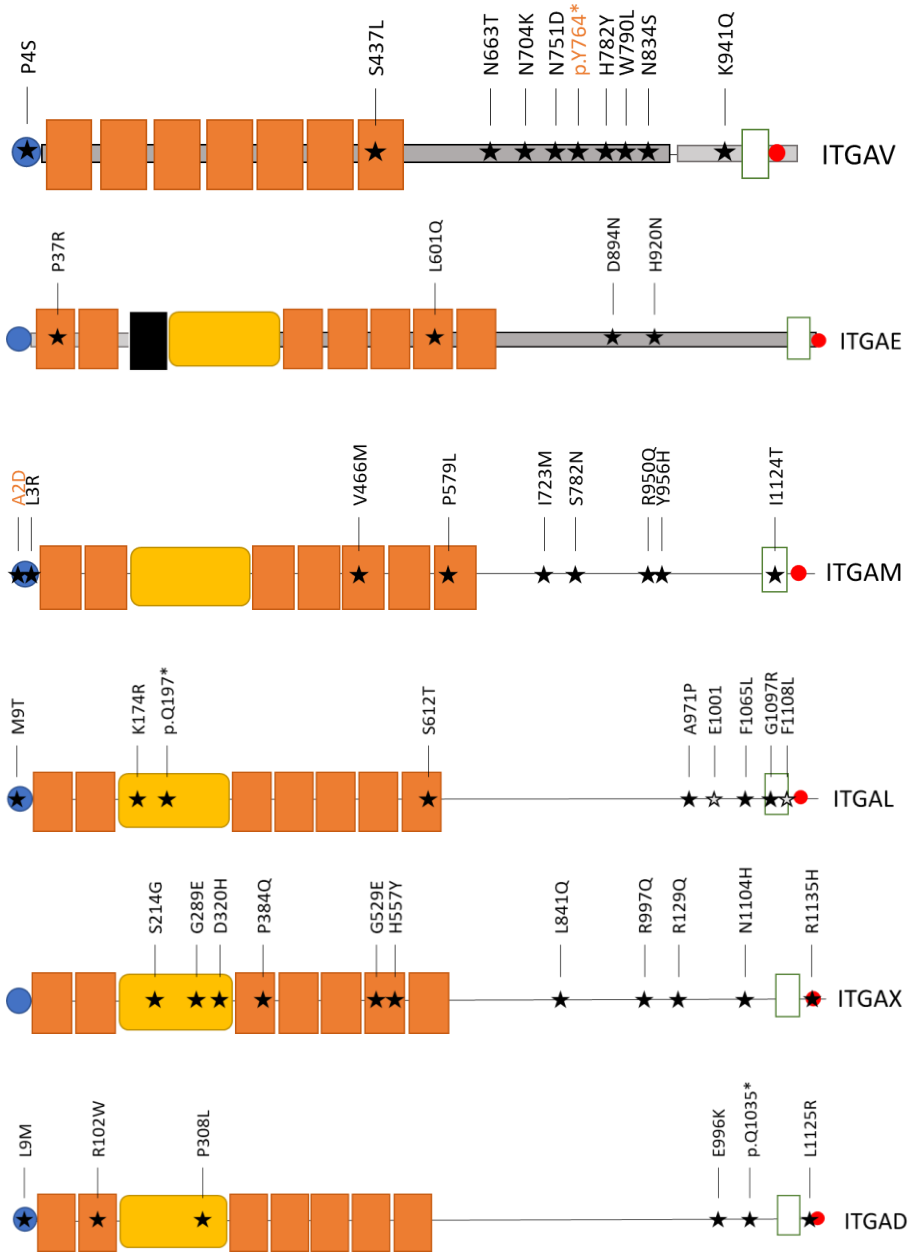


Signal peptide | FG-GAP | VWFA | Helical transmembrane | GFFKR motif | Heavy chain | Light chain | SG1 | X domain | Cell attachment site | Fibronectin type III domain | PSI

Integrin α subunits

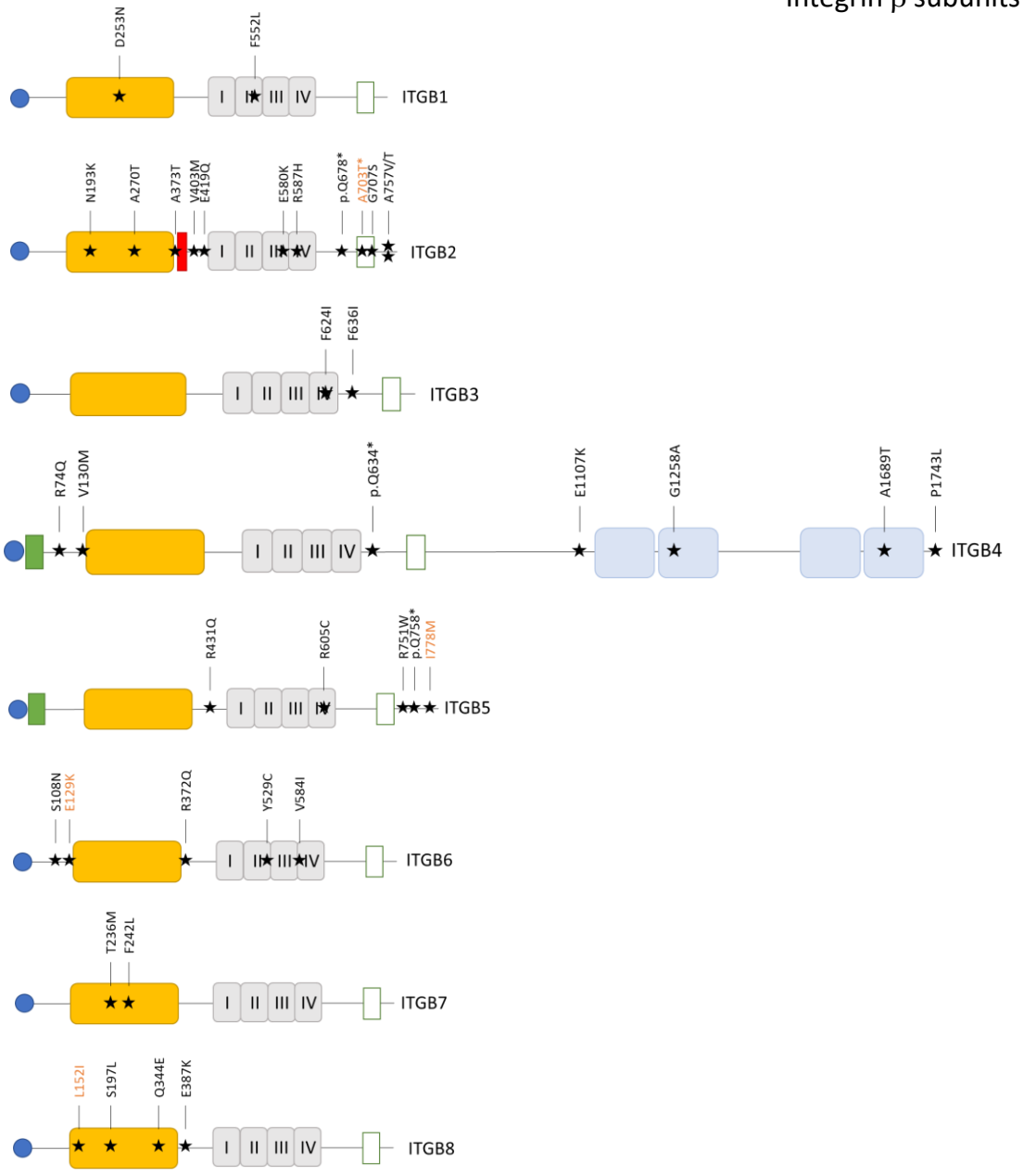


Integrin α subunits

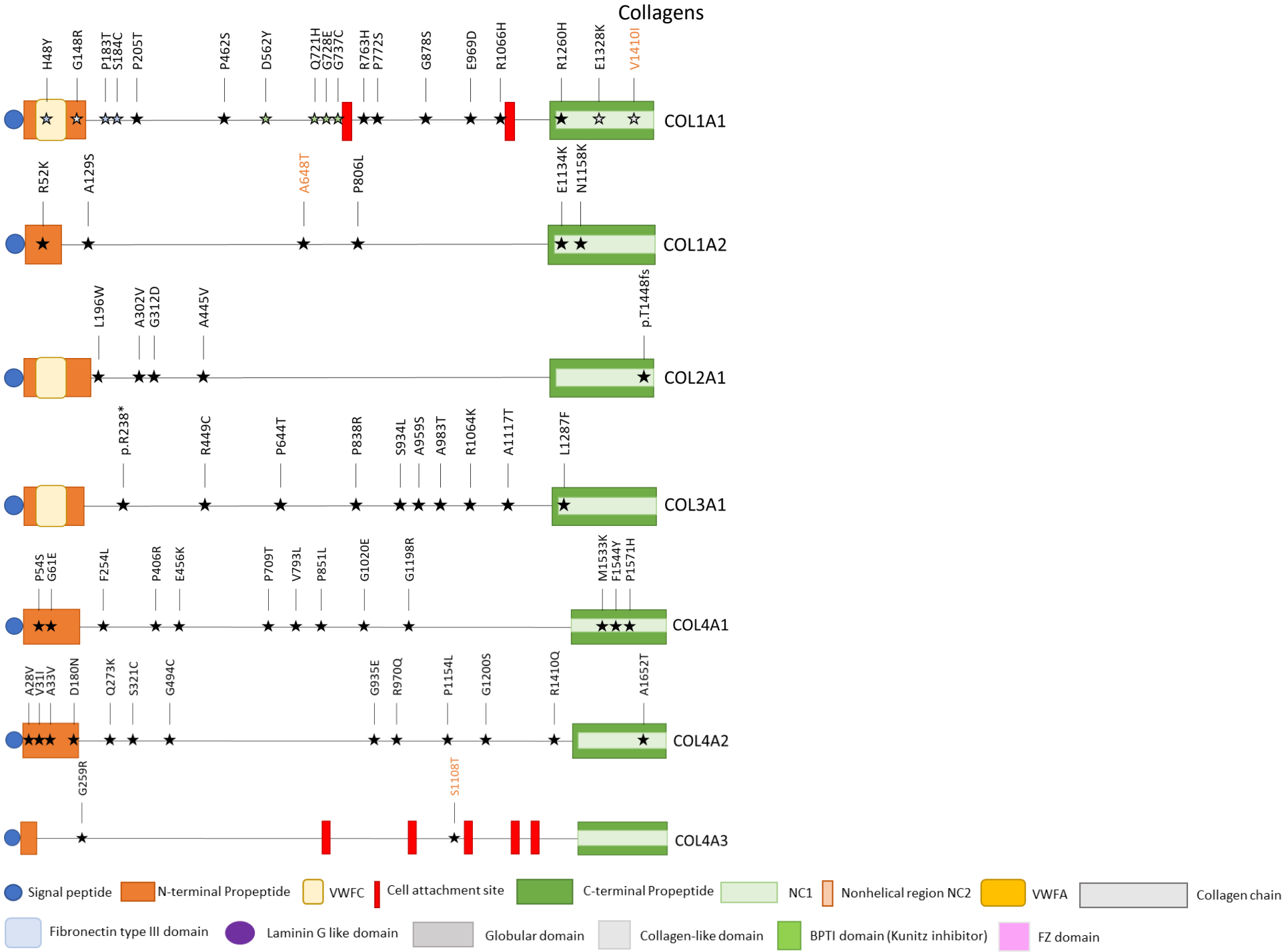


Signal peptide | FG-GAP | VWFA | Helical transmembrane | GFFKR motif | Heavy chain | Light chain | SG1 | X domain | Cell attachment site | Fibronectin type III domain | PSI

Integrin β subunits



Collagens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P205T
P462S
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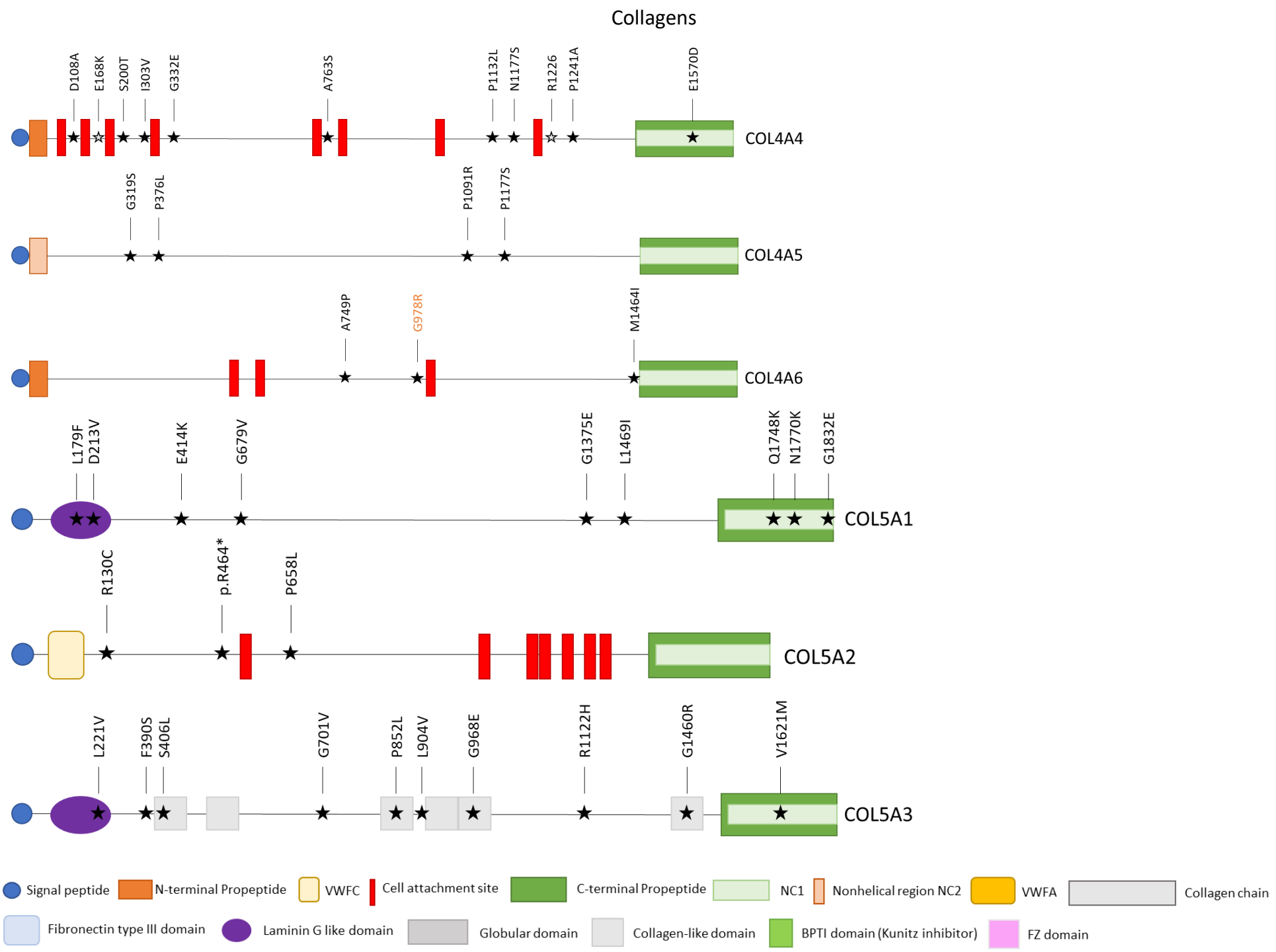
G737C
R763H
P772S
G878S
E969D
R1066H
R1260H
E1328K
V1410I
COL1A1
R52K
A129S
A648T
P806L
E1134K
N1158K
COL1A2
L196W
A302V
G312D
A445V
p.T1448fs
COL2A1
p.R238*
R449C
P644T
P838R
S934L
A959S
A983T
R1064K
A1117T
L1287F
COL3A1
P54S
G61E
F254L
P406R
E456K
P709T
V793L
P851L
G1020E
G1198R
M1533K
F1544Y
P1571H
COL4A1
A28V
V31I
A33V
D180N
Q273K
S321C
G494C
G935E
R970Q
P1154L
G1200S
R1410Q
A1652T
COL4A2
G259R
S1108T
COL4A3
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain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G332E
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R1226
P1241A
E1570D
COL4A4
G319S
P376L
P1091R
P1177S
COL4A5
A749P
G978R
M1464I
COL4A6
L179F
D213V
E414K
G679V
G1375E
L1469I
Q1748K
N1770K
G1832E
COL5A1
R130C
p.R464*
P658L
COL5A2
L221V
F390S
S406L
G701V
P852L
L904V
G968E
R1122H
G1460R
V1621M
COL5A3
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain

Collagens


K53N
A119T
R222H
Q355K
A409V
G443V
A514T
A533T
R677H
D712Y
A807T
T823M
R976H
G985S
V996M
COL6A1
p.Met1?
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P276L
G391R
R876H
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COL6A2
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G139S
p.140fs
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L601M
G753W
V1092I
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P1226S
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Q414R
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V612I
D743N
V815I
R882W
R911L
V922A
A965S
F1027L
I1114M
R1120C
S1157C
K1259R
L1282V
G1431R
T1876R
R1936W
R1952G
P-Q2300*
P2327S
N2396S
G2446V
Y2479C
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A1121S
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G1543R
p.Q1617*
G1659R
S1730C
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V2084F
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R892K
R1120S
R1154C
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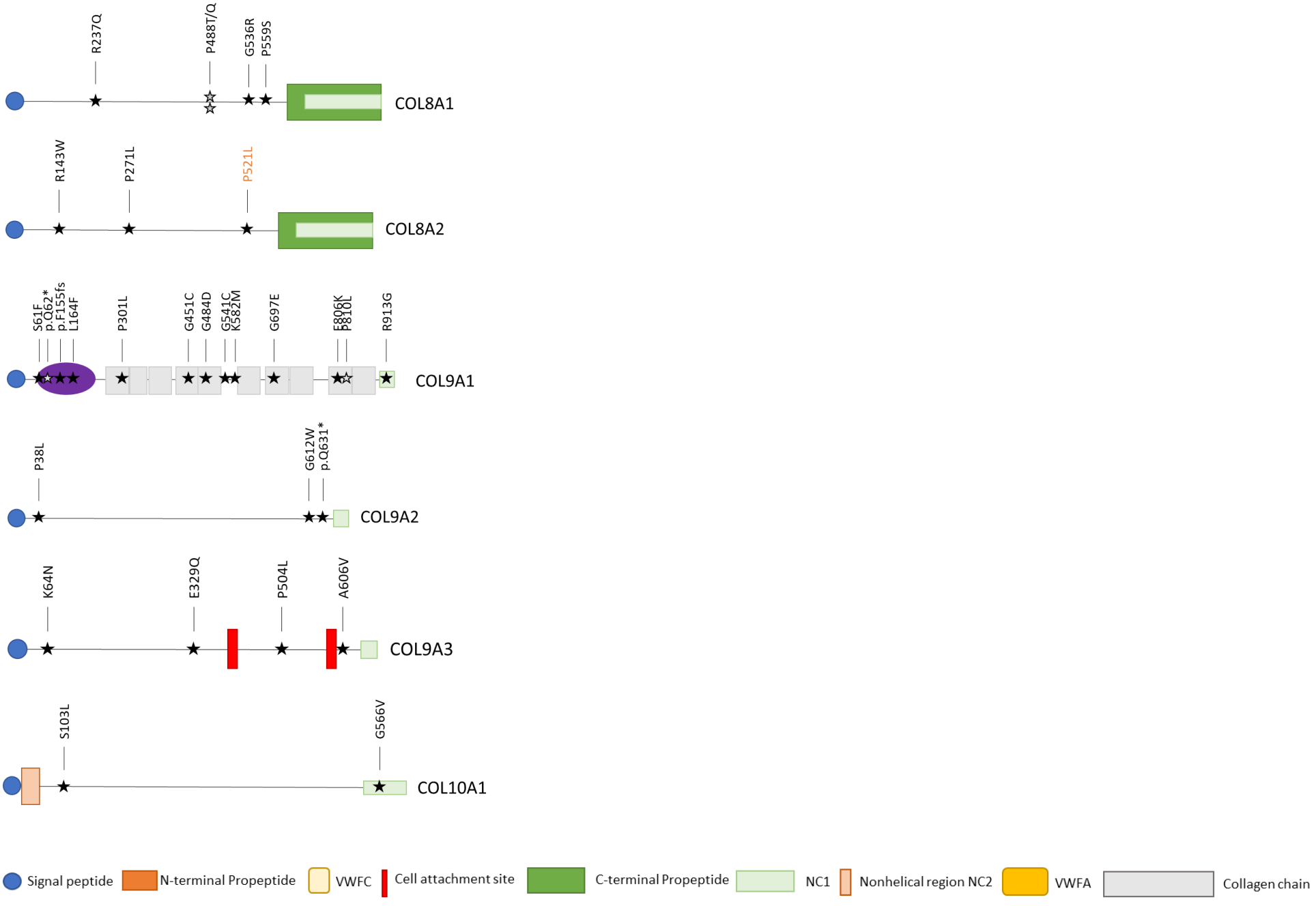
G1290E
A1567V
G1616A
G2257E
G2487D
I2679M
p.G2725fs
I2809F
COL7A1
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain

Collagens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R143W
P271L
P521L
COL8A2
S61F
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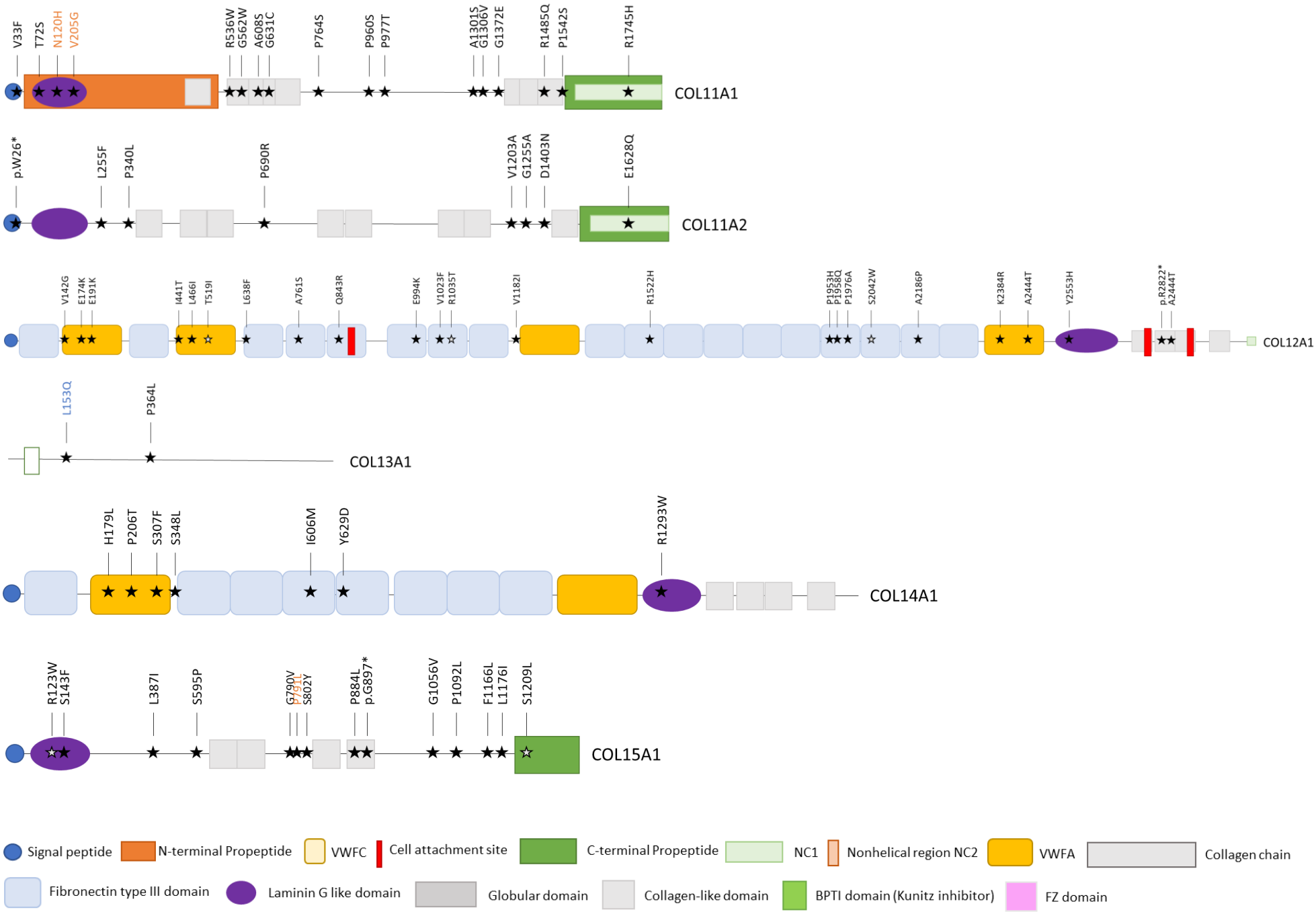
p.F155fs
L164F
P301L
G451C
G484D
G541C
K582M
G697E
F806K
P810L
R913G
COL9A1
P38L
G612W
p.Q631*
COL9A2
K64N
E329Q
P504L
A606V
COL9A3
S103L
G566V
COL10A1
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain

Collagens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P960S
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G1306V
G1372E
R1485Q
P1542S
R1745H
COL11A1
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L255F
P340L
P690R
V1203A
G1255A
D1403N
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COL11A2
V142G
E174K
E191K
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L466I
T519I
L638F
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Q843R
E994K
V1023F
R1035T
V1182I
R1522H
P1953H
P1958Q
P1976A
S2042W
A2186P
K2384R
A2444T
Y2553H
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P206T
S307F
S348L
I606M
Y629D
R1293W
COL14A1
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S143F
L387I
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S802Y
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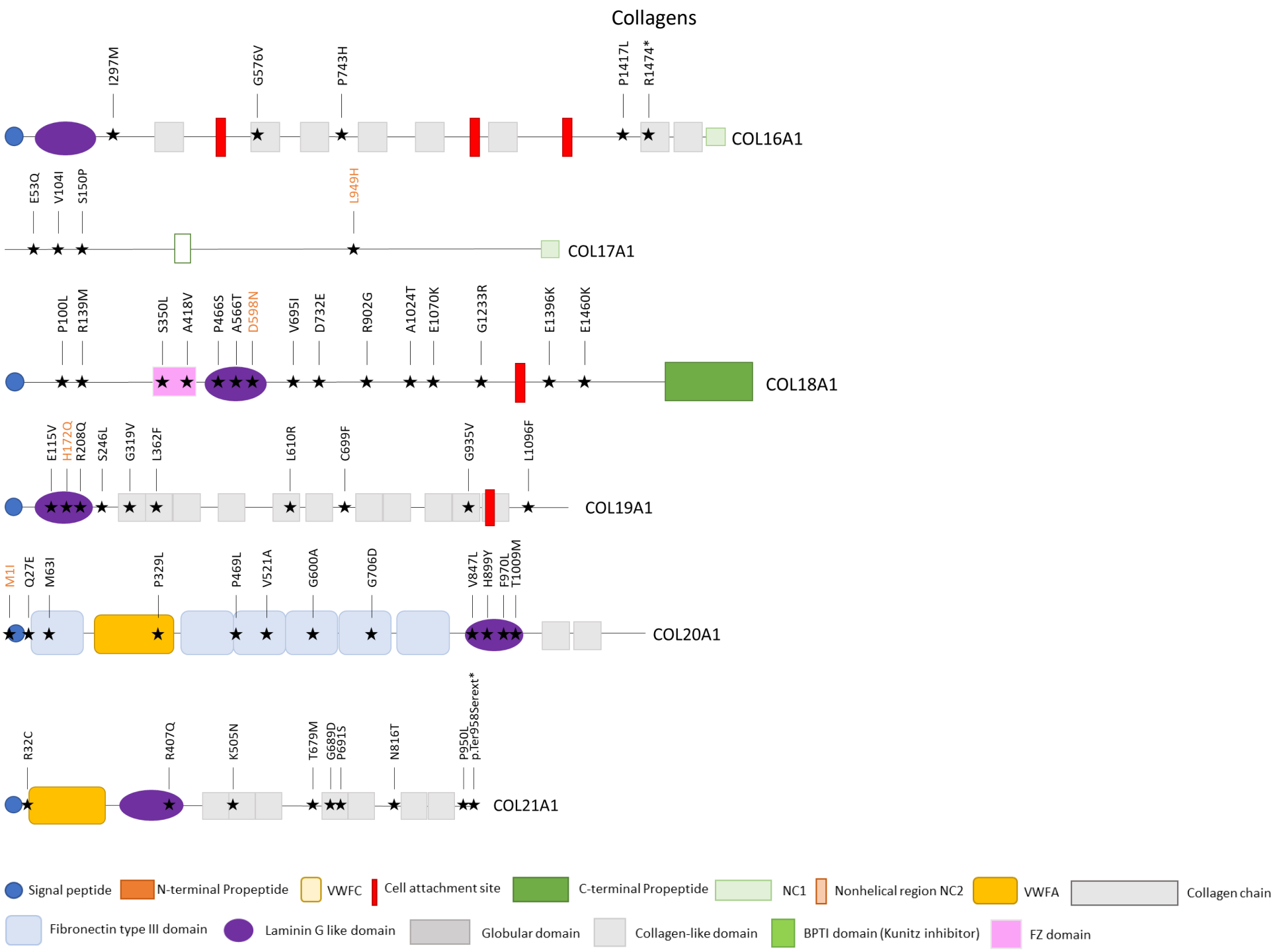
G1056V
P1092L
F1166L
L1176I
S1209L
COL15A1
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain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P100L
R139M
S350L
A418V
P466S
A566T
D598N
V695I
D732E
R902G
A1024T
E1070K
G1233R
E1396K
E1460K
COL18A1
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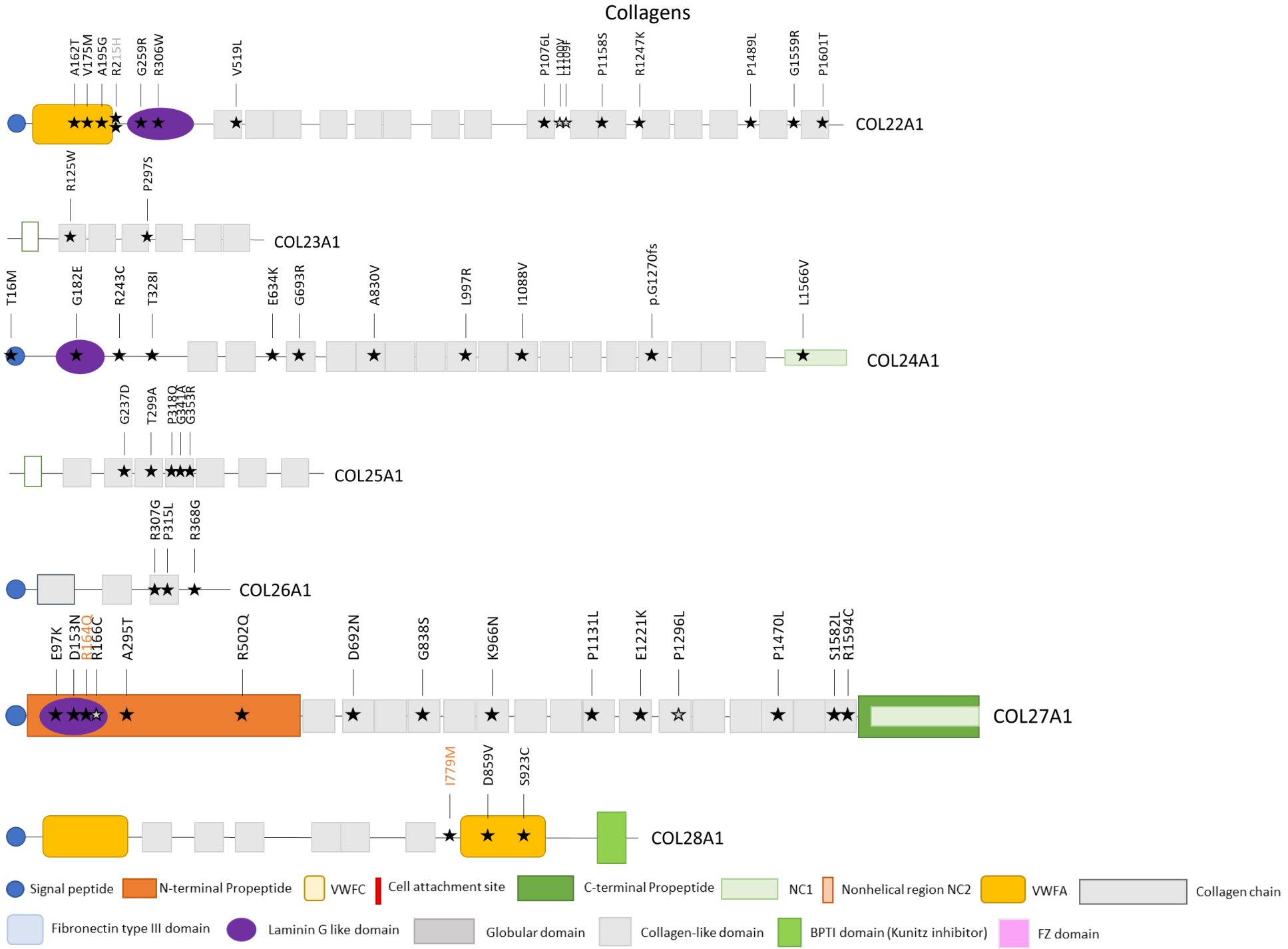
H172Q
R208Q
S246L
G319V
L362F
L610R
C699F
G935V
L1096F
COL19A1
M1I
Q27E
M63I
P329L
P469L
V521A
G600A
G706D
V847L
H899Y
F970L
T1009M
COL20A1
R32C
R407Q
K505N
T679M
G689D
P691S
N816T
P950L
p.Ter958Serext*
COL21A1
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain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V519L
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R1247K
P1489L
G1559R
P1601T
COL22A1
R125W
P297S
COL23A1
T16M
G182E
R243C
T328I
E634K
G693R
A830V
L997R
I1088V
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COL24A1
G237D
T299A
G353R
COL25A1
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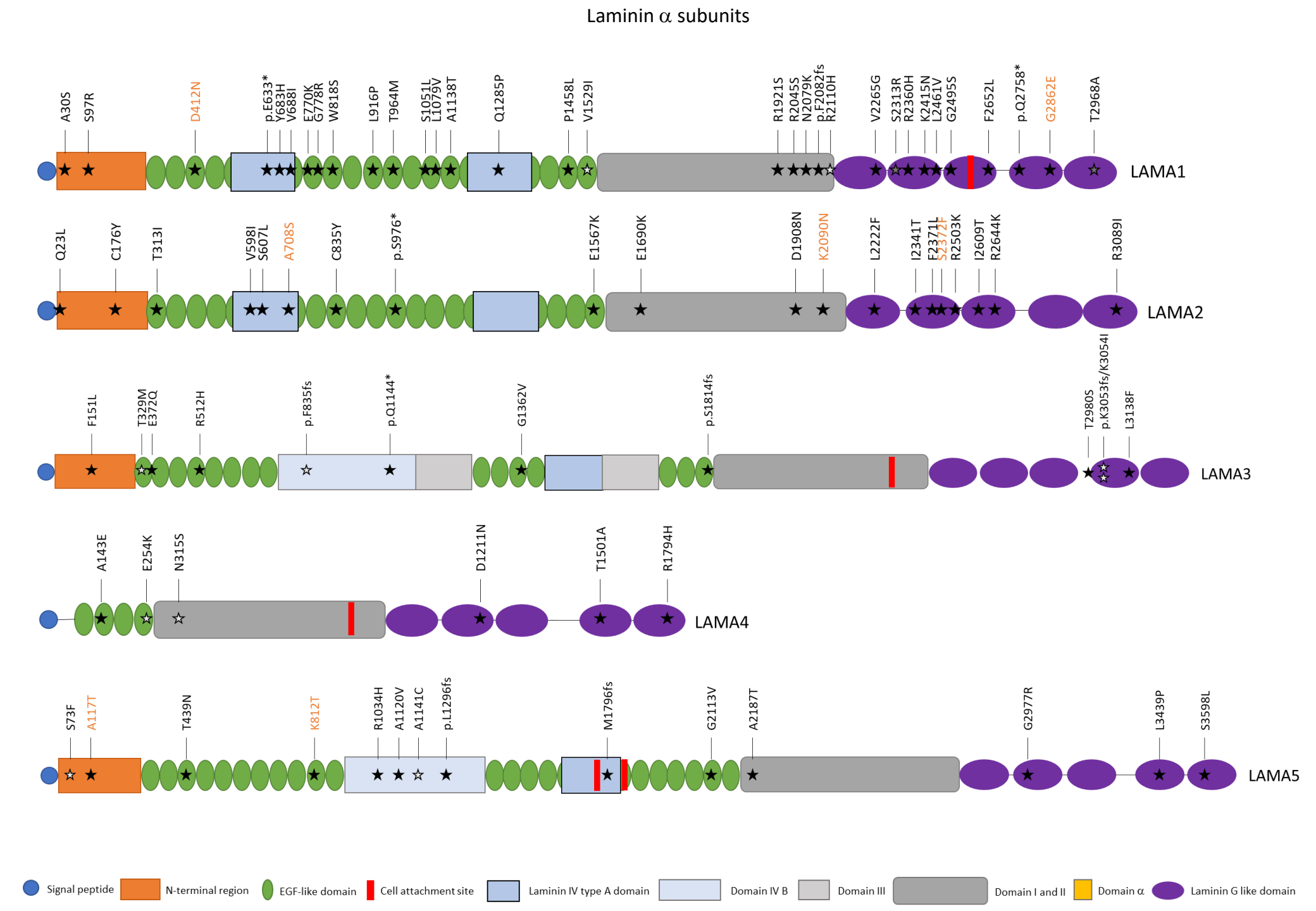
P315L
R368G
COL26A1
E97K
D153N
R166C
A295T
R502Q
D692N
G838S
K966N
P1131L
E1221K
P1296L
P1470L
S1582L
R1594C
COL27A1
I779M
D859V
S923C
COL28A1
Signal peptide
N-terminal Propeptide
VWFC
Cell attachment site
C-terminal Propeptide
NC1
Nonhelical region NC2
VWFA
Collagen chain
Fibronectin type III domain
Laminin G like domain
Globular domain
Collagen-like domain
BPTI domain (Kunitz inhibitor)
FZ domain

Laminins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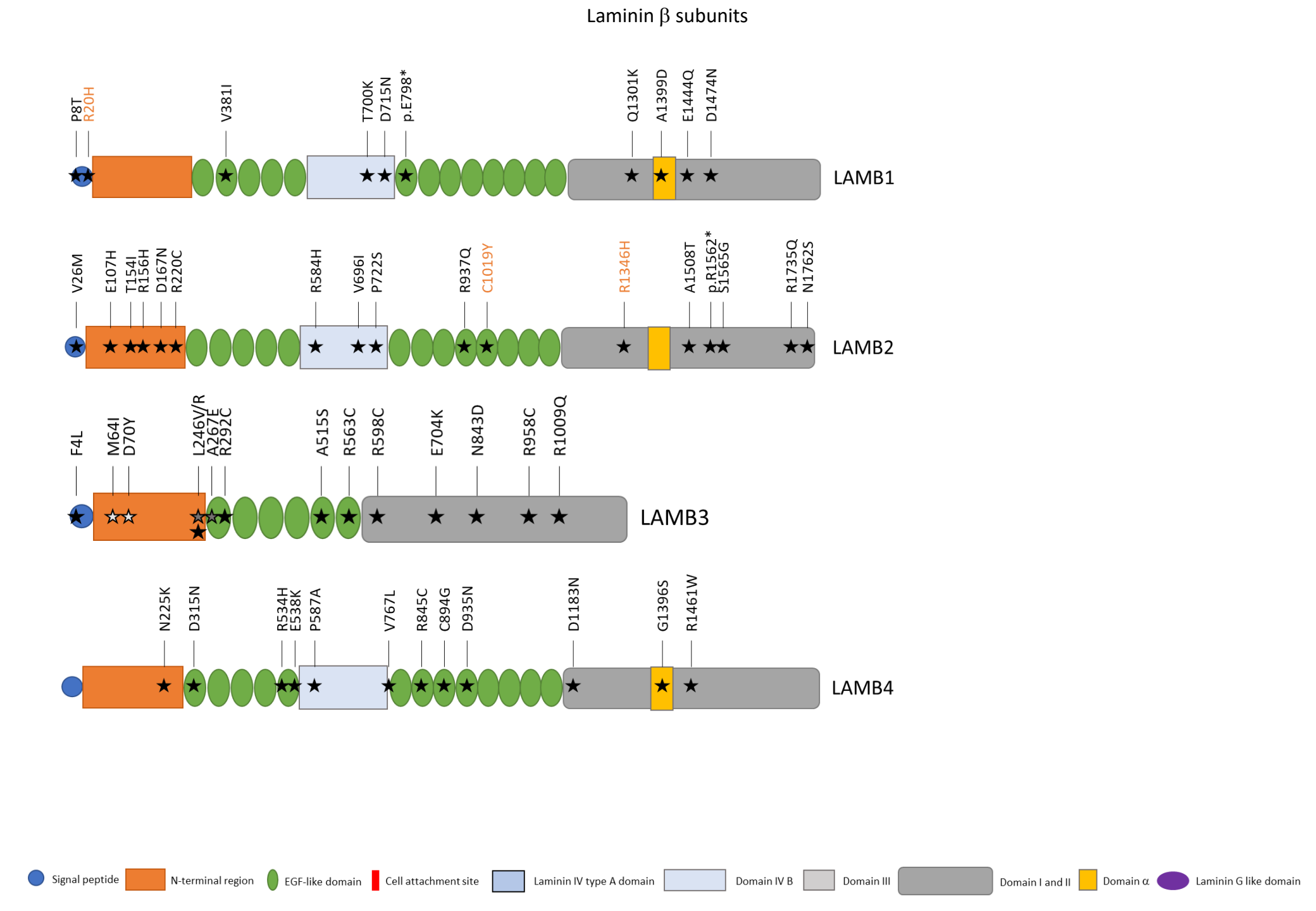
Y683H
V688I
E770K
G778R
W818S
L916P
T964M
S1051L
L1079V
A1138T
Q1285P
P1458L
V1529I
R1921S
R2045S
N2079K
p.F2082fs
R2110H
V2265G
S2313R
R2360H
K2415N
L2461V
G2495S
F2652L
p.Q2758*
G2862E
T2968A
LAMA1
Q23L
C176Y
T313I
V598I
S607L
A708S
C835Y
p.S976*
E1567K
E1690K
D1908N
K2090N
L2222F
I2341T
E2371L
S2372F
R2503K
I2609T
R2644K
R3089I
LAMA2
F151L
T329M
E372Q
R512H
p.F835fs
p.Q1144*
G1362V
p.S1814fs
T2980S
p.K3053fs/K3054I
L3138F
LAMA3
A143E
E254K
N315S
D1211N
T1501A
R1794H
LAMA4
S73F
A117T
T439N
K812T
R1034H
A1120V
A1141C
p.L1296fs
M1796fs
G2113V
A2187T
G2977R
L3439P
S3598L
LAMA5
Signal peptide
N-terminal region
EGF-like domain
Cell attachment site
Laminin IV type A domain
Domain IV B
Domain III
Domain I and II
Domain α
Laminin G like domain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A1399D
E1444Q
D1474N
LAMB1
V26M
E107H
T154I
R156H
D167N
R220C
R584H
V696I
P722S
R937Q
C1019Y
R1346H
A1508T
p.R1562*
S1565G
R1735Q
N1762S
LAMB2
F4L
M64I
D70Y
L246V/R
A267E
R292C
A515S
R563C
R598C
E704K
N843D
R958C
R1009Q
LAMB3
N225K
D315N
R534H
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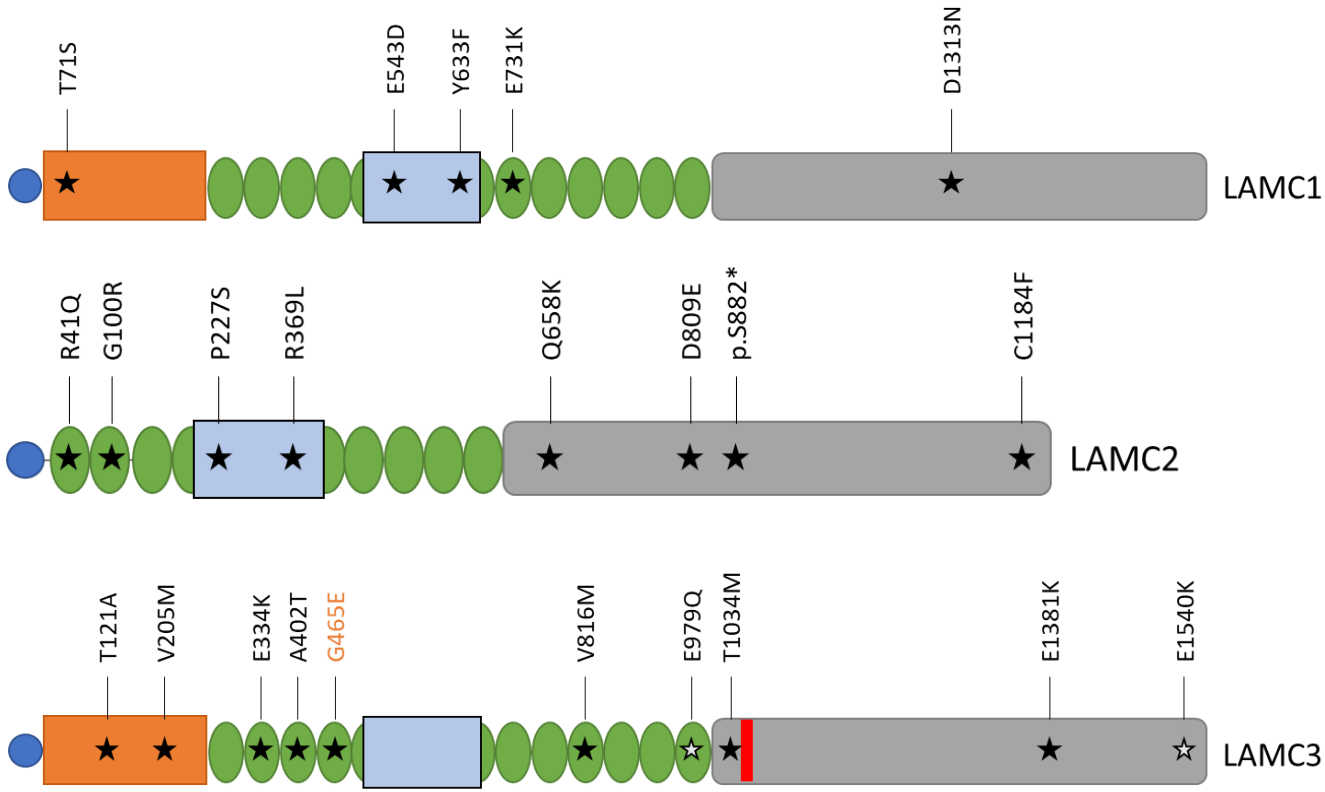
P587A
V767L
R845C
C894G
D935N
D1183N
G1396S
R1461W
LAMB4
Signal peptide
N-terminal region
EGF-like domain
Cell attachment site
Laminin IV type A domain
Domain IV B
Domain III
Domain I and II
Domain α
Laminin G like domain

Laminin γ subunits

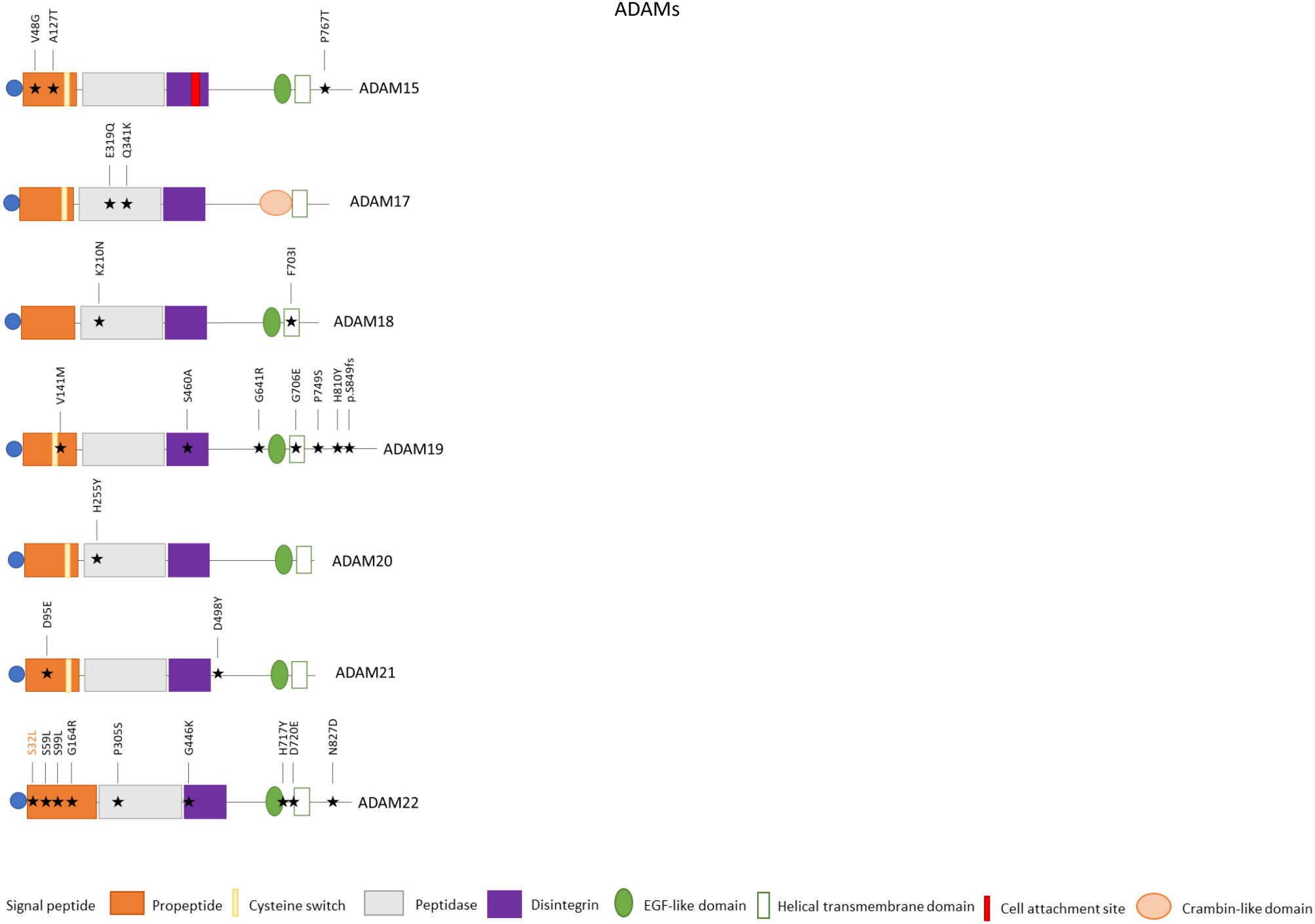


Signal peptide | N-terminal region | EGF-like domain | Cell attachment site | Laminin IV type A domain | Domain IV B | Domain III | Domain I and II | Domain α | Laminin G like domain

ADAMs


ADAMs
V4I
N90I
C452
D615Y
ADAM2
S304F
V358M
S450C
ADAM7
H224Y
T439I
V568M
S683R
ADAM8
V260F
S684I
ADAM9
p.Y225*
p.P289fs
Q307K
ADAM10
K298E
p.440*
T478N
R504Q
S739F
ADAM11
R142W
V309D
D510N
D516N
R616Q
R834S
A845S
ADAM12
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
Crambin-like domain

ADAMs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P767T
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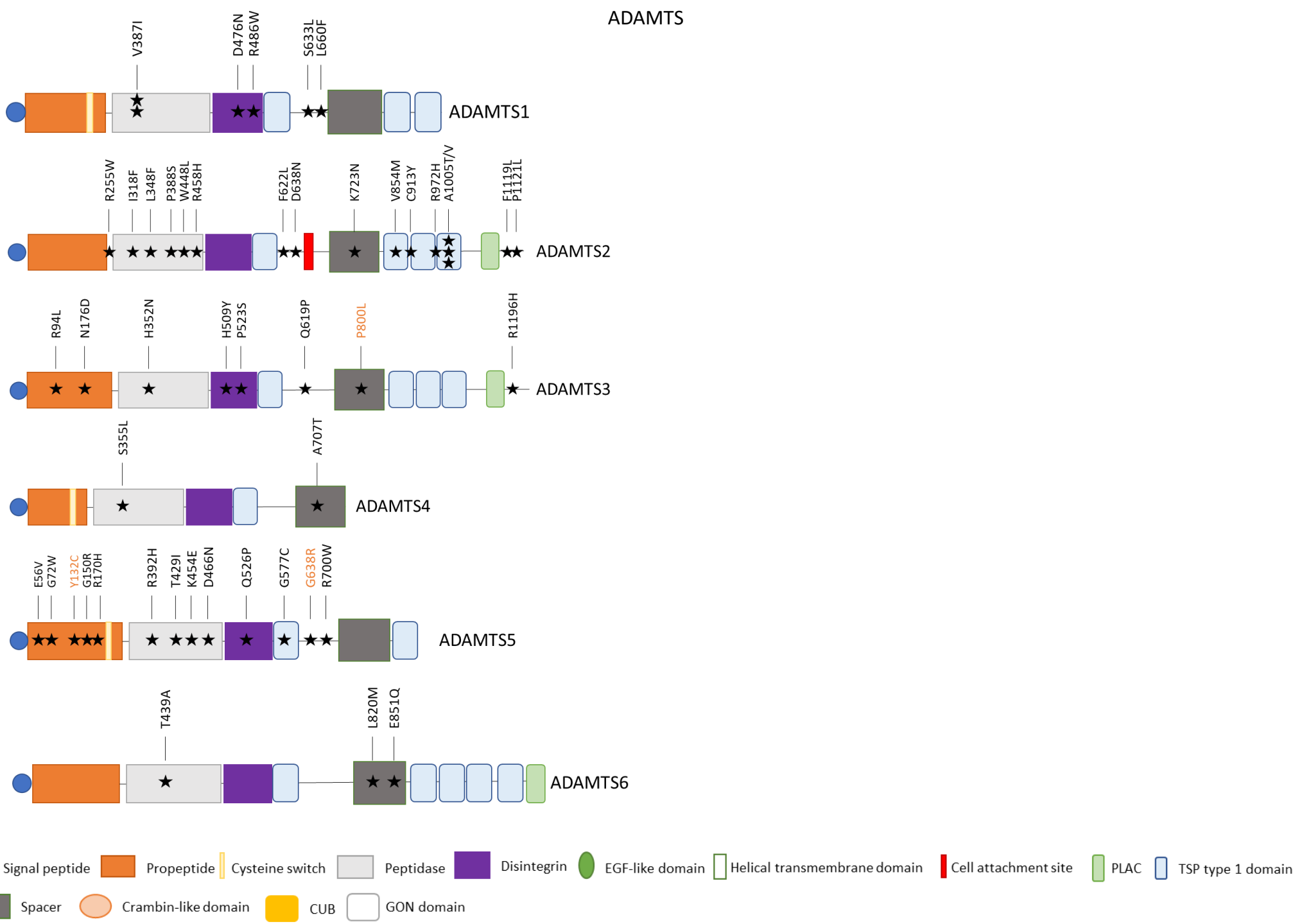
E319Q
Q341K
ADAM17
K210N
F703I
ADAM18
V141M
S460A
G641R
G706E
P749S
H810Y
p.S849fs
ADAM19
H255Y
ADAM20
D95E
D498Y
ADAM21
S32L
S59L
S99L
G164R
P305S
G446K
H717Y
D720E
N827D
ADAM22
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
Crambin-like domain


ADAMs
G413R
R446T
D608G
p.K781fs
ADAM23
C478F
G523E
ADAM28
Y105H
I228F
H310Q
E344K
R348H
R353K
H572L
C693F
Q708K
S741Y
H747Y
p.Q794*
p.Ter821Leuext*
ADAM29
P601R
ADAM30
T61A
V180F
L254F
F258V
P291S
A304E
ADAM32
P294S
E790D
ADAM33
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
Crambin-like domain

ADAMTS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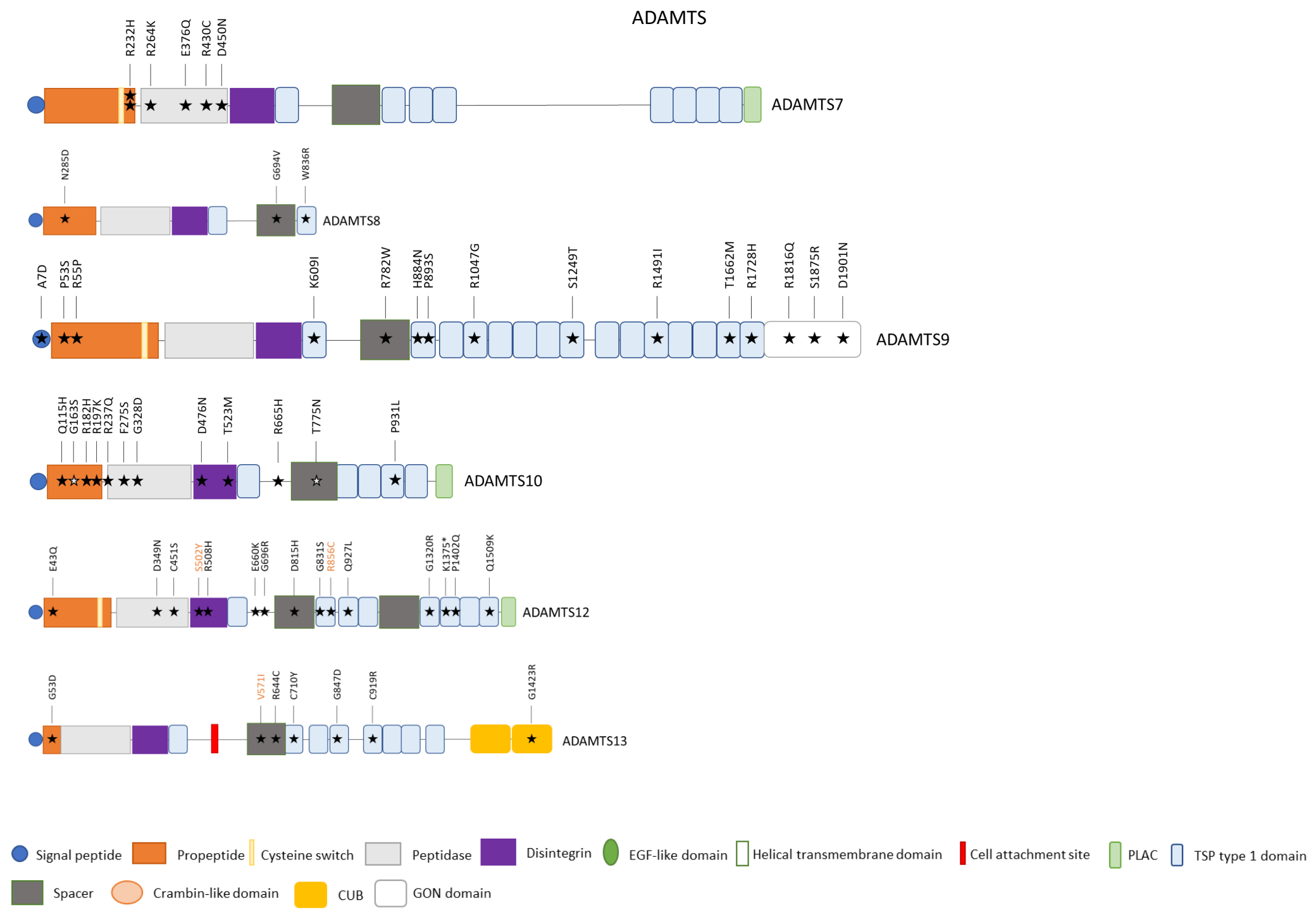
S633L
L660F
ADAMTS1
R255W
I318F
L348F
P388S
W448L
R458H
F622L
D638N
K723N
V854M
C913Y
R972H
A1005T/V
F1119L
P1121L
ADAMTS2
R94L
N176D
H352N
H509Y
P523S
Q619P
P800L
R1196H
ADAMTS3
S355L
A707T
ADAMTS4
E56V
G72W
Y132C
G150R
R170H
R392H
T429I
K454E
D466N
Q526P
G577C
G638R
R700W
ADAMTS5
T439A
L820M
E851Q
ADAMTS6
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
PLAC
TSP type 1 domain
Spacer
Crambin-like domain
CUB
GON domain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E376Q
R430C
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ADAMTS7
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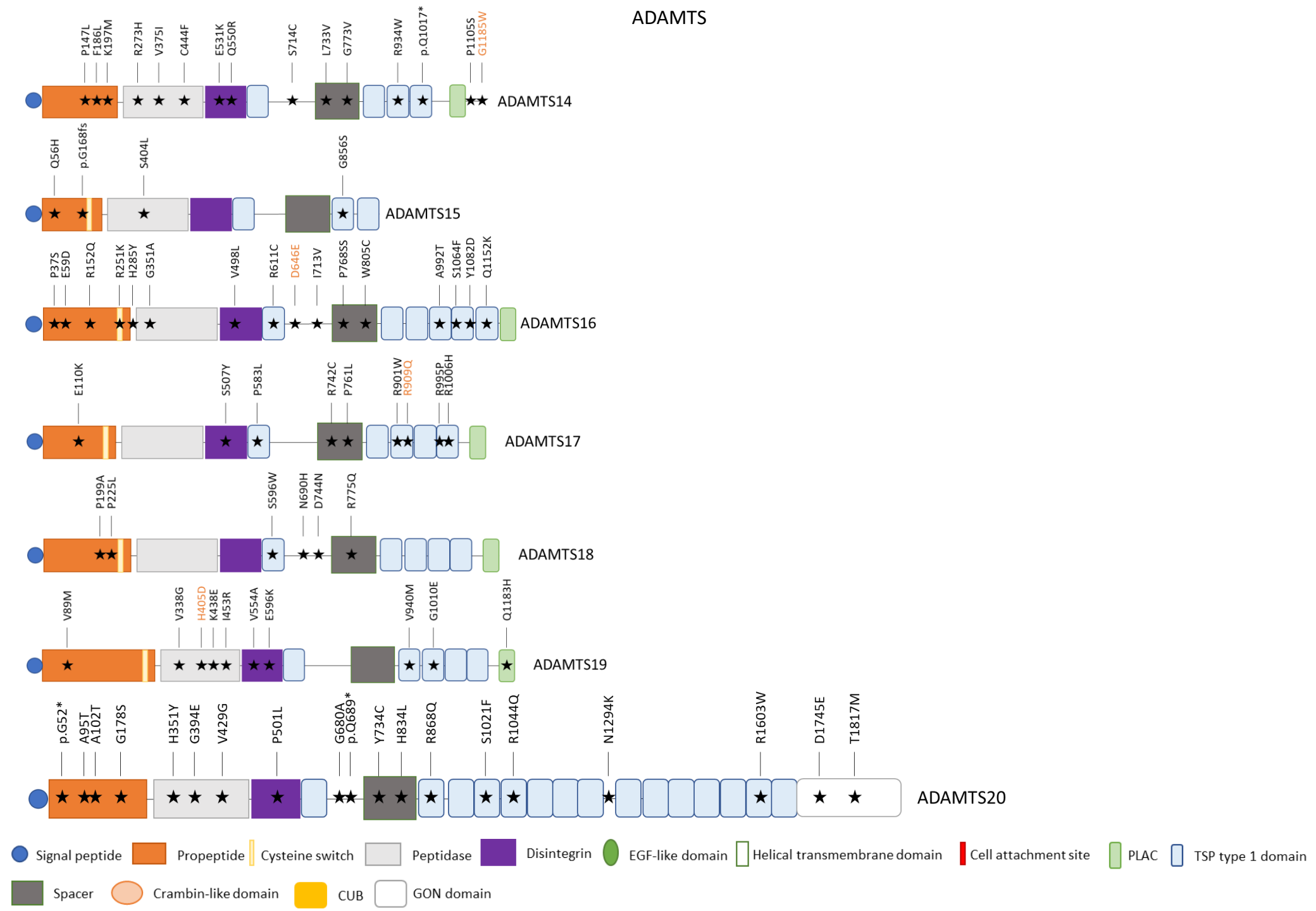
ADAMTS8
A7D
P53S
R55P
K609I
R782W
H884N
P893S
R1047G
S1249T
R1491I
T1662M
R1728H
R1816Q
S1875R
D1901N
ADAMTS9
Q115H
G163S
R182H
R197K
R237Q
F275S
G328D
D476N
T523M
R665H
T775N
P931L
ADAMTS10
E43Q
D349N
C451S
S502Y
R508H
E660K
G696R
D815H
G831S
R856C
Q927L
G1320R
K1375*
P1402Q
Q1509K
ADAMTS12
G53D
V571I
R644C
C710Y
G847D
C919R
G1423R
ADAMTS13
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
PLAC
TSP type 1 domain
Spacer
Crambin-like domain
CUB
GON domain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V375I
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P1105S
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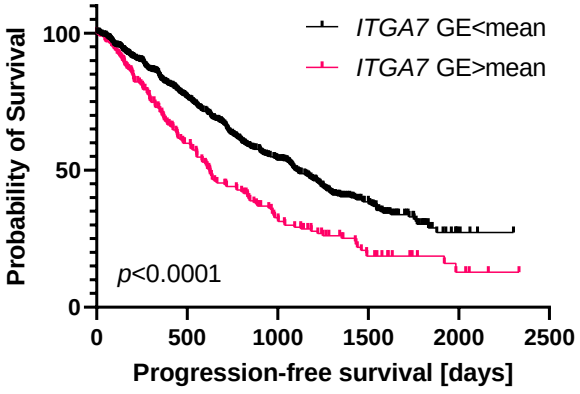
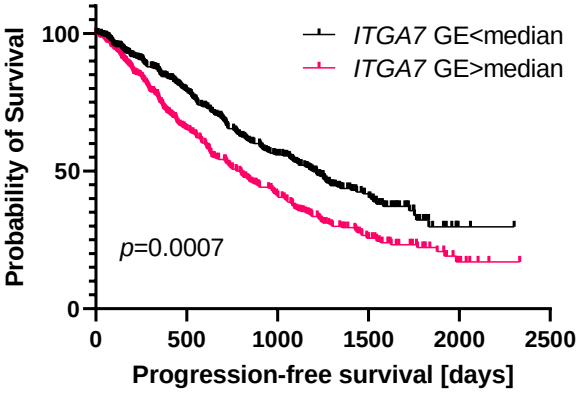
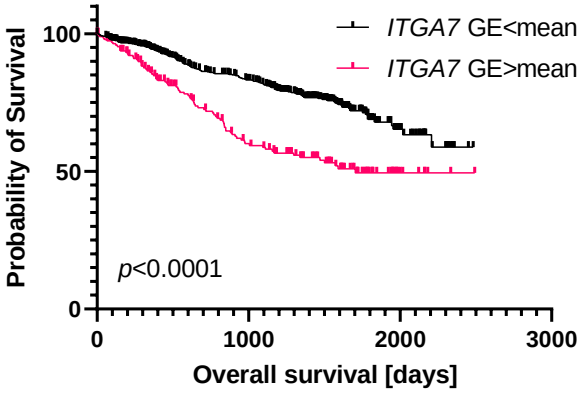
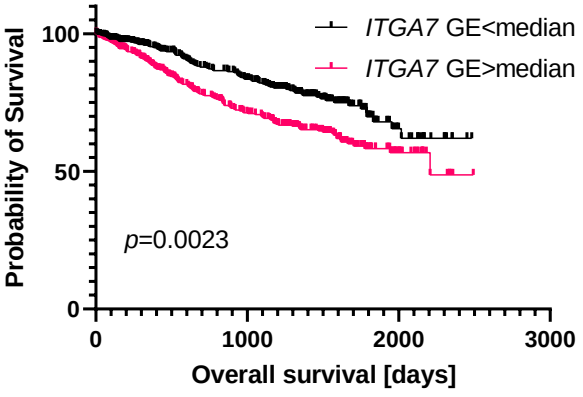
ADAMTS14
Q56H
p.G168fs
S404L
G856S
ADAMTS15
P37S
E59D
R152Q
R251K
H285Y
G351A
V498L
R611C
D646E
I713V
P768SS
W805C
A992T
S1064F
Y1082D
Q1152K
ADAMTS16
E110K
S507Y
P583L
R742C
P761L
R901W
R909Q
R995P
R1006H
ADAMTS17
P199A
P225L
S596W
N690H
D744N
R775Q
ADAMTS18
V89M
V338G
H405D
K438E
I453R
V554A
E596K
V940M
G1010E
Q1183H
ADAMTS19
p.G52*
A95T
A102T
G178S
H351Y
G394E
V429G
P501L
G680A
p.Q689*
Y734C
H834L
R868Q
S1021F
R1044Q
N1294K
R1603W
D1745E
T1817M
ADAMTS20
Signal peptide
Propeptide
Cysteine switch
Peptidase
Disintegrin
EGF-like domain
Helical transmembrane domain
Cell attachment site
PLAC
TSP type 1 domain
Spacer
Crambin-like domain
CUB
GON domain

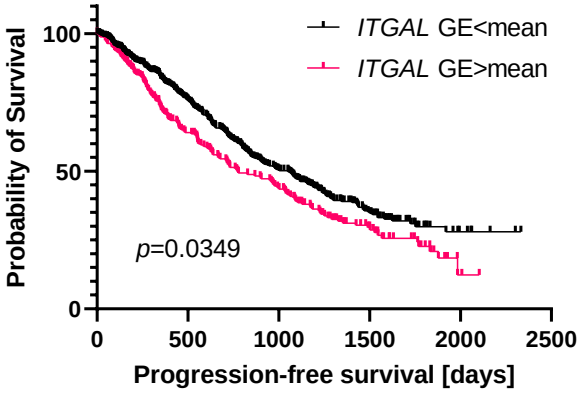
Figure S2: Kaplan Meier plots for the comparison of overall and progression-free survival of MMRF patients with a gene expression (GE) higher or lower than the mean/median expression measured across all samples. Statistical correlations were performed using the Log Rank test. *P* values were adjusted for multiple hypothesis testing using Benjamini-Hochberg correction in R. n=800. Graphs were created using GraphPad Prism 9.

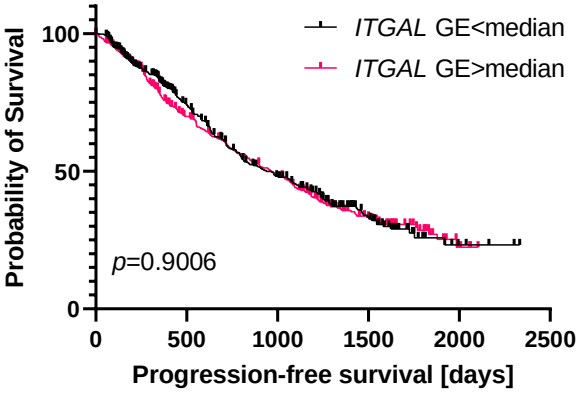


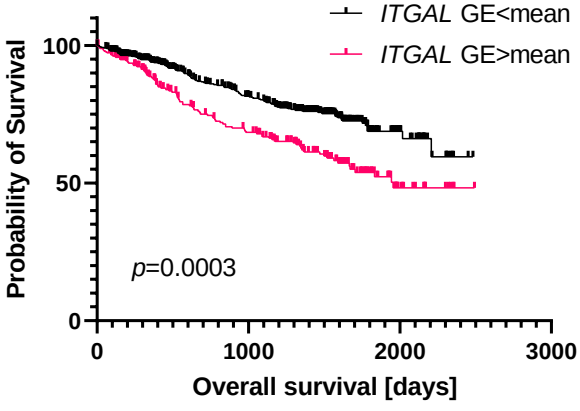


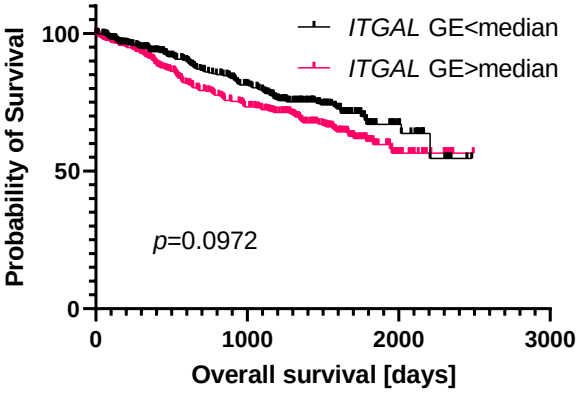


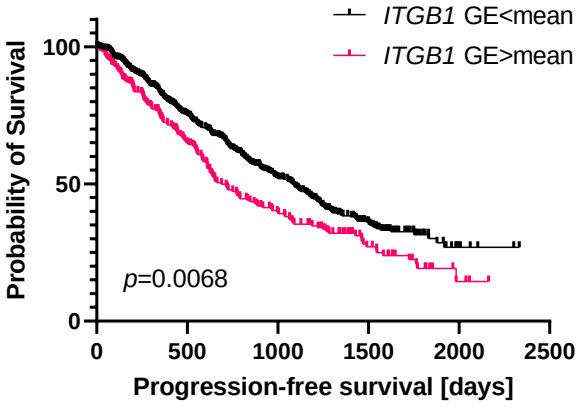


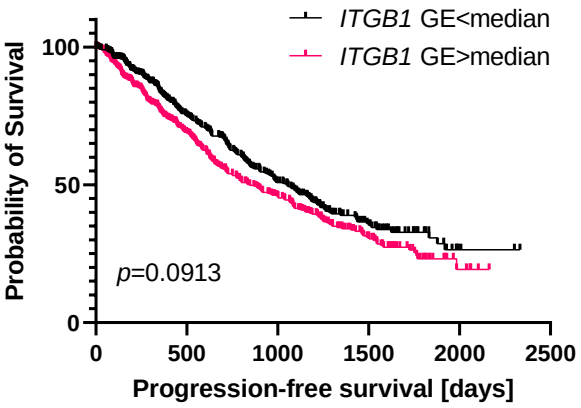


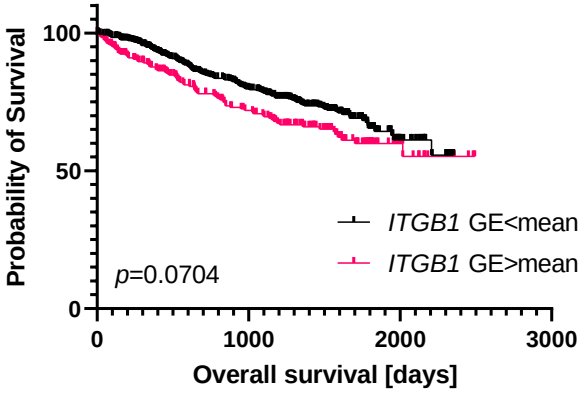


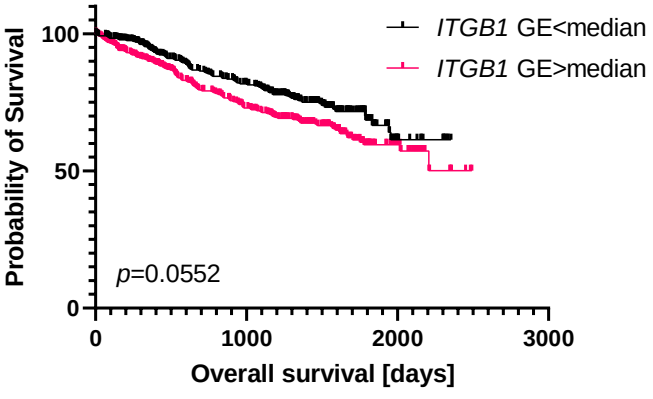


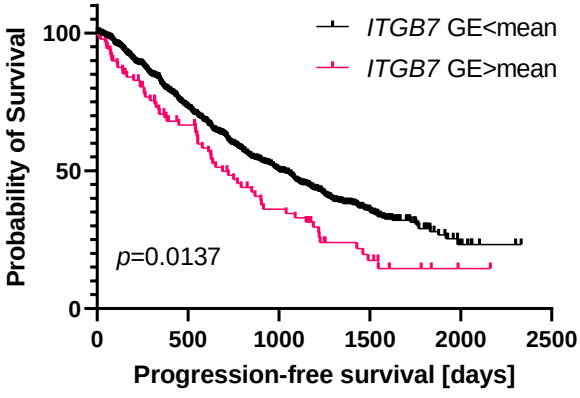


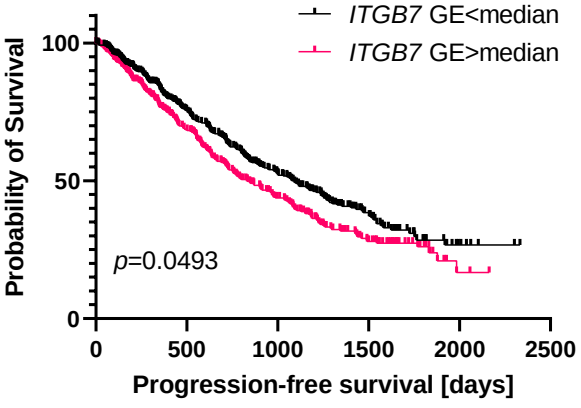

ITGB1 GE<mean
ITGB1 GE>mean
Probability of Survival
100
50
0
p=0.0068
0
500
1000
1500
2000
2500
Progression-free survival [days]

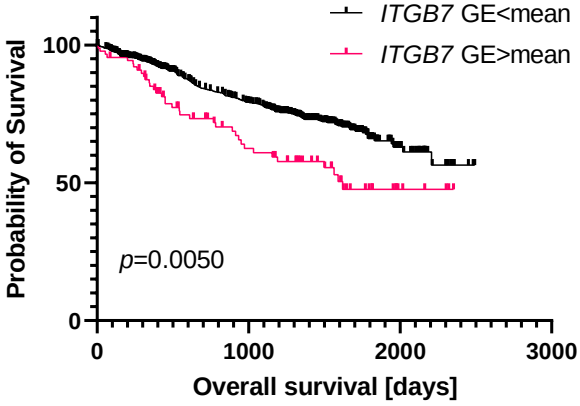

ITGB1 GE<median
ITGB1 GE>median
Probability of Survival
100
50
0
p=0.0913
0
500
1000
1500
2000
2500
Progression-free survival [days]

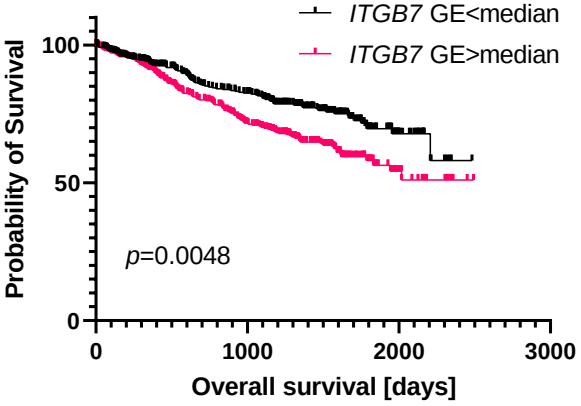

ITGB1 GE<mean
ITGB1 GE>mean
Probability of Survival
100
50
0
p=0.0704
0
1000
2000
3000
Overall survival [days]

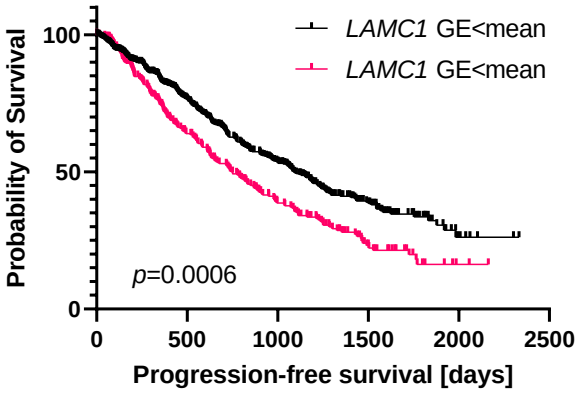

ITGB1 GE<median
ITGB1 GE>median
Probability of Survival
100
50
0
p=0.0552
0
1000
2000
3000
Overall survival [days]

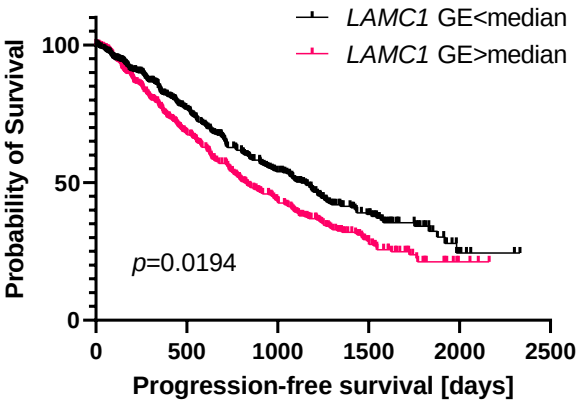

ITGB7 GE<mean
ITGB7 GE>mean
Probability of Survival
100
50
0
p=0.0137
0
500
1000
1500
2000
2500
Progression-free survival [days]

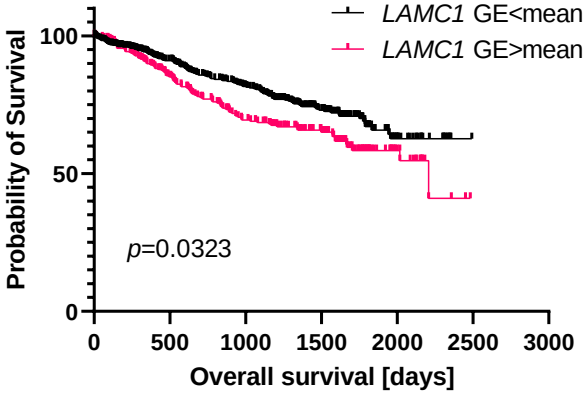

ITGB7 GE<median
ITGB7 GE>median
Probability of Survival
100
50
0
p=0.0493
0
500
1000
1500
2000
2500
Progression-free survival [days]

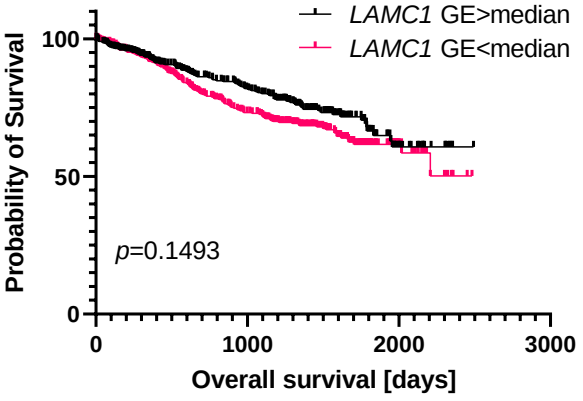

ITGB7 GE<mean
ITGB7 GE>mean
Probability of Survival
100
50
0
p=0.0050
0
1000
2000
3000
Overall survival [days]

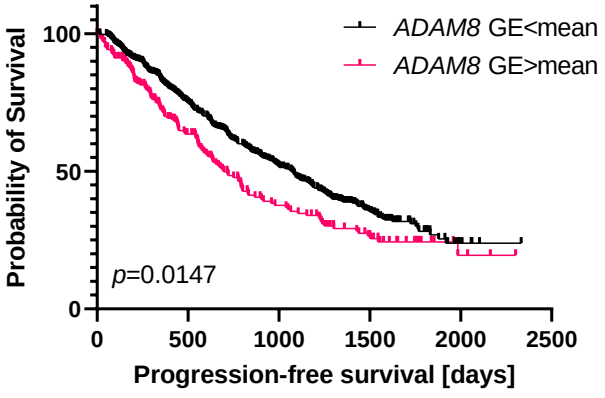

ITGB7 GE<median
ITGB7 GE>median
Probability of Survival
100
50
0
p=0.0048
0
1000
2000
3000
Overall survival [days]

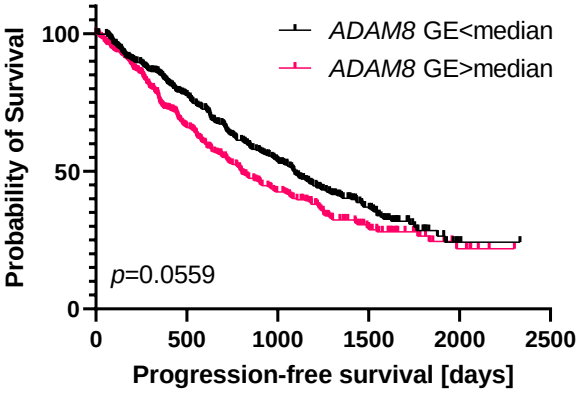

LAMC1 GE<mean
LAMC1 GE<mean
Probability of Survival
100
50
0
p=0.0006
0
500
1000
1500
2000
2500
Progression-free survival [days]

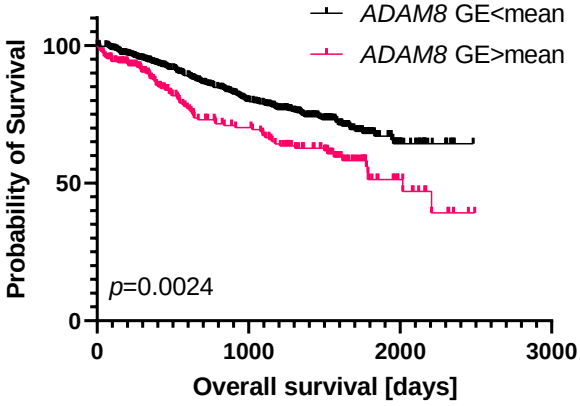

LAMC1 GE<median
LAMC1 GE>median
Probability of Survival
100
50
0
p=0.0194
0
500
1000
1500
2000
2500
Progression-free survival [days]


LAMC1 GE<mean
LAMC1 GE>mean
Probability of Survival
100
50
0
p=0.0323
0
500
1000
1500
2000
2500
3000
Overall survival [days]


LAMC1 GE>median
LAMC1 GE<median
Probability of Survival
100
50
0
p=0.1493
0
1000
2000
3000
Overall survival [days]


ADAM8 GE<mean
ADAM8 GE>mean
Probability of Survival
100
50
0
p=0.0147
0
500
1000
1500
2000
2500
Progression-free survival [days]


ADAM8 GE<median
ADAM8 GE>median
Probability of Survival
100
50
0
p=0.0559
0
500
1000
1500
2000
2500
Progression-free survival [days]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Probability of Survival
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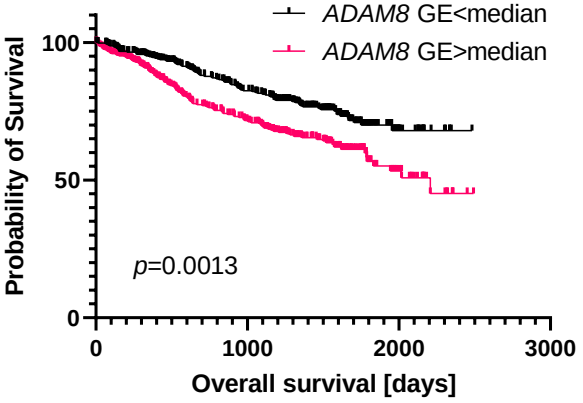
50
0
p=0.0024
0
1000
2000
3000
Overall survival [days]


ADAM8 GE<median
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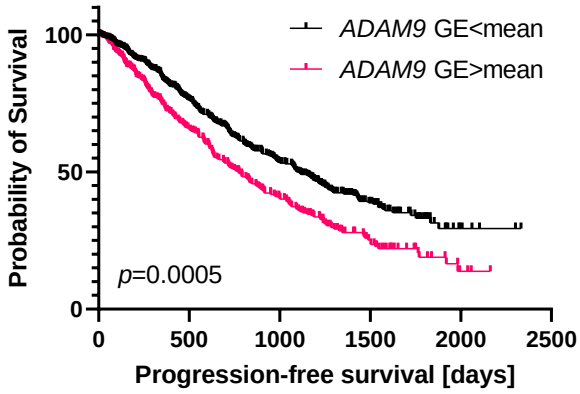
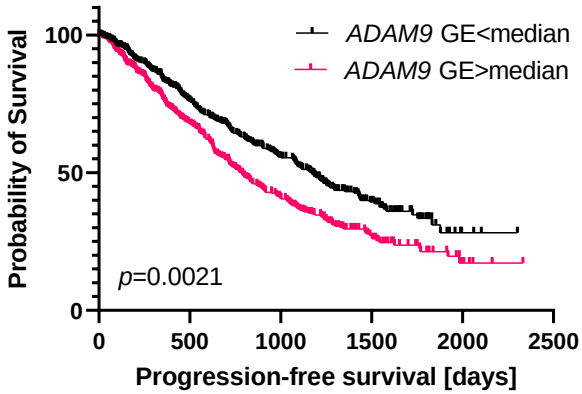
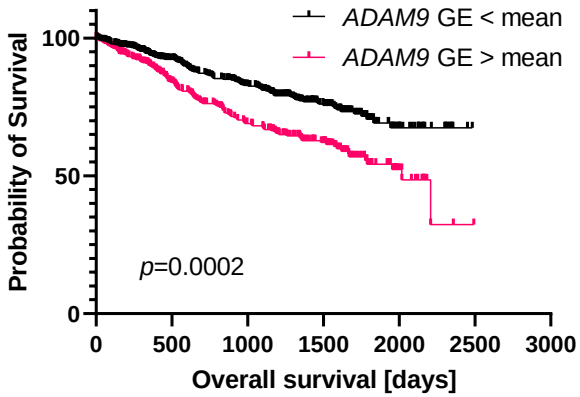
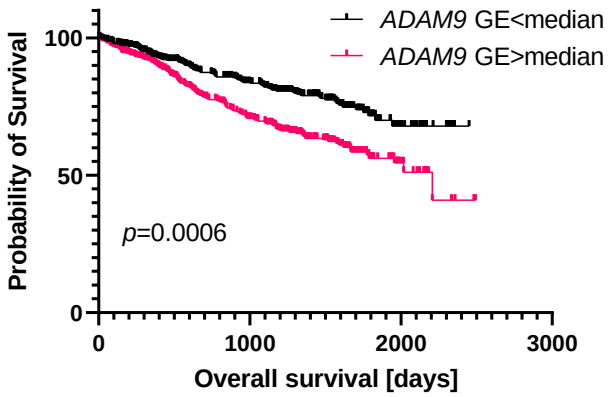
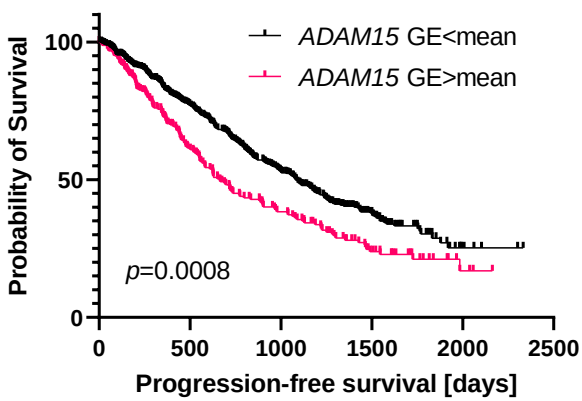
Probability of Survival
100
50
0
p=0.0013
0
1000
2000
3000
Overall survival [days]

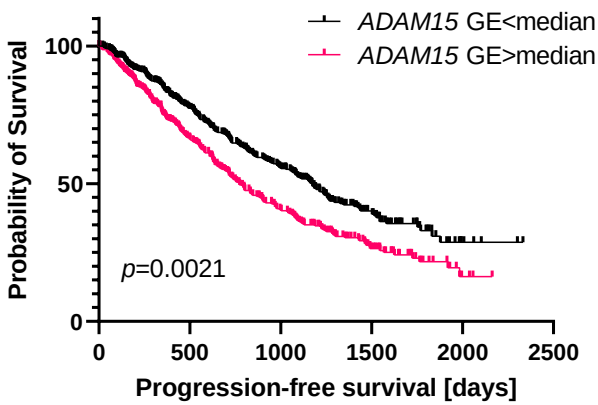

ADAM9 GE<mean
ADAM9 GE>mean
Probability of Survival
100
50
0
p=0.0005
0
500
1000
1500
2000
2500
Progression-free survival [days]

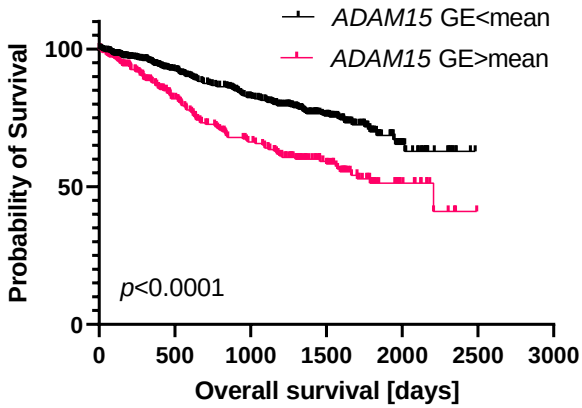

ADAM9 GE<median
ADAM9 GE>median
Probability of Survival
100
50
0
p=0.0021
0
500
1000
1500
2000
2500
Progression-free survival [days]

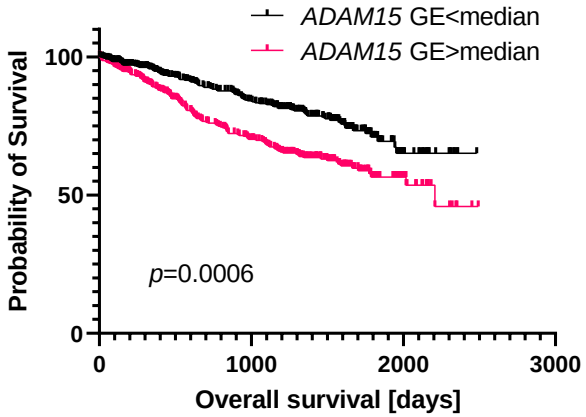

ADAM9 GE < mean
ADAM9 GE > mean
Probability of Survival
100
50
0
p=0.0002
0
500
1000
1500
2000
2500
3000
Overall survival [days]

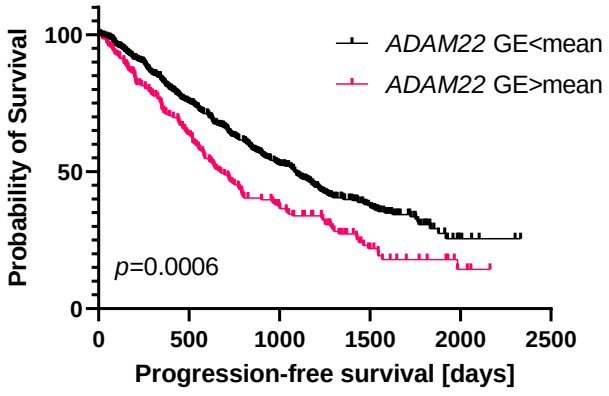

ADAM9 GE<median
ADAM9 GE>median
Probability of Survival
100
50
0
p=0.0006
0
1000
2000
3000
Overall survival [days]

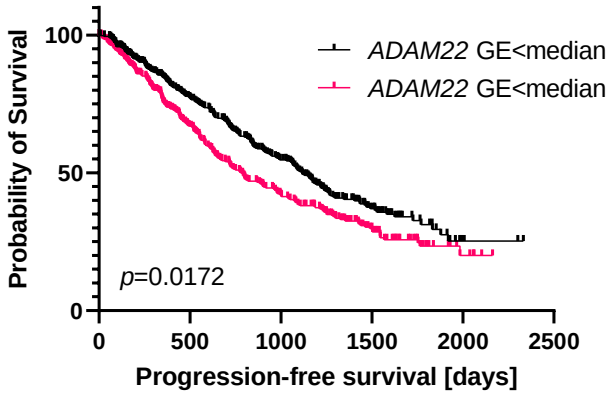

ADAM15 GE<mean
ADAM15 GE>mean
Probability of Survival
100
50
0
p=0.0008
0
500
1000
1500
2000
2500
Progression-free survival [days]


ADAM15 GE<median
ADAM15 GE>median
Probability of Survival
100
50
0
p=0.0021
0
500
1000
1500
2000
2500
Progression-free survival [days]


ADAM15 GE<mean
ADAM15 GE>mean
Probability of Survival
100
50
0
p<0.0001
0
500
1000
1500
2000
2500
3000
Overall survival [days]


ADAM15 GE<median
ADAM15 GE>median
Probability of Survival
100
50
0
p=0.0006
0
1000
2000
3000
Overall survival [days]


Probability of Survival
100
50
0
ADAM22 GE<mean
ADAM22 GE>mean
p=0.0006
0
500
1000
1500
2000
2500
Progression-free survival [days]


Probability of Survival
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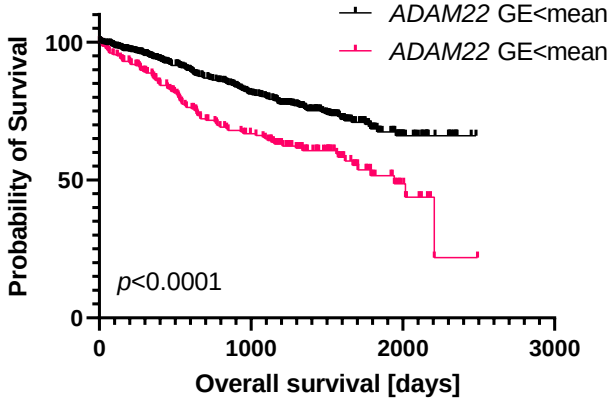
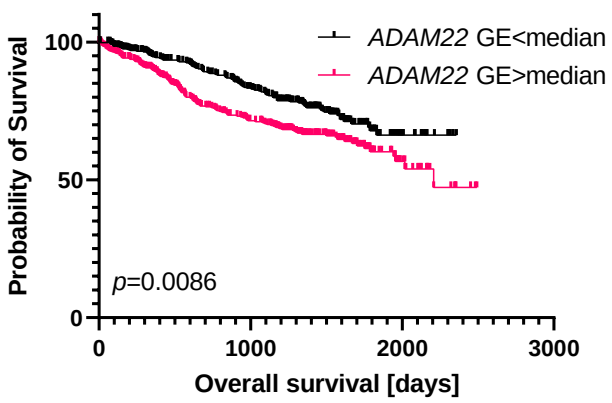
0
ADAM22 GE<median
ADAM22 GE<median
p=0.0172
0
500
1000
1500
2000
2500
Progression-free survival [days]


Probability of Survival
100
50
0
ADAM22 GE<mean
ADAM22 GE<mean
p<0.0001
0
1000
2000
3000
Overall survival [days]


Probability of Survival
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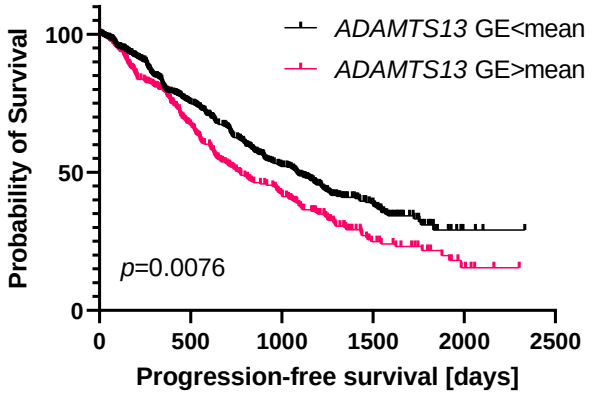
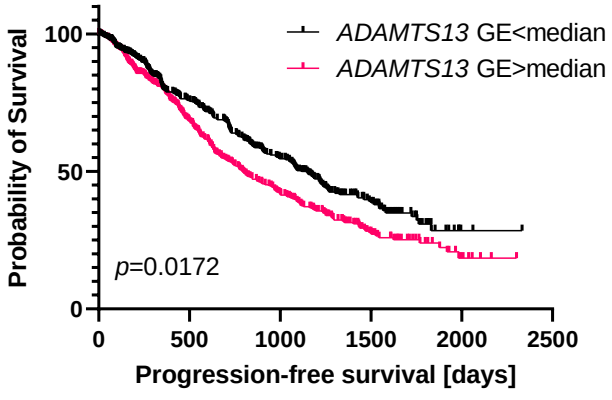
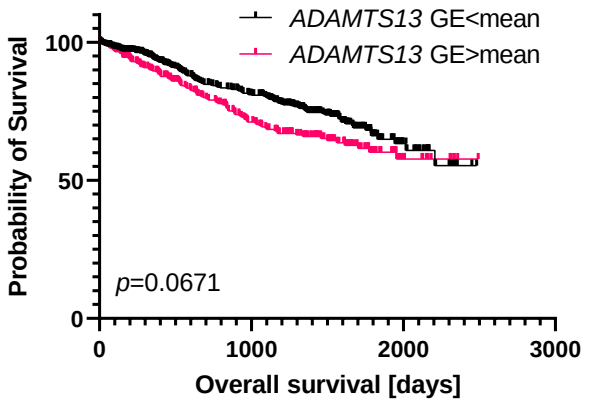
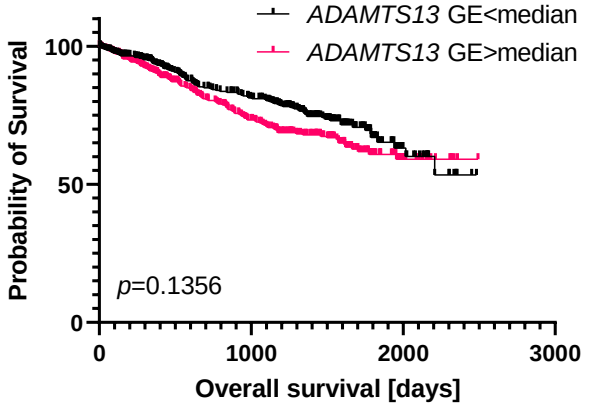
50
0
ADAM22 GE<median
ADAM22 GE>median
p=0.0086
0
1000
2000
3000
Overall survival [days]


Probability of Survival
100
50
0
ADAMTS13 GE<mean
ADAMTS13 GE>mean
p=0.0076
0
500
1000
1500
2000
2500
Progression-free survival [days]


Probability of Survival
100
50
0
ADAMTS13 GE<median
ADAMTS13 GE>median
p=0.0172
0
500
1000
1500
2000
2500
Progression-free survival [days]


Probability of Survival
100
50
0
ADAMTS13 GE<mean
ADAMTS13 GE>mean
p=0.0671
0
1000
2000
3000
Overall survival [days]


Probability of Survival
100
50
0
ADAMTS13 GE<median
ADAMTS13 GE>median
p=0.1356
0
1000
2000
3000
Overall survival [days]