UNC13D is the predominant causative gene with recurrent splicing mutations in Korean patients with familial hemophagocytic lymphohistiocytosis

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Online Supplementary Table S1. The clinical and laboratory findings of 40 Korean pediatric patients with hemophagocytic lymphohistiocytosis.

Patient	P1	P2	P3	P4	P5	P6	P7	P8	Р9	P10	P11	P12	P13
Family history	-	-	-	-	-	-	-	-	-	-	-	-	-
Consanguinity	-	-	-	-	-	-	-	-	-	-	-	-	-
Sex	М	М	М	М	F	М	F	F	М	М	М	М	М
Age at diagnosis	5m	1m	8m	5m	5y 10m	2m	19m	9y 8m	6m	12y 10m	1m	1y 9m.	1y 9m
Fever	+	-	+	+	+	+	-	+	+	+	+	+	+
Splenomegaly	+	+	+	+	+	+	+	+	+	+	+	+	+
Hemoglobin (g/dL)	8.1	7.8	13.7	7.4	7.3	5.5	8.3	11.2	8.1	10.9	8.0	9.8	7.8
Platelets (x10 ³ /mm ³)	8	10	414	76	12	42	45	70	8	45	47	27	173
Neutrophils (/mm ³)	300	1,820	4,300	650	660	600	400	2,180	300	400	4,300	100	2,300
Triglyceride (mg/dL)	401	94	173	127	126	97	45	292	53	177	289	204	258
Fibrinogen (mg/dL)	158	124	236	121	87	138	109	125	28	320	30	280	254
Ferritin (ug/L)	1,798	2,334	403.7	68,910	1292	6,507	2,948	12,075	1,945	3,023	2,000	4,842	720
BM hemophagocytosis	+	+	+	+	+	+	+	+	+	+	+	-	+
NK cell activity (%)	ND	ND	0.8(D)	9.7(D)	ND	24.8(N)	ND	ND	2.1(D)	ND	7.8(D)	ND	ND
Liver dysfunction	+	+	+	+	-	+	+	+	+	+	+	+	+
EBV status	-	-	-	-	-	-	-	+	-	+	-	-	-
CNS symptom	+	-	+	-	+	-	-	-	+	-	+	-	-
Treatment	HLH- 2004												
Response	PR	PR	Relapse	PR	CR	Relapse	CR	CR	Progress	CR	CR	PR	CR
Transplant	Yes	Yes	No	No	Yes	Yes	No	No	No	No	Planned	No	No
Outcome	Dead	Alive	Dead	Alive	Dead	Alive	Alive	Alive	Dead	Alive	Alive	Alive	Alive
FHL mutation	_	UNC13D*	UNC13D	-	UNC13D	UNC13D	-	-	_	_	UNC13D*	-	-

Online Supplementary Table S1. (Continued)

Patient	P14	P15	P16	P17	P18	P19	H	20	P21	P22	P23	P24	P25	P26
Family history	-	-	-	-	-	-		-	-	-	-	-	-	-
Consanguinity	-	-	-	-	-	-		-	-	-	-	-	-	-
Sex	F	М	F	F	М	F		F	М	F	F	М	F	М
Age at diagnosis	5y 8m	3y 10m	4y 9m	3y 1m	7y 9m	2m		9у	1y 10m	2y 2m	3m	8y 4m	12m	9m
Fever	+	+	+	+	+	+		+	+	+	+	+	+	+
Splenomegaly	+	+	+	+	+	+		_	+	+	+	+	+	+
Hemoglobin (g/dL)	6.9	8.9	10.3	9.9	8.4	6.5	5	3.9	9.8	11.6	8.7	7.7	8.3	7.3
Platelets (x10 ³ /mm ³)	42	64	74	16	153	18		32	130	49	43	135	82	179
Neutrophils (/mm ³)	400	350	2,600	1,200	2,500	2,40		50	1,200	250	166	800	10,017	420
Triglyceride (mg/dL)	558	639	151	215	136	147		55	293	162	135	ND	127	546
Fibrinogen (mg/dL)	205	104	104	109	156	30		:11	681	30	87	137	132	302
	344.8	>1,000		797	524	4,842						1,596	15,499	1,490
Ferritin (ug/L)			>2,000			4,84.		806	6,344	25,306	3,917			
BM hemophagocytosis	+	+	+	+	+			- JD	+	+	+	+	+	+
NK cell activity (%)	ND	ND	ND	ND	ND	ND		1D	ND	ND	10.5(D)	ND	15.2(D)	ND
Liver dysfunction	+	+	+	+	+	+		+	+	+	+	+	+	+
EBV status	+	-	+	-	+	-		+	-	+	-	-	-	-
CNS symptom	+ HLH-	– HLH-	– HLH-	+ HLH-	-	– HLH		– LH-	– HLH-	-	– HLH-	– HLH-	– HLH-	– HLH-
Treatment	2004	2004	2004	2004	No	2004		D04	2004	IST	2004	2004	2004	2004
Response	CR	CR	CR	Progress	Relapse	Progre	ess (CR	CR	CR	CR	CR	CR	CR
Transplant	No	No	No	No	No	No	1	No	No	No	No	No	No	No
Outcome	Alive	Alive	Alive	Dead	Dead	Dead	d A	live	Alive	Alive	Alive	Alive	Alive	Alive
FHL mutation	-	-	-	-	_	PRF	1	-	-	-	UNC13D*	-	-	-
Patient	P27	P28	P29		721									
	127	F20	F29	P30	P31	P32	P33	P34	P35	P36	P37	P38	P39	P40
Family history	-	-	-	P30 -	-	P32	P33	P34	P35	P36	P37	P38	P39 -	P40
Family history Consanguinity			- -										P39 - -	P40 - -
Consanguinity			- - F										P39 - - F	P40 - - F
Consanguinity Sex	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Consanguinity Sex Age at diagnosis	- - F	- - F	– – F	- - F	- - M	- - M	- - M	- - F	- - M	- - M	- - F	- - M	- - F	- - F
Consanguinity Sex Age at diagnosis Fever Splenomegaly	- F 3y 2m + +	- F 10y 6m + +	- F 9y 2m + +	- F 3y 5m + +	- M 13m + +	- M 6y 1m +	- M 8y 11m + +	- F 3m +	- M 8m + +	- M 21m +	- F 2y +	- M 8y 7m + -	- F 3y 9m + +	- F 2m +
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL)	- F 3y 2m + + 10.5	- F 10y 6m + + 11.2	- F 9y 2m + 11.1	- F 3y 5m + + 10.4	- M 13m + + 7.1	- M 6y 1m + + 9.3	- - M 8y 11m + + 11.6	- F 3m + +	- M 8m + + 6.4	- M 21m + +	- F 2y + +	- M 8y 7m + - 8.0	- F 3y 9m + +	- F 2m + +
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³)	- F 3y 2m + + 10.5 20	- F 10y 6m + 11.2 36	- F 9y 2m + 11.1 166	- F 3y 5m + 10.4 33	- M 13m + + 7.1 110	- M 6y 1m + 9.3 92	 M 8y11m + 11.6 127	- F 3m + + 10.1	- M 8m + + 6.4	- M 21m + 10.7 45	- F 2y + 10.9 71	- M 8y 7m + - 8.0 79	- F 3y 9m + + 10.4 91	- F 2m + + 8.9
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³)	- F 3y 2m + 10.5 20 350	- F 10y 6m + 11.2 36 930	- F 9y 2m + 11.1 166 4,006	- F 3y 5m + 10.4 33 930	- M 13m + + 7.1 110 1,210	- M 6y 1m + 9.3 92 2,720		- F 3m + 10.1 13 6,900	- M 8m + + 6.4 133 890	- M 21m + 10.7 45	- F 2y + + 10.9 71 586	- M 8y 7m + - 8.0 79 2,695	- F 3y 9m + 10.4 91 820	- F 2m + 8.9 19 2,200
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL)	- F 3y 2m + + 10.5 20 350 453	- F 10y 6m + + 11.2 36 930 321	- F 9y 2m + 11.1 166 4,006 186	- F 3y 5m + + 10.4 33 930 571	- M 13m + + 7.1 110 1,210 305	- M 6y 1m + 9,3 92 2,720 352	- M 8y11m + 11.6 127 600	 F 3m + 10.1 13 6,900 260	- M 8m + + 6.4 133 890 158	- M 21m + 10.7 45 1,200 366	- F 2y + 10.9 71 586 467	- M 8y 7m + - 8.0 79 2,695 232	- F 3y 9m + 10.4 91 820 336.5	- F 2m + + 8.9 19 2,200 134
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL)	- F 3y 2m + 10.5 20 350 453 162	- F 10y 6m + 11.2 36 930 321 138	- F 9y 2m + 11.1 166 4,006 186 232	- F 3y 5m + 10.4 33 930 571 63	- M 13m + + 7.1 110 1,210 305 ND	- M 6y 1m + 9.3 92 2,720 352 125	- M 8y11m + 11.6 127 600 221 135	 F 3m + 10.1 13 6,900 260 322	- M 8m + 6.4 133 890 158 134	 M 21m + 10.7 45 1,200 366 156	- F 2y + 10.9 71 586 467 89	- M 8y 7m + - 8.0 79 2,695 232 136	- F 3y 9m + 10.4 91 820 336.5 167.8	- F 2m + 4 8.9 19 2,200 134 27.1
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL)	- F 3y 2m + + 10.5 20 350 453 162 9,309	- F 10y 6m + 11.2 36 930 321 138 6,000	- F 9y 2m + 11.1 166 4,006 186 232 1,259	- F 3y 5m + 10.4 33 930 571 63 16,500	- M 13m + + 7.1 110 1,210 305 ND 1,650	- M 6y 1m + 9.3 92 2,720 352 125 591	- M 8y11m + 11.6 127 600 221 135 4,220	- F 3m + 10.1 13 6,900 260 322 4,857	- M 8m + + 6.4 133 890 158 134 15,331	- M 21m + 10.7 45 1,200 366 156 19,020	 F 2y + 10.9 71 586 467 89 >16,500	- M 8y 7m + - 8.0 79 2,695 232 136 66,188	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000	- F 2m + + 8.9 19 2,200 134 27.1 45,767
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Ferritin (ug/L) BM hemophagocytosis	- F 3y 2m + + 10.5 20 350 453 162 9,309 +	- F 10y 6m + 11.2 36 930 321 138 6,000 +	- F 9y 2m + 11.1 166 4,006 186 232 1,259 +	- F 3y 5m + + 10.4 33 930 571 63 16,500 +	- M 13m + + 7.1 110 1,210 305 ND 1,650 -	- M 6y 1m + 9,3 92 2,720 352 125 591 +	- M 8y11m + 11.6 127 600 221 135 4,220	- F 3m + 10.1 13 6,900 260 322 4,857	- M 8m + + 6.4 133 890 158 134 15,331 +	- M 21m + 10.7 45 1,200 366 156 19,020 +	 F 2y + 10.9 71 586 467 89 >16,500 +	- M 8y 7m + - 8.0 79 2,695 232 136 66,188 +	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 +	- F 2m + + 8.9 19 2,200 134 27.1 45,763 +
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) Ferritin (ug/L) BM hemophagocytosis	- F 3y 2m + 10.5 20 350 453 162 9,309 + 5.3(D)	- F 10y 6m + 11.2 36 930 321 138 6,000 + ND	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND	- F 3y 5m + 10.4 33 930 571 63 16,500 + ND	- M 13m + 7.1 110 1,210 305 ND 1,650 - 25.5(N)	- M 6y 1m + 9.3 92 2,720 352 125 591 + 30.5(N)	- M 8y11m + 11.6 127 600 221 135 4,220 4,220 + ND	 F 3m + 10.1 13 6,900 260 322 4,857 - ND	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N)	- M 21m + 10.7 45 1,200 366 156 19,020 + ND	 F 2y + 10.9 71 586 467 89 >16,500 + ND	- M 8y 7m + - 8.0 79 2,695 232 136 66,188 + +	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,767 + ND
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) SM hemophagocytosis NK cell activity (%)	- F 3y 2m + 10.5 20 350 453 162 9,309 + 5.3(D) +	F 10y 6m + 11.2 36 930 321 138 6,000 + ND +	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND + ND	F 3y 5m + 10.4 33 930 571 63 16,500 + ND +	- M 13m 13m 4 - 7.1 110 1,210 305 ND 1,650 - 25.5(N) 4	- M 6y 1m + 9.3 92 2,720 352 125 591 + 30.5(N)	 M 8y11m + 11.6 127 600 221 135 4,220 4,220 + ND	 F 3m + 10.1 13 6,900 260 322 4,857 ND +	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N) +	- M 21m + 10.7 45 1,200 366 156 19,020 + ND +	 F 2y + 10.9 71 586 467 89 >16,500 + ND +	- M 8y 7m + - 8.0 79 2,695 232 136 66,188 + 5.1(D) +	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,767 + ND +
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) Ferritin (ug/L) BM hemophagocytosis NK cell activity (%) Liver dysfunction	- F 3y 2m + + 10.5 20 350 453 162 9,309 + 5.3(D) + +	- F 10y 6m + 11.2 36 930 321 138 6,000 + ND + ND +	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND + ND	- F 3y 5m + 10.4 33 930 571 63 16,500 + ND + ND +	- M 13m + + 7.1 110 1,210 305 ND 1,650 - 25.5(N) + +	- M 6y 1m + 9,3 92 2,720 352 125 352 125 3591 + 30.5(N) + +	- M 8y11m + 11.6 127 600 221 135 4,220 4,220 4,220 + ND ND	 F 3m + + 10.1 13 6,900 260 322 4,857 ND + -	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N) + -	 M 21m + + 10.7 45 1,200 366 156 19,020 + ND + + ND	 F 2y + 10.9 71 586 467 89 >16,500 + ND + ND	 M 8y 7m + 8.0 79 2,695 232 136 66,188 + 5.1(D) +	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,767 + ND +
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) SM hemophagocytosis NK cell activity (%) Liver dysfunction EBV status	- F 3y 2m + + 10.5 20 350 453 162 9,309 + 5.3(D) + + +	F 10y 6m + 11.2 36 930 321 138 6,000 + ND + ND + + HLH-	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND + ND	F 3y 5m + 10.4 33 930 571 63 16,500 + ND +	- M 13m 13m 4 - 7.1 110 1,210 305 ND 1,650 - 25.5(N) 4	- M 6y 1m + 9.3 92 2,720 352 2,720 352 125 591 + 30.5(N) 4 + 30.5(N)	 M 8y11m + 11.6 127 600 221 135 4,220 4,220 + ND	F 3m + 10.1 13 6,900 260 322 4,857 ND + - ND + HLH-	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N) +		 F 2y + 10.9 71 586 467 89 >16,500 + ND +	- M 8y 7m + - 8.0 79 2,695 232 136 66,188 + 5.1(D) +	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,765 + ND + - ND + HLH-
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) SM hemophagocytosis NK cell activity (%) Liver dysfunction EBV status CNS symptom	- F 3y 2m + + 10.5 20 350 453 162 9,309 + 5.3(D) + 5.3(D) + + + 10.5	F 10y 6m + 1102 36 930 321 138 6,000 + ND + ND + 1 ND + 1 ND + ND + ND + ND	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND + ND + ND + ND	F 3y 5m + 10.4 33 930 571 63 16,500 + ND + ND + 10,100 + 1000	 M 13m + + 7.1 110 1,210 305 ND 1,650 1,650 - 25.5(N) + + + HLH- 2004	- M 6y 1m + 9.3 92 2,720 352 352 352 352 352 352 352 125 30.5(N) + 30.5(N)	- M 8y 11m + 11.6 127 600 221 135 4,220 4,220 135 4,220 135 4,220 135 4,220 135 4,220 135 4,220 135 145 155 155 155 155 155 155 15	 F 3m + + 10.1 13 6,900 260 322 4,857 ND + + ND	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N) + 14.1(N) + - -		F 2y + 10.9 71 586 467 89 >16,500 + ND + ND + + 10.9 10,9 10,9 10,9 10,9 10,9 10,9 10,9 10,	 M 8y 7m + 8.0 79 2,695 232 136 66,188 + 5.1(D) + 5.1(D) + + + HLH- 2004	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,765 + ND + - ND + - - HLH- 2004
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Platelets (×10 ³ /mm ³)	- F 3y 2m + + 10.5 20 350 453 162 9,309 + 5.3(D) + 5.3(D) + + HLH- 2004 CR	F 10y 6m + 11.2 36 930 321 138 6,000 + ND + ND + HLH 2004 CR		F 3y 5m + 10.4 33 930 571 63 16,500 + ND 16,500 + HLH- 2004 CR		- M 6y 1m + 9,3 92 2,720 352 125 352 125 30.5(N) 30.5(N) 4 + 30.5(N) 4 - - - NLH- 2004 (CR		 F 3m + 10.1 13 6,900 260 322 4,857 - ND + ND + 1 - ND + 1 - ND 2004 Progress			F 2y 4 2y 4 10.9 71 586 467 89 >16,500 4 1,00 1,00 4 1,	 M 8y 7m + 8.0 79 2,695 232 136 66,188 + 5.1(D) + 5.1(D) + + + HLH- 2004 CR	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND + ND + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,763 + ND + - ND + HLH- 2004 CR
Consanguinity Sex Age at diagnosis Fever Splenomegaly Hemoglobin (g/dL) Platelets (×10 ³ /mm ³) Neutrophils (/mm ³) Triglyceride (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) Fibrinogen (mg/dL) Eibrinogen (mg/dL) SM hemophagocytosis NK cell activity (%) Liver dysfunction EBV status	- F 3y 2m + + 10.5 20 350 453 162 9,309 + 5.3(D) + 5.3(D) + + + 10.5	F 10y 6m + 1102 36 930 321 138 6,000 + ND + ND + 1 ND + 1 ND + ND + ND + ND	- F 9y 2m + 11.1 166 4,006 186 232 1,259 + ND + ND + ND + ND	F 3y 5m + 10.4 33 930 571 63 16,500 + ND + ND + 10,100 + 1000	 M 13m + + 7.1 110 1,210 305 ND 1,650 1,650 - 25.5(N) + + + HLH- 2004	- M 6y 1m + 9.3 92 2,720 352 352 352 352 352 352 352 125 30.5(N) + 30.5(N)	- M 8y 11m + 11.6 127 600 221 135 4,220 4,220 135 4,220 135 4,220 135 4,220 135 4,220 135 4,220 135 145 155 155 155 155 155 155 15	 F 3m + + 10.1 13 6,900 260 322 4,857 ND + + ND	- M 8m + + 6.4 133 890 158 134 15,331 + 14.1(N) + 14.1(N) + - -		F 2y + 10.9 71 586 467 89 >16,500 + ND + ND + + 10.9 10,9 10,9 10,9 10,9 10,9 10,9 10,9 10,	 M 8y 7m + 8.0 79 2,695 232 136 66,188 + 5.1(D) + 5.1(D) + + + HLH- 2004	- F 3y 9m + 10.4 91 820 336.5 167.8 >2,000 + ND + ND + ND + ND	- F 2m + + 8.9 19 2,200 134 27.1 45,765 + ND + - ND + - - HLH- 2004

BM, bone marrow; NK, natural killer; EBV, Epstein-Barr virus; CNS, central nervous system; FHL, familial hemophagocytic lymphohistiocytosis; –, absent; +, present; ND, not determined; D, decreased NK cell activity; N, normal NK cell activity; HLH, hemophagocytic lymphohistiocytosis; CR, complete remission; PR, partial response; *, one mutant allele of UNC13D. The reference range for the NK cell activity was determined as 11.8-31.9% based on data from 63 control individuals.