

Figure 1

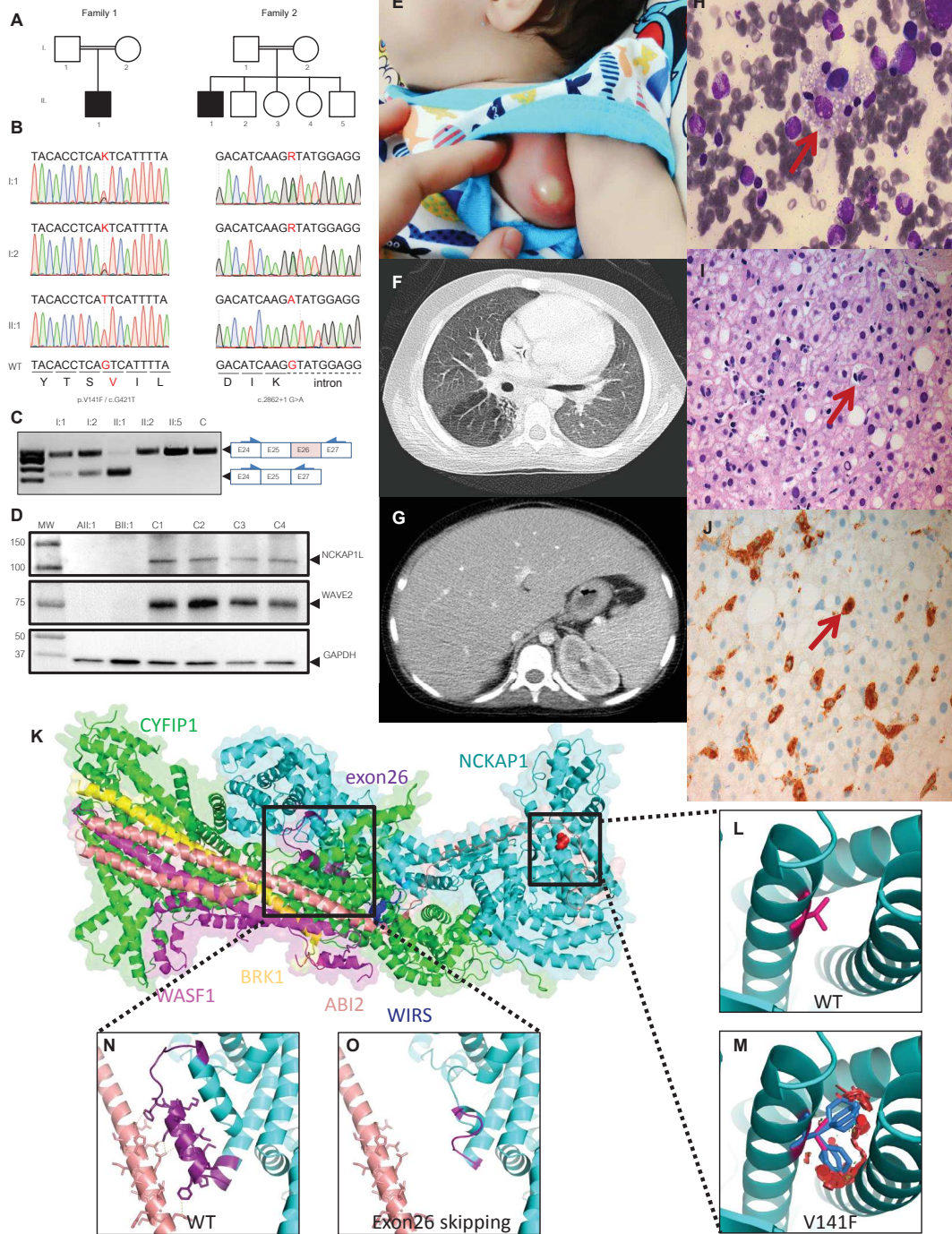


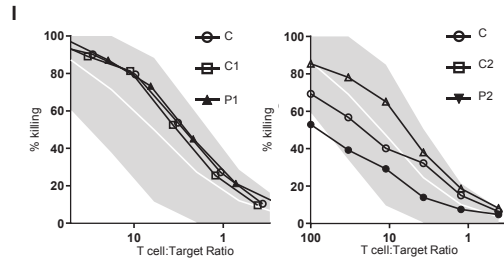
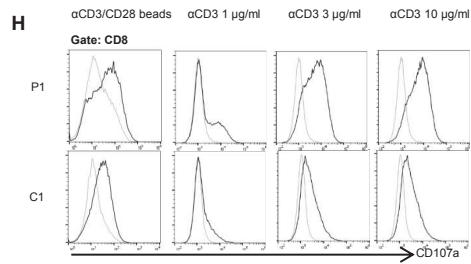
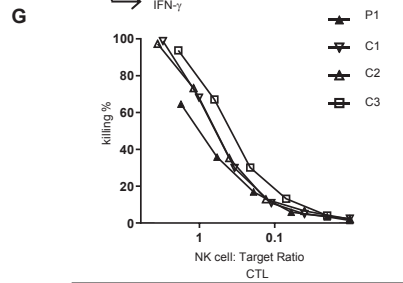
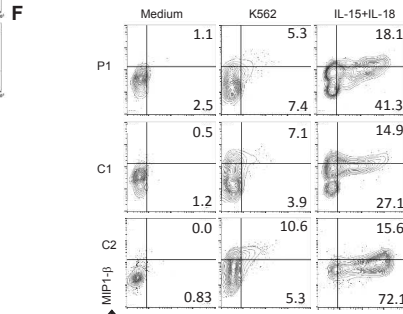
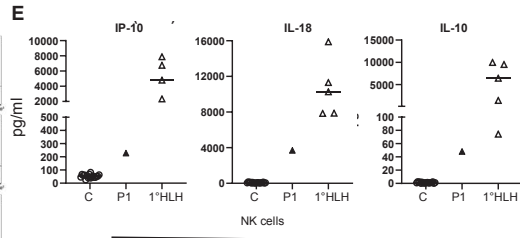
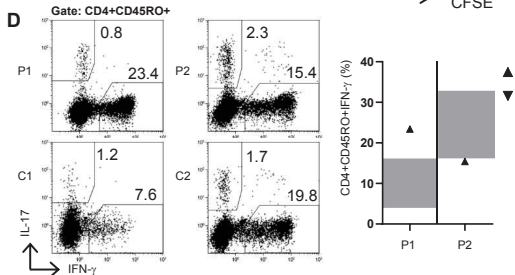
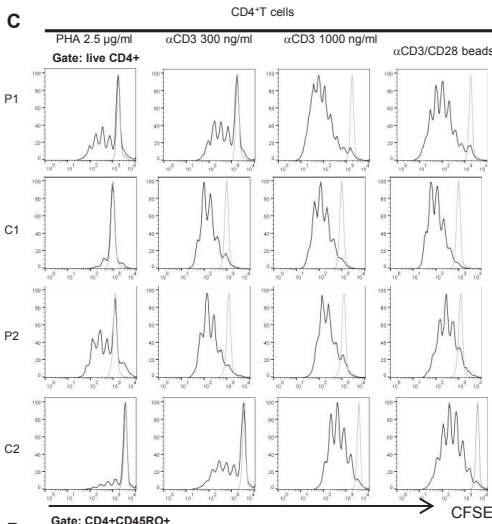
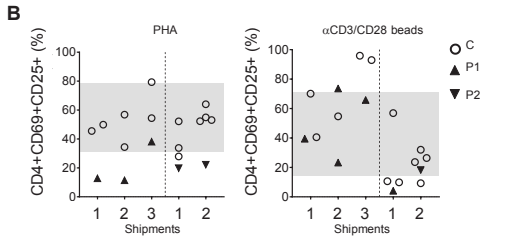
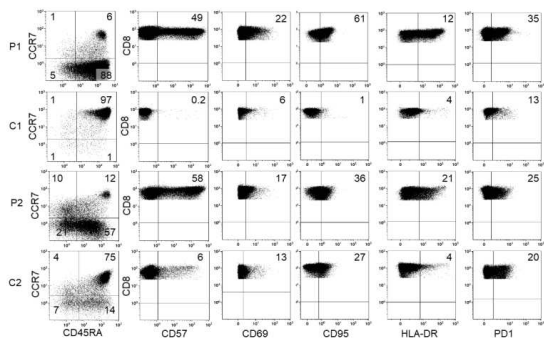
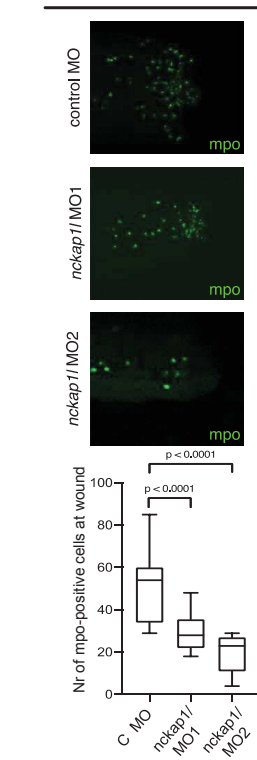
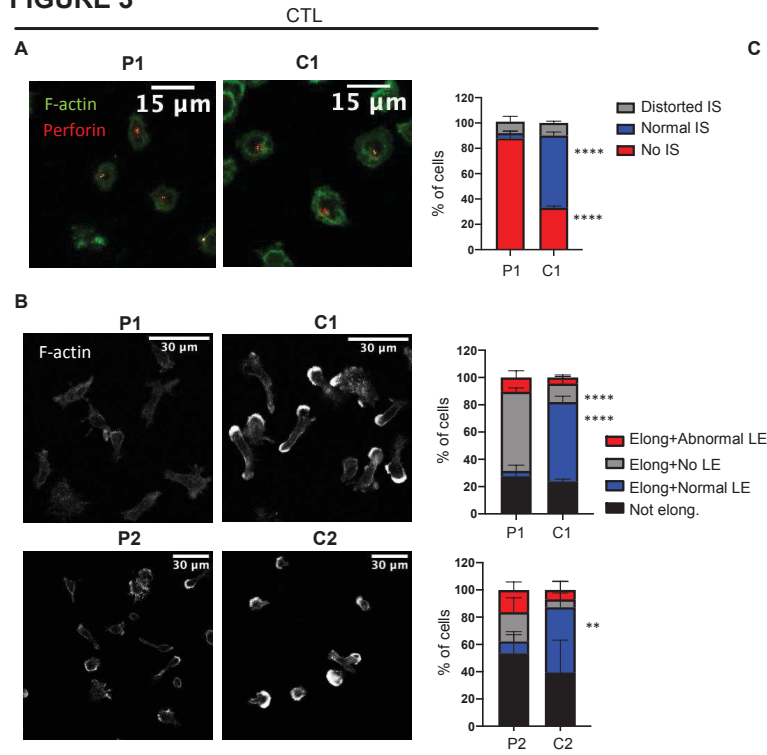
FIGURE 2CD8⁺T cells

FIGURE 3

zebrafish neutrophils



Dear Martina:
please insert
ZF MO
and rescue here

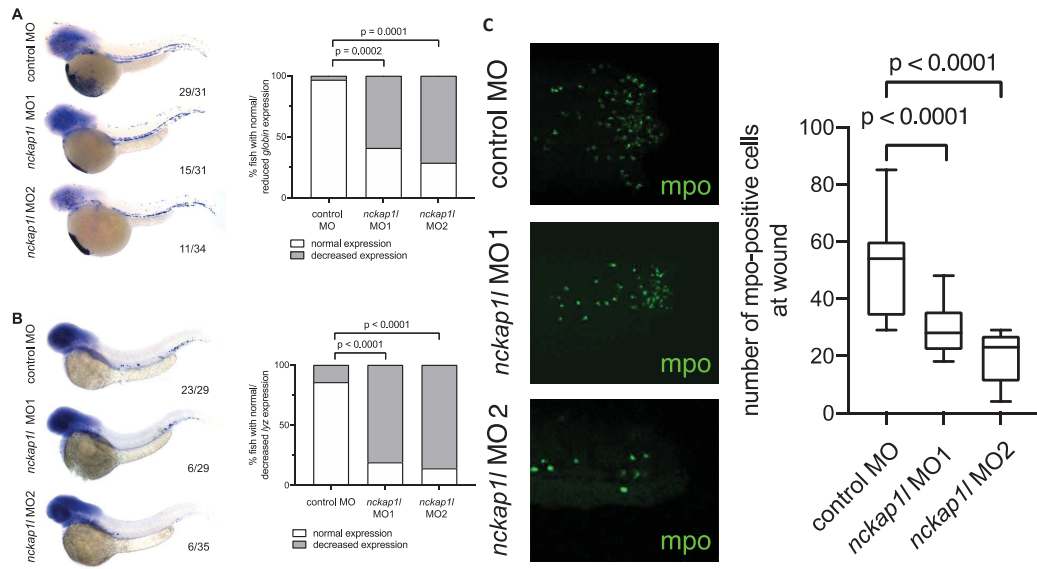


Figure 4

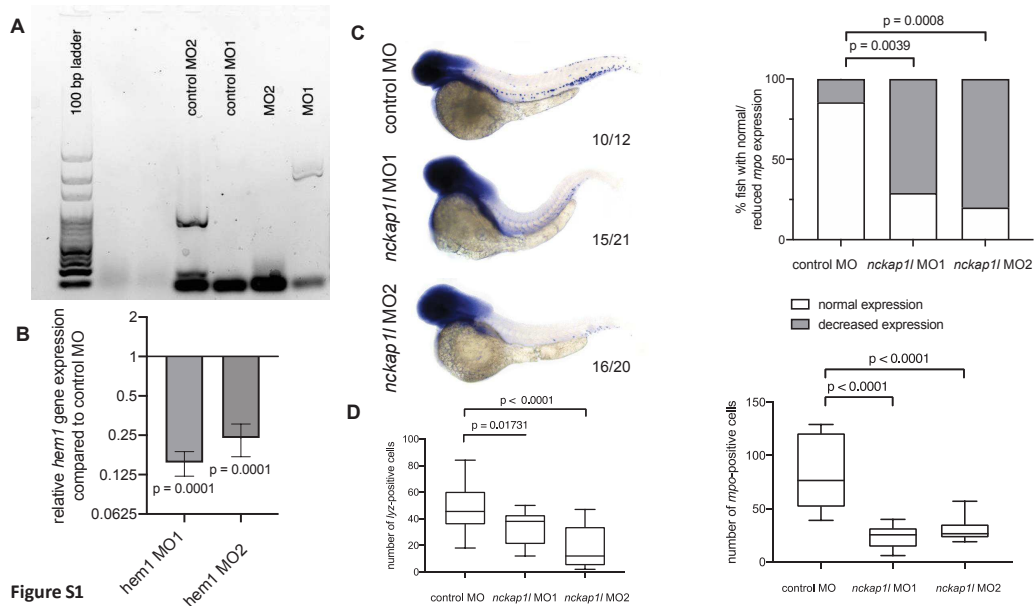


Figure S1

Table 1. Blood and immunological parameters of NCKAP1L patients.

	Patient 1 3 months	Patient 1 8 months	Normal range	Patient 2 9 years	Patient 2 11 years	Normal range
Peripheral blood						
White blood cells (x10 ⁹ /μL)	85.5	7.4	6-17.5	3.46	10.6	5.4-9.7
Hemoglobin (g/dL)	9.5	11	9.5-13.5	6.60	12.4	11.3-13.4
RBC (x10 ⁶ /μL)	3.16	4.84	3.5-5.5	3.02	5.65	4.00-5.20
MCV (fl)	95.9	82	80-100	66.4	62.5	77-90
MCH (pg)	30.1	27.5	27-31	22	18.9	25-30
Reticulocyte count (%)	2.4		0.5-1.5		0.3	0.5-1.5
Direct Coombs test	Negative	Negative		Negative	Negative	
Platelets (x10 ³ /μL)	234	236	150-450	71	188	150-450
Neutrophils (x10 ³ /μL)	21.4	2.1	1-8.5	1.66	2.84	2.5-5.95
Lymphocytes (x10 ³ /μL)	51	3.3	4.0-10.5	1.38	5.07	1.23-2.76
Monocytes (x10 ³ /μL)	7.7	1.8	0.2-1.2	0.42	0.87	0.10-1.11
Eosinophils (x10 ³ /μL)	1.5		<0.81	0	0.12	0.04-0.19
Lymphocyte subsets^a						
CD3 (x10 ³ cells/mL)	40.8	4.67	1.85-5.96	0.43	3.78	1-2.6
CD3/CD4 (x10 ³ cells/mL)	10.2	1.28	1.14-3.8	0.25	1.69	0.53-1.5
CD3/CD8 (x10 ³ cells/mL)	30.6	3.24	0.54-1.97	0.16	2.38	0.33-1.1
CD4/CD8 ratio	0.3	0.39	1.6-3.8	1.05	0.58	1.1-1.6
CD3/CD25 (x10 ³ cells/mL)	-	-		56	328	100-400
CD19 (x10 ³ cells/mL)	5.6	0.69	0.64-1.96	0.57	1.55	0.27-8.6
CD16/CD56 (x10 ³ cells/mL)	4.5	0.40	0.15-1.33	0.57	0.21	0.07-0.48
% in CD4⁺ T cells						
Treg (CD25 ⁺ CD127 ⁻ Foxp3 ⁺)	-	5.6	6.3-8.5*	-	7.4	7.6-9.9*
Naive (CD45RA ⁺ CCR7 ⁺)	-	33	74-90*	-	34	67-83*
CM (CD45RA ⁺ CCR7 ⁻)	-	20	8-18*	-	50	12-23*
EM (CD45RA ⁻ CCR7 ⁺)	-	34	2-5*	-	15	4-9*
TEMRA (CD45RA ⁻ CCR7 ⁻)	-	3	0-5*	-	1	1-2*
CD57 ⁺	-	6.5	1-2*	-	3.8	0-2*
CD69 ⁺	-	21	5-9*	-	5.0	5-7*
CD95 ⁺	-	69	12-24*	-	66.9	18-36*
HLA-DR ⁺	-	7	2-4*	-	5.3	2-9*
PD1 ⁺	-	36	16-26*	-	34.3	17-22*
% in CD8⁺ T cells						
Naive (CD45RA ⁺ CCR7 ⁺)	-	6	80-85*	-	12	56-74*
CM (CD45RA ⁺ CCR7 ⁻)	-	1	0-6*	-	10	2-4*
EM (CD45RA ⁻ CCR7 ⁺)	-	5	2-10*	-	21	6-14*
TEMRA (CD45RA ⁻ CCR7 ⁻)	-	88	6-28*	-	57	13-30*
CD57 ⁺	-	49	0-16*	-	58	4-20*
CD69 ⁺	-	22	6-21*	-	17	12-24*
CD95 ⁺	-	61	0-18*	-	36	14-34*
HLA-DR ⁺	-	12	5-17*	-	21	5-15*
PD1 ⁺	-	35	19-25*	-	25	16-31*
% in CD19⁺ B cells						
Naive (IgD ⁺ CD27 ⁻)	-	90	69-86*	-	93	64-86*
Switched Memory (IgD ⁻ CD27 ⁺)	-	1	3-10*	-	3	5-17*
Unswitched Memory (IgD ⁺ CD27 ⁺)	-	1	7-10*	-	3	5-15*
Transitional (CD24 ⁺ CD38 ⁺)	-	10	8-19*	-	9	7-15*
CD21 ⁺	-	77	4-14*	-	2	2-5*
% in Monocytes						
Classical (CD14 ⁺ CD16 ⁻)	-	9	59-80*	-	72	80-85*
Transient (CD14 ⁺ CD16 ⁺)	-	10	6-14*	-	17	3-5*
Resident (CD14 ⁺ CD16 ⁺)	-	75	5-12*	-	2	2-6*
% In CD3⁺CD56⁺ NK cells						
CD16 ⁺ CD56 ⁺⁺	-	18	2-8*	-	18	5-10*
NKp30 ⁺	-	26	69-86**	-	51	64-81*
NKp44 ⁺	-	8	0-11*	-	7	1-4*
NKp46 ⁺	-	96	96-98*	-	95	94-97*
NKG2C ⁺	-	11	0-69**	-	10	7-19**
NKG2D ⁺	-	98	97-98*	-	93	84-100*
CD57 ⁺	-	10	0-49*	-	28	10-23**
Immunoglobulins						
IgA (mg/dL)	130	169	4-69	1820	680	70-400

IgG (mg/dL)	2581	1680	196-560	15900	22500	700-1600
IgM (mg/dL)	>1000	9550	25-93	1340	1160	40-230
IgE (IU/mL)	60	22.9	<15	358	197	0-500
Serology						
Antinuclear antibodies titer	-	Positive at 1/1280 dilution	<1/80	Negative	-	<1/80
Anti-dsDNA (IU/mL)	-	Negative	<50	Negative	-	<200
Tetanus titer (IU/mL)	Protective	Protective	> 0.15	Protective	Protective	> 0.15
Others						
Ferritin (ng/mL)	1190	241	36-100	14280	76.9	21-274
Fibrinogen (mg/L)	0.64	0.83	1.5-3.5	1.07	3.83	1.50-4.10
Triglycerides (mg/dL)	1140	1940	20-150	612	174	20-150
AST (U/L)	141	84	6-50	301	102	5-34
ALT (U/L)	21	35	20-60	313	121	5-55
Total Bilirubin (μmol/L)	6.84	3.42	3.4-17.1	15.1	5.1	3.4-17.1
<i>conjugated</i>	3.42		<5.9	14.2		<5.9
<i>unconjugated</i>	3.42		<17.1	0.9		<17.1
Alk Phos (IU/L)	709	680	110-320	174	221	141-460
Haptoglobin (g/L)				0.47		<2.7
LDH (IU/L)		2835	500-920	948		432-700
ESR (mm/hr)	1	20	0-10	28	25	0-15
CRP (mg/L)	1	1	<6	208	5	< 8
sIL-2R (U/ml)	-	3202	223-710	-	1701	223-710
IFN-γ (pg/ml)	-	5.3	1.7-66.5 ^b	-	339	0.3-11.0 ^c
IL-18 (pg/ml)	-	3698	17-145 ^b	-	2130	266-1300 ^c
IP-10 (pg/ml)	-	228	25- 68 ^b	-	518	37- 245 ^c
IL12p40 (pg/ml)	-	676	0.0- 74 ^b	-	152	0.0- 65 ^c
IL-12 (pg/ml)		451.5	35 (±18.7)		34.1	35 (±18.7)
IL-15 (pg/ml)		5862.9	76 (±0.0)		75.7	76 (±0.0)
IL-17A (pg/ml)		36.0	11 (±0.0)		11.1	11 (±0.0)
IL-17F (pg/ml)		5620.3	138 (±0.0)		138.3	138 (±0.0)
IL-1a (pg/ml)		526.4	8 (±0.0)		8.3	8 (±0.0)
IL-b (pg/ml)		157.9	8 (±0.0)		8.0	8 (±0.0)
IL-6 (pg/ml)		18.7	19 (±52.9)		221.7	19 (±52.9)
TNF-a (pg/ml)		21.7	11 (±28.5)		10.2	11 (±28.5)
IFN-a (pg/ml)		31.3	11 (±0.0)		11.0	11 (±0.0)
IL-1Ra (pg/ml)		63.7	16 (±10.0)		16.3	16 (±10.0)
IL-2R (pg/ml)		519.9	76 (±12.1)		287.3	76 (±12.1)
IL-4 (pg/ml)		705.9	343 (±821.1)		498.4	343 (±821.1)
IL-13 (pg/ml)		26.9	13 (±19.9)		4.7	13 (±19.9)
IL-5 (pg/ml)		5.3	5 (±11.2)		1.0	5 (±11.2)
MCP-1 (pg/ml)		2425.1	170 (±160.7)		144.5	170 (±160.7)
Rantes (pg/ml)		192.8	114 (±48.9)		212.0	114 (±48.9)
Eotaxin (pg/ml)		105.1	14 (±9.1)		11.8	14 (±9.1)
MIG (pg/ml)		84.8	10 (±2.8)		21.3	10 (±2.8)
IL-8 (pg/ml)		7.0	124 (±113.2)		7.0	124 (±113.2)
IL-3 (pg/ml)		300.7	20 (±0.0)		19.5	20 (±0.0)
GCSF (pg/ml)		65.3	55 (±0.0)		55.2	55 (±0.0)
GM-CSF (pg/ml)		15.9	4 (±1.4)		4.0	4 (±1.4)
EGF (pg/ml)		940.2	35 (±10.2)		21.8	35 (±10.2)
HGF (pg/ml)		6686.4	118 (±17.9)		120.2	118 (±17.9)
FGF-basic (pg/ml)		100.6	13 (±0.0)		12.8	13 (±0.0)
Granzyme A (pg/ml)		20.0	486 (±1473.5)		1111.5	486 (±1473.5)
Granzyme B (pg/ml)		15.6	5 (±13.0)		20.4	5 (±13.0)
sFas (pg/ml)		2902.2	14,169 (±7555.2)		28529.2	14,169 (±7555.2)
sFasL (pg/ml)		10.0	10 (±0.0)		10.0	10 (±0.0)

*- indicates test not done. Normal range values are either those of the local diagnostic laboratory and/or reported from Gregory's Pediatric Anesthesia, Fifth Edition. Edited by George A. Gregory, Dean B. Andropoulos. Published 2012 by Blackwell Publishing Ltd. #: Normal range for absolute numbers of lymphocytes subsets were from age-matched routine clinical lab values. For other markers: * and ** correspond to 5th and 95th percentile of values obtained from 8 age-matched controls and in some rare cases from 3 age-matched controls respectively. ^bNormal range shows 5th and 95th percentile of serum cytokine levels calculated among 21 healthy subjects. ^cNormal range shows 5th and 95th percentile of plasma cytokine levels calculated among 9 healthy subjects.

Table S1: Blood and immunological parameters of both patients.

"-" indicates test not done.

	Patient 1 3 months	Patient 1 8 months	Normal range	Patient 2 9 years	Patient 2 11 years	Normal range
Peripheral blood						
White blood cell count	85.5	7.4	6-17.5 x10 ³ /µL	3.46	10.6	5.4 – 9.7x10 ³ /µL
Hemoglobin	9.5	11	9.5-13.5 g/dL	6.60	12.4	11.3 -13.4 g/dL
RBC					5.65	4.00–5.20 x10 ⁹ /µL
MCV					62.5	77-90 fL
MCH					18.9	25-30 pg
Platelets	234000	236000	150,000-450,000 /µL	71000	188000	150,000-450,000 /µL
Neutrophils	21.4	2.1	1-8.5 x10 ³ /µL	1.66	2.84	2.5-5.95 x10 ³ /µL
Lymphocytes	51	3.3	4.0-10.5 x10 ³ /µL	1.38	5.07	1.23 - 2.76 x10 ³ /µL
Monocytes	7.7	1.8	0.2-1.2 x10 ³ /µL	0.42	0.87	0.10-1.11 x10 ³ /µL
Eosinophils	1.5	-	<0.81 x10 ³ /µL	0	0.12	0.04 - 0.19 x10 ³ /µL
Lymphocyte subsets						
CD3 (cells/mL)		4.67	1.85-5.96K	0.43	3.78	1K - 2.6K
CD3/CD4 (cells/mL)		1.28	1.14-3.8K	0.25	1.69	0.53K - 1.5K
CD3/CD8 (cells/mL)		3.24	0.54-1.97	0.16	2.38	0.33K - 1.1K
CD4/CD8 ratio		0.39	1.6-3.8	1.05	0.58	1.1 - 1.6
CD3/CD25 (cells/mL)		-		56	328	100-400
CD19 (cells/mL)		0.69	0.64-1.96	0.57	1.55	0.27K - 8.6K
CD16/CD56 (cells/mL)		0.40	0.15-1.33	0.57	0.21	0.07K - 0.48K
% in CD4+Tcells						
Treg (CD25 ⁺ CD127 ⁺ Foxp3 ⁺)		5.6			7.4	
Naive (CD45RA ⁺ CCR7 ⁺)		31.3	82-93		26	48-85
CM (CD45RA ⁺ CCR7 ⁻)		21.7	5-11		48	1-10
EM (CD45RA ⁺ CCR7 ⁻)		37.1	1-4		25	3-16
TEMRA (CD45RA ⁺ CCR7 ⁻)		10.0	0-3		7	6-39
% in CD8+ T cells						
Naive (CD45RA ⁺ CCR7 ⁺)		7.4	78-96		9	47-79
CM (CD45RA ⁺ CCR7 ⁻)		0.7	0-3		10	14-37
EM (CD45RA ⁺ CCR7 ⁻)		5.0	0-3		31	4-20
TEMRA (CD45RA ⁺ CCR7 ⁻)		86.9	1-19		48	0-3
% in CD19+ B cells						
Naive (IgD ⁺ CD27 ⁺)		92.7	87- 99		82	64-84
Switched Memory (IgD ⁻ CD27 ⁻)		1.0	0.6-3.7		6	6-16
Unswitched Memory (IgD ⁻ CD27 ⁺)		2.5	2.4-9.9		11	4-14
Transitional (CD24 ⁺ CD38 ⁺)		10.4	8-27		9	8-21
CD21 ⁺		77.1	1-7		2	2-7
% in Monocytes						
Classical (CD14 ⁺ CD16 ⁻)		9.3	66-92		72	82-94
Transient (CD14 ⁺ CD16 ⁺)		9.7	1-10		18	1-5
Resident (CD14 ⁺ CD16 ⁺)		75.5	2-12		2	1-5
Immunoglobulins						
IgA (mg/dL)	130	169	4–69	1820	680	70 - 400
IgG (mg/dL)	2581	1680	196–560	15900	22500	700 - 1600
IgM (mg/dL)	>1000	9550	25-93	1340	1160	40 - 230
IgE IU/mL	60	22.9	<15	358	197	0 - 500
Serology						
ANA UNIT		Positive at 1/1280 dilution		Negative	-	<20
Anti-dsDNA IU/mL	-	Negative		Negative	-	<200
C-ANCA UNIT	-	-		Negative	-	<20
B-ANCA UNIT	-	-		Negative	-	<20
ASMA titer	-	-		Negative	-	<1:40
L/K mic Ab UNIT				Negative		<20
Tetanus titer (IU/mL)	Protective	Protective		Protective	Protective	> 0.15
Others						
Ferritin ng/mL	1190	241	36-100	14280	76.9	21-274
Fibrinogen mg/L	0.64	0.83		1.07	3.83	1.50-4.10
Triglyceride mg/dL	1140	1940	20-150mg/dL	612	174	20-150mg/dL

AST U/L	141			301	102	5-34
ALT U/L	21			313	121	5-55
Total Bilirubin □mol/L	6.84	3.42		15.1	5.1	3.50-20.5
Alk Phos IU/L	709	680		174	221	141-460
ESR mm/hr				28	25	0-15
CRP mg/L				208	5	< 8
sIL-2R (U/ml)		3202			1701	