Supplemental Table S3 | Individuals with PIDs born outside pilot test region. TRECs and PIDv2 panel testing on the original DBS and on new samples.

Patient ID	PID_1	PID_2	PID_3	PID_4		PID_5		PID_6
Year	2016	2016	2017	2017		2017		2017
Symptoms at time of diagnosis	SGA, microcephaly, transient lymphopenia, persistent neutropenia and low number of platelets	SGA, microcephaly, failure to thrive, pigment patches skin	Heart defect, choanal atresia, coloboma, infections	Heart defect, prematurity, Downs syndrome		Heart defect, dysmorphic features		Infections, failure to thrive
Gender	Female	Male	Male	Male		Male		Female
GA w	35	36	36	33		34		40
BW g	1920	1534	2445	1844		1570		3430
TRECs/µl at birth	4.69	1.9	0	9.7		15.7		71.8
Repeated TRECs/ul (age)	23.8 (3 months) 0 (12 months)	0 (4 months)	0 (1.5 months)	0 (2 months) 17-32 (2.5 months)		ND		12.2 (6.8 months)
1st FACS (age):	2.5 months	3 months	1.5 months	2 months	2.5 months	Day 1	3 months	6.8 months
CD3 x10^6/L	**918 (2300-6500)**	**98 (2300-6500) x10^6/L**	**617 (2300-7000) x10^6/L**	**212 (2300-6500) x10^6/L**	**1249 (2300-6500) x10^6/L**	**1146 (600-5000) x10^6/L**	**3922 (2300-6500) x10^6/L**	**1319 (2400-6900) x10^6/L**
CD4 x10^6/L	**190 (1500-5000) x10^6/L**	**90 (1500-5000) x10^6/L**	**552 (1700-5300) x10^6/L**	**149 (1500-5000) x10^6/L**	**890 (1500-5000) x10^6/L**	**673 (400-3500) x10^6/L**	2199 (1500-5000) x10^6/L	**918 (1400-5100) x10^6/L**
CD8 x10^6/L	**443 (500-1600) x10^6/L**	**9 (500-1600) x10^6/L**	**73 (400-1700) x10^6/L**	**60 (500-1600) x10^6/L**	**356 (500-1600) x10^6/L**	**465 (200-1900) x10^6/L**	1597 (500-1600) x10^6/L	**383 (600-2200) x10^6/L**
CD19 x10^6/L	3506 (600-3000) x10^6/L	**72 (600-3000) x10^6/L**	4067 (600-1900) x10^6/L	**256 (600-3000) x10^6/L**	**308 (600-3000) x10^6/L**	**269 (100-1900) x10^6/L**	3367 (600-3000) x10^6/L	**9 (700-2500) x10^6/L**
NK x10^6/L	477 (100-1300) x10^6/L	**7 (100-1300) x10^6/L**	4551 (200-1400) x10^6/L	**64 (100-1300) x10^6/L**	**117 (100-1300) x10^6/L**	**236 (100-1900) x10^6/L**	1928 (100-1300) x10^6/L	**40 (100-1000) x10^6/L**
Lymphocytes x10^9/L	7.2 (2-17) x10^9/L	**0.3 (2-17) x10^9/L**	NA (2-17) x10^9/L	0.6 (2-17) x10^9/L	NA (2-17) x10^9/L	1.6 (2-15) x10^9/L	6.1 (2-17) x10^9/L	**1 (3.5-13.5) x10^9/L**
Neutrophils x10^9/L	**0.4 (1-9) x10^9/L**	**1.0 (1-9) x10^9/L**	6.3 (1-9) x10^9/L	8.5 (1-9) x10^9/L	1.4 (1-9) x10^9/L	4.0 (3-25) x10^9/L	3.6 (1-9) x10^9/L	3.1 (1-8.5) x10^9/L
WBC x10^9/L	8.4 (5-19) x10^9/L	**2.1 (5-19) x10^9/L**	11.6 (5-19) x10^9/L	10.8-(5-19) x10^9/L	4.3 (5-19) x10^9/L	6.1 (9-30) x10^9/L	10.9 (5-19) x10^9/L	**4.4 (6-17) x10^9/L**
IgG g/L	**10.6 (3-7) g/L**	**2.4 (3-7) g/**L	4.3 (3-7) g/L	2.4 (3-7) g/L	NA	NA	3.3 (3-7) g/L	**< 1.0 (3-7) g/L**
IgA g/L	< 0.1 (0-0.3) g/L	< 0.2 (0-0.3) g/L	0.11 (0-0.3) g/L	0.4 (0-0.3) g/L	NA	NA	0.12 (0-0.3) g/L	< 0.1 (0-0.3) g/L
IgM g/L	0.22 (0.1-0.8) g/L	0.5 (0.1-0.8) g/L	0.44 (0.1-0.8) g/L	0.2 (0.1-0.8) g/L	NA	NA	0.77 (0.1-0.8) g/L	1.1 (0.1-0.8) g/L
Gene	unknown	unknown	*CHD7*	Trisomy 21		*TBX1*		*IKZF1*
SNV/CNV	NA	NA	c.[5833C>T];[=]	47,XY,+21		22q11.21 del		c.[476A<G];[=]
protein	NA	NA	p.Arg1945*	NA		NA		p.Asn159Ser
Refseq	NA	NA	NM_017780.3	NA		NA		NM_006060.4
Classification ACMG[1]	NA	NA	5	NA		NA		4
HGMD/ClinVar	NA	NA	RCV-000258138.1 CM060228	NA		NA		CM173423[2]
gnomAD allele frequency	NA	NA	0 in gnomAD	NA		NA		0 in gnomAD, but one heterozygote individual reported among 60 000 in ExAC
Gene panel	PIDv2 and IEM	PIDv2 and Hematology	NBSv1	NBSv1		NBSv1		PIDv2
Other gene tests	mtDNA deletion test normal. WES trio and WGS trio, No pathogenic variants detected	Fanconi anemia on Mitomycin C test. WES trio and WGS trio, No pathogenic variants detected	Sanger validation	Trisomy test		MLPA		Sanger validation
Disease development	Short stature, Microcephaly and DD/ID. Developed diabetes mellitus, but Pearson syndrome excluded	DD/ID, Microcephaly OFC 44.3cm at 2y3m = 3 cm below 2.5p Short stature 86 cm at 2.5y, at 3p	Short stature, Microcephaly, Seizures, Tracheostomia, needs respiratory support.	Heart surgery of ASD, VSD, PDA at 2 months				*P.jirovecii*

Treatment and outcome	Treated with immunomodulatory agents, steroids, tacrolimus. Deceased at 1.5 years of age after *P.jirovecii* infection followed by respiratory failure.	Successful HSCT 6,5 months old 10/10 MUD Preconditioning regimen: RIC Fanconi anemia protocol Flu, CP, ATG	At 2 years of age: prophylactic antibiotics, antifungal, antiviral and Sc immunoglobulins. Thymus transplantation were considered earlier	Lymphopenia 1.9x10^9/L at 1 years of age, but no recurrent infections	Prophylactic antibiotics	Successful HSCT[3] 9 months of age 11/12 MUD
Parental ethnicity	Norwegian	Norwegian	Arab	Norwegian	Pakistan	Norwegian

Abnormal laboratory results are marked in bold in the table above.

Abbreviations:
aCGH, array comparative genomic hybridization chromosomal/chromosomal microarray; ACMG, American College of Medical Genetics and Genomics' Guidelines for variant interpretation and classification; ATG, Antithymocyte globulin; BW, Birth weight; CNV, Copy number variation; CP, Cyclophosphamide; DD/ID, Developmental delay/Intellectual disability; FACS, fluorescence-activated cell sorting /lymphocyte flow cytometry; Flu, Fludarabine; g, gram; GA, Gestational age; gnomAD, The Genome Aggregation Database; Hematology, Ion Ampliseq™ Hematology research panel; HGMD, The Human Gene Mutation Database; HGNC, The HUGO Gene Nomenclature Committee; HSCT, Hematopoietic Stem Cell Transplantation; IEM, Ion Ampliseq™ Inborn Errors of Metabolism research panel; MLPA, multiplex ligation-dependent probe amplification; MUD, Matched unrelated donor; NA, Not applicable; NBS, Newborn screening; NBSv1, Newborn screening customized 160-gene panel version 1; ND, Not done; OFC, occipital frontal circumference; PIDv2, Primary immunodeficiency research panel version 2; PID, Primary immunodeficiency; Refseq, The National Center for Biotechnology Information Reference Database; RIC, Reduced intensity conditioning; SCID, Severe combined immunodeficiency; Sc, Subcutaneous; SGA, Small for gestational age; SNV, Single nucleotide variant; TREC, T-cell receptor excision circles; Trio-test; testing the child and both parents in comparison; WES, whole exome sequencing; WGS, whole genome sequencing; y, year; w, week; WBC, white blood cells

Resources:

ClinVar, https://www.ncbi.nlm.nih.gov/clinvar/
Gene names according to HGNC, https://www.genenames.org/
Gene variant classification according to ACMG standards and guidelines, Genetics in Medicine, 2015
gnomAD, https://gnomad.broadinstitute.org

References:

1. Richards, S., Aziz, N., Bale, S., Bick, D., Das, S., Gastier-Foster, J., Grody, W.W., Hegde, M., Lyon, E., Spector, E., et al. (2015). Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 17, 405-424.

2. Yoshida, N., Sakaguchi, H., Muramatsu, H., Okuno, Y., Song, C., Dovat, S., Shimada, A., Ozeki, M., Ohnishi, H., Teramoto, T., et al. (2017). Germline IKAROS mutation associated with primary immunodeficiency that progressed to T-cell acute lymphoblastic leukemia. Leukemia 31, 1221-1223.

3. Kellner, E.S., Krupski, C., Kuehn, H.S., Rosenzweig, S.D., Yoshida, N., Kojima, S., Boutboul, D., Latour, S., Barlogis, V., Galambrun, C., et al. (2019). Allogeneic hematopoietic stem cell transplant outcomes for patients with dominant negative IKZF1/IKAROS mutations. J Allergy Clin Immunol 144, 339-342.