Table 1 Other well-defined immunodeficiency syndromes

	Disease	Circulating T cells	Circulating B cells	Serum Ig	Associated features	Inheritance	Genetic defects/presumed pathogenesis	OMIM	HGNC symbol	HGNC ID(s)	ENSEMBL ID
1.	**Wiskott-Aldrich syndrome**	Progressive decrease	Normal	Decreased IgM: antibody to polysaccharides particularly decreased; often increased IgA and IgE bacterial and viral infections	**Thrombocytopenia**; small platelets; eczema; lymphomas; autoimmune disease; bacterial infections	XL	Mutations in *WASP* gene; cytoskeletal defect affecting haematopoietic stem cell derivatives	301000,	*WAS*	12731	ENSG00000015285
2.	**DNA repair defects (other than those in Table I and Table II)**										
A	**Ataxia-telangiectasia**	Decreased	Normal	Often decreased IgA, IgE, and IgG subclasses; increased IgM monomers; antibodies variably decreased	Ataxia, telangiectasis, increased AFP levels, lymphoreticular and other malignancies, increased x-ray sensitivity	AR	Mutation in A-T gene (*ATM*); disorder of cell cycle check-point pathway leading to chromosomal instability and defect in DNA double strand breaks repair	208900, 607585	*ATM*	795	ENSG00000149311
B	**Ataxia-like syndrome**	Decreased	Normal	Often decreased IgA, IgE, and IgG subclasses; increased IgM monomers; antibodies variably decreased	Moderate ataxia, microcephaly, severely increased radiosensitivity, normal AFP levels, no telangiectasis	AR	Mutation in *MRE11*; disorder of cell-cycle checkpoint and defect in DNA double strand breaks repair	604391, 600814	*MRE11A*	7230	ENSG00000020922
C	**Nijmegen breakage syndrome**	Decreased	Normal	Often decreased IgA, IgE, and IgG subclasses; increased IgM monomers; antibodies variably decreased	Microcephaly, lymphomas, ionizing radiation sensitivity, chromosomal instability, normal AFP levels, no telangiectasis	AR	Hypomophic mutation in *NBS1* (*Nibrin*); disorder of cell-cycle checkpoint and defect in DNA double strand breaks repair	251260, 602667	*NBN*	7652	ENSG00000104320
D	**Bloom syndrome**	Normal	Normal	Reduced	Chromosomal instability, marrow failure, leukemia, lymphoma, short stature, bird-like face, sensitivity to the sun, telangiectasias	AR	Mutation in *BLM*, a RecQ-like helicase	210900, 604610	*BLM*	1058	ENSG00000197299
E	**Immunodeficiency with centromeric instabilityand facialanomalies (ICF)**	Decreased or normal; Responses to PHAmay be decreased	Decreased or normal	Hypogamma-globulinemia; variableantibody deficiency	Facialdysmorphicfeatures; macroglossia; bacterial/opportunisticinfections; malabsorption; cytopenias; malignancies; multiradial configurations ofchromosomes 1, 9,16;noDNAbreaks	AR	MutationsinDNA methyltransferase *DNMT3B* (ICF1) resulting in defectiveDNA methylation;orin *ZBTB24* (ICF2)	242860, 602900	*DNMT3B*	2979	ENSG00000088305
F	**PMS2 deficiency (class switch recombination deficiency due to impaired mismatch repair)**	Normal	Switched and non-switched B cells are reduced	Low IgG and IgA, elevated IgM, abnormal antibody responses	Recurrent infections; café-au-lait spots; lymphoma, colorectal carcinoma, brain tumor	AR	Mutations in *PMS2*, resultingin defective CSR-induced DNA double-strand breaks inIgswitch regions	600259	*PMS2*	9122	ENSG00000122512
G	**Riddle syndrome**	Normal	Normal	Low IgG	Mild motor control and learning difficulties, mild facial dysmorphism, and short stature	AR	Mutations in *RNF168*, resulting in defective DNA double-strand break repair	611943, 612688	*RNF168*	26661	ENSG00000163961
3.	**Thymic defects**										
	Di George anomaly	Decreased or normal	Normal	Normal or decreased	Hypoparathyroidism, conotruncal malformation; abnormal facies; partial monosomy of 22q11-pter or 10p in some patients	*De novo* defect or AD	Contiguous gene defect in 90% affecting thymic development; deletion or mutation in *TBX1* (22q11) or deletion involving the *NEBL* gene (10p)	188400, 602054	*TBX1*	11592	ENSG00000184058
4.	**Immuno-osseous dysplasias**										
A	**Cartilage hair hypoplasia***	Decreased or normal	Normal	Normal or reduced; antibodies variably decreased	Short-limbed dwarfism with metaphyseal dysostosis, sparse hair, anemia, neutropenia, susceptibility to cancer, impaired spermatogenesis; neuronal dysplasia of the intestine	AR	Mutation in *RMRP* *	250250	*RMRP*	10031	ENSG00000199916
B	**Schimke immunoosseus dysplasia**	Decreased	Normal	Normal	Short stature, spondiloepiphyseal dysplasia, intrauterine growth retardation, nephropathy	AR	Mutation in *SMARCAL1*	242900, 606622	*SMARCAL1*	11102	ENSG00000138375
	Comel– Netherton syndrome	Normal	Switched and non-switched B cells are reduced	Elevated IgE and IgA antibody variably decreased	Congenitalichthyosis,bamboo hair,atopicdiathesis,increased bacterial infections,failureto thrive	AR	Mutations in *SPINK* 5 resulting in lack of the serine protease inhibitor LEKTI, expressed in epithelial cells	256500, 605010	*SPINK5*	15464	ENSG00000133710
6.	**Hyper-IgE syndrome**										
A	**Job syndrome (AD HIES)**	Normal Th-17 cells decreased	Normal (switched and non-switched memoryB cells are reduced; BAFFlevel increased)	Elevated IgE specific antibody production decreased	Recurrent skin boils and pneumonia caused by *Staph aur*; pneumatoceles; exzema; nail candidiasis, facial dysmorphism, hyperextensible joints, delayed shedding primary teeth.	*De novo* defect or AD	Mutation in *STAT3*	102582	*STAT3*	11364	ENSG00000168610
B	**AR HIES with mycobacterial and viral infections**	Normal	Normal	Elevated IgE	Susceptibility to fungi (*Candida*), intracellular bacteria (mycobacteria, *Salmonella*), and viruses	AR	Mutations in *TYK2*	611521, 176941	*TYK2*	12440	ENSG00000105397
C	**AR HIES with viral infections and CAN vasculitis/hemorrhage**	Normal	Normal	Elevated IgE	Susceptibility to bacterial, viral and fungal *Candida* infections; eczema; vasculitis; CNS hemorrhage		Unknown				
8.	**APECED, autoimmune polyendocrinopathy with candidiasis and ectodermal dystrophy**	Normal, increased $CD4^+$ cells	Normal	Normal	Autoimmune disease of parathyroid, adrenal and other organs plus candidiasis, dental enamel hypoplasia and other abnormalities	AR	Defects in *AIRE*, encoding a transcription regulator needed to establish thymic self-tolerance	607358	*AIRE*	360	ENSG00000160224
9.	**Hepatic veno-occlusive disease with immunodeficiency**	Normal (decreased memory T cells)	Normal (decreased memory B cells)	Decreased IgG, IgA, IgM, absent germinal centers absent tissue plasma cells	Hepatic veno-occlusive disease; *Pneumocystis jiroveci* pneumonia; thrombocytopenia, hepatosplenomegaly	AR	Mutation in *SP110*	235550, 604457	*SP110*	5401	ENSG00000135899
10. A	**Hoyerall-Hreidarsson syndrome**	Progressive decrease	Progressive decrease	Variable	Intrauterine growth retardation, microcephaly, digestive tract involvement, develops pancytopenia, reduced number and function of NK cells	XL	Mutation in *Dyskerin*	305000, 300126	*DKC1*	2890	ENSG00000130826
B	AR-DKC	Abnormal	Variable	Variable	Pancytopenia, sparse scalp hair and eyelashes, prominent periorbital telangiectasia, and hypoplastic/dysplastic nails	AR	Mutation in *NOLA2* (*NHP2*) or in *NOLA3* (*NOP10*)	224230, 606470	*NHP2*	14377	ENSG00000145912
						AR	*NOLA3* (*NOP10*)	606471	*NOP10*	14378	ENSG00000182117
					Dyskeratosis congenita, autosomal recessive 3	AR	WD repeat containing, antisense to TP53	612661	*WRAP53*	25522	ENSG00000141499
C	AD-DKC	Variable	Variable	Variable	Reticular hyperpigmentation of the skin, dystrophic nails, osteoporosis, premalignant leukokeratosis of the mouth mucosa, palmar hyperkeratosis, anemia, pancytopenia	AD	TERC	127550	*TERC*	11727	ENSG00000200182
					Dyskeratosis congenita, autosomal dominant 2 Dyskeratosis congenita, autosomal recessive 4	AD/AR	Mutationin *TERT*	187270, 609135,	*TERT*	11730	ENSG00000164362

								178500, 127550				
					Dyskeratosis congenita	AD or de novo	Mutationin *TINF2*	604319	*TINF2*	11824	ENSG00000092330
	Hoyerall-Hreidarsson syndrome 2				Dyskeratosis congenita	De novo/AD	DCLRE1B/ SNM1B/ APOLLO	609683	*DCLRE1B*	17641	ENSG00000118655
					Dyskeratosis congenita		TERF2	602027	*TERF2*	11729	ENSG00000132604
	Other relevant PID-like diseases/ DNA repair/immundysregulation:				Noonan phenotype & ALPS like disease with immunodysregulation and JMML risk	AD or de novo	Cbl proto-oncogene, E3 ubiquitin protein ligase	613563, 165360	*CBL*	1541	ENSG00000110395
						De novo	HMGB1		*HMGB1*	4983	ENSG00000189403
	Werner syndrome					AR	WRN	277700, 604611, 114500	*WRN*	12791	ENSG00000165392
	Rothmund Thomson					AR	*RECQL4*	268400	*RECQL4*	9949	ENSG00000160957

WASP, Wiskott-Aldrich syndrome protein; *MRE11*, meiotic recombination 11; *XL*, X-linked inheritance; *AR*, autosomal recessive inheritance; *AD*, autosomal dominant inheritance; AFP, alpha fetoprotein, *RMRP*, RNA component of mitochondrial RNA-processing endoribonuclease; *SMARCAL1*, SWI/SNF-related, matrix-associated, actin-dependent regulator of chromatin, subfamily alpha-like 1; *AP3B1*, adaptor-related protein complex 3, β-1 subunit.

* Patients with cartilage-hair hypoplasia can also present with typical severe combined immunodeficiency syndrome or with Omenn syndrome.