Supplementary Table 2. Detailed list of 105 enriched pathways from STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) database

No.	Enriched pathways	Total number of proteins involved	p-value	Gene symbols
1	Extracellular matrix organization	37	8.90E-24	*A2M, ACAN, ASPN, BGN, CD47, COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, COMP, DCN, FGA, FGB, FGG, FMOD, GDF5, HAPLN1, HSPG2, HTRA1, LOX, LUM, MMP10, PCOLCE, PCOLCE2, PPIB, THBS1, TIMP1, TNC, TTR, VCAN, VTN*
2	ECM proteoglycans	18	9.26E-16	*ACAN, ASPN, BGN, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, COMP, DCN, FMOD, HAPLN1, HSPG2, LUM, TNC, VCAN, VTN*
3	Integrin cell surface interactions	17	6.49E-14	*CD47, COL10A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, COMP, FGA, FGB, FGG, HSPG2, LUM, THBS1, TNC, VTN*
4	Collagen biosynthesis and modifying enzymes	13	1.63E-10	*COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, PCOLCE, PCOLCE2, PPIB*
5	Collagen formation	14	2.61E-10	*COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, LOX, PCOLCE, PCOLCE2, PPIB*
6	Glycosaminoglycan metabolism	12	4.88E-07	*ACAN, B3GNT7, BGN, DCN, FMOD, HSPG2, LUM, OGN, OMD, PRELP, VCAN, XYLT1*
7	Keratan sulfate degradation	6	5.80E-07	*ACAN, FMOD, LUM, OGN, OMD, PRELP*
8	Gluconeogenesis	5	0.00054	*ENO1, GAPDH, PGAM2, PGK1, TPI1*
9	Formation of the cornified envelope	29	1.66E-24	*CDSN, DSG1, DSP, JUP, KRT1, KRT10, KRT14, KRT15, KRT16, KRT17, KRT19, KRT2, KRT33A, KRT4, KRT5, KRT6A, KRT6B, KRT6C, KRT72, KRT73, KRT76, KRT77, KRT78, KRT79, KRT8, KRT80, KRT84, KRT9, TGM5*
10	Platelet degranulation	22	1.04E-16	*A1BG, A2M, ALB, ANXA5, APOA1, CD109, CLEC3B, CLU, F13A1, FGA, FGB, FGG, HRG, ITIH4, QSOX1, SERPINA1, SERPING1, TF, THBS1, TIMP1, TIMP3, TTN*
11	Platelet activation, signalling and aggregation	25	6.50E-14	*A1BG, A2M, ALB, ANXA5, APOA1, CD109, CLEC3B, CLU, COL1A1, COL1A2, F13A1, FGA, FGB, FGG, HRG, ITIH4, QSOX1, RASGRP2, SERPINA1, SERPING1, TF, THBS1, TIMP1, TIMP3, TTN*
12	Innate immune system	45	2.71E-13	*A1BG, ACTG1, ANXA2, ARG1, C1S, C3, C9, CALML5, CASP8, CD47, CFB, CFI, CHI3L1, CLU, DCD, DSG1, DSP, FABP5, FGA, FGB, FGG, FLG2, FTL, GSN, HBB, HP, HRNR, JUP, KRT1, LTF, LYZ, MIF, PKM, PLA2G2A, QSOX1, RASGRP2, S100A1, S100A8, S100A9, SERPINA1, SERPINB1, SERPING1, TNFAIP6, TTR, VTN*
13	Hemostasis	34	1.31E-12	*A1BG, A2M, ALB, ANXA2, ANXA5, APOA1, CD109, CD47, CLEC3B, CLU, COL1A1, COL1A2, F13A1, FGA, FGB, FGG, HBB, HBD, HRG, ITIH4, KIF1B, MIF, QSOX1, RASGRP2, SERPINA1, SERPINA5, SERPINC1, SERPINE2, SERPING1, TF, THBS1, TIMP1, TIMP3, TTN*
14	Neutrophil degranulation	29	1.53E-11	*A1BG, ANXA2, ARG1, C3, CALML5, CD47, CHI3L1, DSG1, DSP, FABP5, FLG2, FTL, GSN, HBB, HP, HRNR, JUP, KRT1, LTF, LYZ, MIF, PKM, QSOX1, S100A8, S100A9, SERPINA1, SERPINB1, TNFAIP6, TTR*
15	Degradation of the extracellular matrix	17	7.17E-11	*A2M, ACAN, COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, DCN, HSPG2, HTRA1, MMP10, TIMP1*
16	Post-translational protein phosphorylation	15	1.94E-10	*ALB, APOA1, C3, CP, FGA, FGG, MFGE8, MFI2, QSOX1, SERPINA1, SERPINC1, TF, TIMP1, TNC, VCAN*
17	Immune system	57	3.58E-10	*A1BG, ACTG1, ANXA1, ANXA2, ARG1, BLMH, C1S, C3, C9, CA1, CALML5, CASP8, CD47, CFB, CFI, CHI3L1, CLU, COL1A1, COL1A2, COL2A1, CSF3R, DCD, DSG1, DSP, F13A1, FABP5, FGA, FGB, FGG, FLG2, FTL, GSN, HBB, HP, HRNR, JUP, KRT1, LTF, LYZ, MIF, MSN, PKM, PLA2G2A, QSOX1, RASGRP2, S100A1, S100A8, S100A9, SERPINA1, SERPINB1, SERPING1, TIMP1, TNFAIP6, TNFRSF11B, TTR, VIM, VTN*

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Supplementary Table 2. Continued

No.	Enriched pathways	Total number of proteins involved	p-value	Gene symbols
18	Assembly of collagen fibrils and other multimeric structures	12	6.15E-10	*COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, LOX, PCOLCE*
19	regulation of insulin-like growth factor transport and uptake by insulin-like growth factor binding proteins	15	1.03E-09	*ALB, APOA1, C3, CP, FGA, FGG, MFGE8, MFI2, QSOX1, SERPINA1, SERPINC1, TF, TIMP1, TNC, VCAN*
20	Diseases associated with glycosaminoglycan metabolism	10	3.96E-09	*ACAN, BGN, DCN, FMOD, HSPG2, LUM, OGN, OMD, PRELP, VCAN*
21	Collagen chain trimerization	10	8.43E-09	*COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3*
22	Developmental biology	37	1.28E-08	*ACTG1, ANK2, CDSN, COL2A1, COL6A1, COL6A2, COL6A3, DSG1, DSP, H2AFV, JUP, KRT1, KRT10, KRT14, KRT15, KRT16, KRT17, KRT19, KRT2, KRT33A, KRT4, KRT5, KRT6A, KRT6B, KRT6C, KRT72, KRT73, KRT76, KRT77, KRT78, KRT79, KRT8, KRT80, KRT84, KRT9, MSN, TGM5*
23	Collagen degradation	11	1.37E-08	*COL10A1, COL11A2, COL14A1, COL15A1, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, MMP10*
24	Formation of fibrin clot (clotting cascade)	9	5.04E-08	*A2M, F13A1, FGA, FGB, FGG, SERPINA5, SERPINC1, SERPINE2, SERPING1*
25	Defective ST3GAL3 causes MCT12 and EIEE15	6	5.33E-08	*ACAN, FMOD, LUM, OGN, OMD, PRELP*
26	Binding and uptake of ligands by scavenger receptors	9	5.63E-08	*ALB, APOA1, COL1A1, COL1A2, FTL, HBA1, HBB, HP, HPX*
27	Nonintegrin membrane-ECM interactions	10	6.87E-08	*COL10A1, COL11A2, COL1A1, COL1A2, COL2A1, HSPG2, THBS1, TNC, TTR, VTN*
28	Amyloid fiber formation	11	7.28E-08	*APCS, APOA1, APOA4, FGA, GSN, HSPG2, LTF, LYZ, MFGE8, TGFBI, TTR*
29	Defective CHST6 causes MCDC1	6	7.93E-08	*ACAN, FMOD, LUM, OGN, OMD, PRELP*
30	Defective B4GALT1 causes B4GALT1-CDG (CDG-2d)	6	7.93E-08	*ACAN, FMOD, LUM, OGN, OMD, PRELP*
31	Metabolism of carbohydrates	17	3.11E-07	*ACAN, B3GNT7, BGN, DCN, ENO1, FMOD, GAPDH, HSPG2, LUM, OGN, OMD, PGAM2, PGK1, PRELP, TPI1, VCAN, XYLT1*
32	Common pathway of fibrin clot formation	7	3.54E-07	*F13A1, FGA, FGB, FGG, SERPINA5, SERPINC1, SERPINE2*
33	Scavenging of heme from plasma	6	5.80E-07	*ALB, APOA1, HBA1, HBB, HP, HPX*
34	Keratan sulfate biosynthesis	7	1.03E-06	*ACAN, B3GNT7, FMOD, LUM, OGN, OMD, PRELP*
35	Regulation of complement cascade	8	2.02E-06	*C1S, C3, C9, CFB, CFI, CLU, SERPING1, VTN*
36	Regulation of TLR by endogenous ligand	6	3.19E-06	*FGA, FGB, FGG, S100A1, S100A8, S100A9*
37	Diseases of glycosylation	11	9.04E-06	*ACAN, BGN, DCN, FMOD, HSPG2, LUM, OGN, OMD, PRELP, THBS1, VCAN*

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Supplementary Table 2. Continued

No.	Enriched pathways	Total number of proteins involved	p-value	Gene symbols
38	Erythrocytes take up oxygen and release carbon dioxide	4	7.48E-05	*CA1, CA2, HBA1, HBB*
39	Platelet aggregation (plug formation)	6	8.18E-05	*COL1A1, COL1A2, FGA, FGB, FGG, RASGRP2*
40	Intrinsic pathway of fibrin clot formation	5	0.00011	*A2M, SERPINA5, SERPINC1, SERPINE2, SERPING1*
41	A tetrasaccharide linker sequence is required for GAG synthesis	5	0.00022	*BGN, DCN, HSPG2, VCAN, XYLT1*
42	Syndecan interactions	5	0.00022	*COL1A1, COL1A2, THBS1, TNC, VTN*
43	Erythrocytes take up carbon dioxide and release oxygen	4	0.00024	*CA1, CA2, HBA1, HBB*
44	Apoptotic execution phase	6	0.00037	*CASP8, DSG1, DSP, GSN, HIST1H1C, VIM*
45	Signaling by PDGF	6	0.00054	*COL2A1, COL6A1, COL6A2, COL6A3, THBS1, THBS3*
46	Antimicrobial peptides	7	0.00076	*CLU, DCD, LTF, LYZ, PLA2G2A, S100A8, S100A9*
47	Crosslinking of collagen fibrils	4	0.0008	*COL1A1, COL1A2, LOX, PCOLCE*
48	Scavenging by class A receptors	4	0.0008	*APOA1, COL1A1, COL1A2, FTL*
49	Apoptotic cleavage of cellular proteins	5	0.00082	*CASP8, DSG1, DSP, GSN, VIM*
50	Metal sequestration by antimicrobial proteins	3	0.00088	*LTF, S100A8, S100A9*
51	Defective B4GALT7 causes EDS, progeroid type	4	0.0011	*BGN, DCN, HSPG2, VCAN*
52	Defective B3GAT3 causes JDSSDHD	4	0.0011	*BGN, DCN, HSPG2, VCAN*
53	Defective B3GALT6 causes EDSP2 and SEMDJL1	4	0.0011	*BGN, DCN, HSPG2, VCAN*
54	Signaling by receptor tyrosine kinases	15	0.0013	*ACTG1, CILP, COL11A2, COL1A1, COL1A2, COL2A1, COL6A1, COL6A2, COL6A3, FGFBP2, HSPB1, JUP, MST1, THBS1, THBS3*
55	Defective CHST3 causes SEDCJD	3	0.0016	*BGN, DCN, VCAN*
56	Defective CHST14 causes EDS, musculocontractural type	3	0.0016	*BGN, DCN, VCAN*
57	Defective CHSY1 causes TPBS	3	0.0016	*BGN, DCN, VCAN*
58	Retinoid metabolism and transport	5	0.0016	*APOA1, APOA4, HSPG2, RBP4, TTR*
59	Integrin alphaIIb beta3 signaling	4	0.002	*FGA, FGB, FGG, RASGRP2*

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Supplementary Table 2. Continued

No.	Enriched pathways	Total number of proteins involved	p-value	Gene symbols
60	Dermatan sulfate biosynthesis	3	0.0029	*BGN, DCN, VCAN*
61	MET activates PTK2 signaling	4	0.0031	*COL11A2, COL1A1, COL1A2, COL2A1*
62	Caspase-mediated cleavage of cytoskeletal proteins	3	0.0035	*CASP8, GSN, VIM*
63	Disease	24	0.0039	*ACAN, ACTG1, ALB, BGN, CP, DCN, FGA, FGB, FGG, FMOD, HSPG2, IPO5, LTF, LUM, OGN, OMD, PRDX1, PRDX2, PRELP, RBP4, THBS1, TTR, VCAN, YWHAE*
64	GRB2:SOS provides linkage to MAPK signaling for Integrins	3	0.0042	*FGA, FGB, FGG*
65	Dissolution of fibrin clot	3	0.0042	*ANXA2, HRG, SERPINE2*
66	Cell-Cell communication	7	0.0045	*ACTG1, ANG, CD47, FLNC, JUP, KRT14, KRT5*
67	Cell junction organization	6	0.0045	*ACTG1, ANG, FLNC, JUP, KRT14, KRT5*
68	CS/DS degradation	3	0.0047	*BGN, DCN, VCAN*
69	p130Cas linkage to MAPK signaling for integrins	3	0.0047	*FGA, FGB, FGG*
70	Signaling by high-kinase activity BRAF mutants	4	0.0051	*ACTG1, FGA, FGB, FGG*
71	Visual phototransduction	6	0.0055	*APOA1, APOA4, HSPG2, RBP4, RDH8, TTR*
72	Glycolysis	5	0.0064	*ENO1, GAPDH, PGAM2, PGK1, TPI1*
73	Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation	4	0.0065	*ANXA2, CA1, MIF, MSN*
74	MAP2K and MAPK activation	4	0.007	*ACTG1, FGA, FGB, FGG*
75	Signaling by moderate kinase activity BRAF mutants	4	0.007	*ACTG1, FGA, FGB, FGG*
76	Paradoxical activation of RAF signaling by kinase inactive BRAF	4	0.007	*ACTG1, FGA, FGB, FGG*
77	Plasma lipoprotein assembly	3	0.008	*A2M, APOA1, APOA4*
78	NCAM1 interactions	4	0.0085	*COL2A1, COL6A1, COL6A2, COL6A3*
79	Chondroitin sulfate biosynthesis	3	0.0089	*BGN, DCN, VCAN*
80	TLR cascades	7	0.0099	*CASP8, FGA, FGB, FGG, S100A1, S100A8, S100A9*
81	Initial triggering of complement	3	0.0113	*C1S, C3, CFB*
82	Alternative complement activation	2	0.012	*C3, CFB*

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Supplementary Table 2. Continued

No.	Enriched pathways	Total number of proteins involved	p-value	Gene symbols
83	Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer disease models	3	0.0123	*PRDX1, PRDX2, YWHAE*
84	Apoptosis	7	0.0135	*CASP8, DSG1, DSP, GSN, HIST1H1C, VIM, YWHAE*
85	The canonical retinoid cycle in rods (twilight vision)	3	0.0135	*RBP4, RDH8, TTR*
86	Signaling by RAS mutants	4	0.0155	*ACTG1, FGA, FGB, FGG*
87	Activation of C3 and C5	2	0.0185	*C3, CFB*
88	HDL assembly	2	0.0185	*A2M, APOA1*
89	Terminal pathway of complement	2	0.0222	*C9, CLU*
90	Signaling by BRAF and RAF fusions	4	0.0225	*ACTG1, FGA, FGB, FGG*
91	Plasma lipoprotein remodeling	3	0.024	*ALB, APOA1, APOA4*
92	HDL remodeling	2	0.026	*ALB, APOA1*
93	Adherens junctions interactions	3	0.0278	*ACTG1, ANG, JUP*
94	Chylomicron assembly	2	0.0304	*APOA1, APOA4*
95	Chylomicron remodeling	2	0.0304	*APOA1, APOA4*
96	Vesicle-mediated transport	15	0.0308	*ACTG1, ALB, ANK2, APOA1, COL1A1, COL1A2, FTL, HBA1, HBB, HP, HPX, KIF1B, SERPINA1, TF, YWHAE*
97	Plasma lipoprotein assembly, remodeling, and clearance	4	0.0318	*A2M, ALB, APOA1, APOA4*
98	Interleukin-4 and Interleukin-13 signaling	5	0.0318	*ANXA1, COL1A2, F13A1, TIMP1, VIM*
99	Detoxification of reactive oxygen species	3	0.0332	*PRDX1, PRDX2, SOD3*
100	Apoptotic cleavage of cell adhesion proteins	2	0.0338	*DSG1, DSP*
101	GP1b-IX-V activation signalling	2	0.0338	*COL1A1, COL1A2*
102	Type I hemidesmosome assembly	2	0.0338	*KRT14, KRT5*
103	Reversible hydration of carbon dioxide	2	0.0382	*CA1, CA2*
104	Retinoid cycle disease events	2	0.0382	*RBP4, TTR*
105	G alpha (i) signalling events	10	0.0499	*AGT, ANXA1, APOA1, APOA4, C3, HSPG2, INSL5, RBP4, RDH8, TTR*

ECM, extracellular matrix; TLR, Toll-like receptor; GAG, glycosaminoglycans; PDGF, platelet-derived growth factor; EDS, Ehlers–Danlos syndrome; TPBS, temtamy preaxial brachydactyly syndrome; PTK2, protein tyrosine kinase 2; MAPK, mitogen-activated protein kinase; HDL, high-density lipoprotein.