

# 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	P9	P10	P11	P12	P13
Family history	-	-	-	-	-	-	-	-	-	-	-	-	-
Consanguinity	-	-	-	-	-	-	-	-	-	-	-	-	-
Sex	M	M	M	M	F	M	F	F	M	M	M	M	M
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 <sup>3</sup> /mm <sup>3</sup> )	8	10	414	76	12	42	45	70	8	45	47	27	173
Neutrophils (/mm <sup>3</sup> )	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	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004
Response	PR	PR	Relapse	PR	CR	Relapse	CR	CR	CR	Progress	CR	CR	PR
Transplant	Yes	Yes	No	No	Yes	Yes	No	No	No	No	Planned	No	No
Outcome	Dead	Alive	Dead	Alive	Dead	Alive	Alive	Alive	Alive	Dead	Alive	Alive	Alive
FHL mutation	-	UNC13D*	UNC13D	-	UNC13D	UNC13D	-	-	-	-	UNC13D*	-	-

Online Supplementary Table S1. (Continued)

Patient	P14	P15	P16	P17	P18	P19	P20	P21	P22	P23	P24	P25	P26
Family history	-	-	-	-	-	-	-	-	-	-	-	-	-
Consanguinity	-	-	-	-	-	-	-	-	-	-	-	-	-
Sex	F	M	F	F	M	F	F	M	F	F	M	F	M
Age at diagnosis	5y 8m	3y 10m	4y 9m	3y 1m	7y 9m	2m	9y	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	8.9	9.8	11.6	8.7	7.7	8.3	7.3
Platelets ( $\times 10^3/\text{mm}^3$ )	42	64	74	16	153	18	32	130	49	43	135	82	179
Neutrophils ( $/\text{mm}^3$ )	400	350	2,600	1,200	2,500	2,400	350	1,200	250	166	800	10,017	420
Triglyceride (mg/dL)	558	639	151	215	136	147	155	293	162	135	ND	127	546
Fibrinogen (mg/dL)	205	104	104	109	156	30	211	681	30	87	137	132	302
Ferritin (ug/L)	344.8	>1,000	>2,000	797	524	4,842	4,806	6,344	25,306	3,917	1,596	15,499	1,490
BM hemophagocytosis	+	+	+	+	+	-	-	+	+	+	+	+	+
NK cell activity (%)	ND	ND	ND	ND	ND	ND	ND	ND	ND	10.5(D)	ND	15.2(D)	ND
Liver dysfunction	+	+	+	+	+	+	+	+	+	+	+	+	+
EBV status	+	-	+	-	+	-	+	-	+	-	-	-	-
CNS symptom	+	-	-	+	-	-	-	-	-	-	-	-	-
Treatment	HLH-2004	HLH-2004	HLH-2004	HLH-2004	No	HLH-2004	HLH-2004	HLH-2004	IST	HLH-2004	HLH-2004	HLH-2004	HLH-2004
Response	CR	CR	CR	Progress	Relapse	Progress	CR	CR	CR	CR	CR	CR	CR
Transplant	No	No	No	No	No	No	No	No	No	No	No	No	No
Outcome	Alive	Alive	Alive	Dead	Dead	Dead	Alive	Alive	Alive	Alive	Alive	Alive	Alive
FHL mutation	-	-	-	-	-	<i>PRF1</i>	-	-	-	<i>UNC13D*</i>	-	-	-

  

Patient	P27	P28	P29	P30	P31	P32	P33	P34	P35	P36	P37	P38	P39	P40
Family history	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Consanguinity	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Sex	F	F	F	F	M	M	M	F	M	M	F	M	F	F
Age at diagnosis	3y 2m	10y 6m	9y 2m	3y 5m	13m	6y 1m	8y 11m	3m	8m	21m	2y	8y 7m	3y 9m	2m
Fever	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Splenomegaly	+	+	+	+	+	+	+	+	+	+	+	-	+	+
Hemoglobin (g/dL)	10.5	11.2	11.1	10.4	7.1	9.3	11.6	10.1	6.4	10.7	10.9	8.0	10.4	8.9
Platelets ( $\times 10^3/\text{mm}^3$ )	20	36	166	33	110	92	127	13	133	45	71	79	91	19
Neutrophils ( $/\text{mm}^3$ )	350	930	4,006	930	1,210	2,720	600	6,900	890	1,200	586	2,695	820	2,200
Triglyceride (mg/dL)	453	321	186	571	305	352	221	260	158	366	467	232	336.5	134
Fibrinogen (mg/dL)	162	138	232	63	ND	125	135	322	134	156	89	136	167.8	27.1
Ferritin (ug/L)	9,309	6,000	1,259	16,500	1,650	591	4,220	4,857	15,331	19,020	>16,500	66,188	>2,000	45,767
BM hemophagocytosis	+	+	+	+	-	+	+	-	+	+	+	+	+	+
NK cell activity (%)	5.3(D)	ND	ND	ND	25.5(N)	30.5(N)	ND	ND	14.1(N)	ND	ND	5.1(D)	ND	ND
Liver dysfunction	+	+	+	+	+	+	+	+	+	+	+	+	+	+
EBV status	+	+	ND	+	+	+	-	-	-	+	+	-	-	-
CNS symptom	-	-	-	-	+	-	-	-	-	-	-	+	-	-
Treatment	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004	HLH-2004
Response	CR	CR	CR	CR	Relapse	CR	Progress	Progress	CR	CR	PR	CR	CR	CR
Transplant	Yes	No	No	No	No	No	No	No	No	No	Yes	No	No	No
Outcome	Alive	Alive	Alive	Alive	Alive	Alive	Alive	Dead	Alive	Alive	Alive	Alive	Alive	Alive
FHL mutation	<i>UNC13D*</i>	-	-	-	-	-	-	<i>UNC13D</i>	-	-	-	-	-	-

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.