Table 1 Predominantly antibody deficiencies

	Disease	B-cell numbers	Pro-B	Serum Ig	Associated features	Inheritance	Genetic defects /presumed pathogenesis	OMIM	HGNC symbol	HGNC ID(s)	ENSEMBL ID
1.	**Severe reduction in all serum Ig isotypes with absent B cells**										
A	**Btk deficiency** **Bruton's agammaglobulinemia**	Profoundly decreased or absent.	Normal	All isotypes decreased	Severe bacterial infections	XL	Mutations in *BTK;* a cytoplasmic tyrosine kinase activated by crosslinking of the BCR	300300	*BTK*	1133	ENSG00000010671
B	**m heavy chain deficiency**	Absent	Normal	All isotypes decreased	Severe bacterial infections	AR	Mutations in μ heavy chain	147020	*IGHM*	5541	ENSG00000211899
C	**lambda 5 deficiency**	Profoundly decreased or absent	Normal	All isotypes decreased	Severe bacterial infections	AR	Mutations in λ5	146770	*IGLL1*	5870	ENSG00000128322
D	**Igα deficiency**	Absent	Normal	All isotypes decreased	Severe bacterial infections	AR	Mutations in Igα; part of the pre-BCR and BCR	112205	*CD79A*	1698	ENSG00000105369
E	**Igβ deficiency**	Absent	Normal	All isotypes decreased	Severe bacterial infections	AR	Mutations in Igβ; part of the pre-BCR and BCR	147245	*CD79B*	1699	ENSG00000007312
F	**BLNK deficiency**	Profoundly decreased or absent	Normal	All isotypes decreased	Severe bacterial infections	AR	Mutations in *BLNK* ; a scaffold protein that binds to BTK	604515	*BLNK*	14211	ENSG00000095585
G	**Thymoma with immunodeficiency**	Profoundly decreased or absent	Decreased	All isotypes decreased	Infections	None	Unknown				
H	**Myelodysplasia with hypogammaglobulinemia**	Profoundly decreased or absent	Decreased	One or more isotypes decreased	Infections	Variable	May have monosomy 7, trisomy 8 or dyskeratosis congenital				
2.	**Severe reduction in at least 2 serum Ig isotypes with normal or low numbers of B cells**										
	Common variable immunodeficiency disorders[I]	Normal or decreased		Decrease in IgG and IgA; IgM might be normal	All have recurrent bacterial infections. Clinical phenotype vary: autoimmune, lymphoproliferative, and/or granulomatous disease	AR or AD	*TACI*, *BAFFR*, *Msh5* contributing polymorfisms[II]				
A	**ICOS deficiency**	Normal or decreased		Decrease in IgG and IgA; IgM might be normal	Recurrent bacterial infections	AR	Mutation in *ICOS*	604558	*ICOS*	5351	ENSG00000163600
B	**CD19 deficiency**	Normal		Decrease in IgG and IgA; IgM might be normal	Recurrent bacterial infections	AR	Mutation in *CD19*	107265	*CD19*	1633	ENSG00000177455
	CD20 deficiency	Normal or decreased		Low IgG, normal or elevated IgM, and IgA	Recurrent bacterial infections	AR	CD20	112210	*MS4A1*	7315	ENSG00000156738
	CD81 deficiency	Normal or decreased		Low IgG, low or normal IgA, and IgM	Recurrent bacterial infections, May have glomerulonephritis	AR	CD81	186845	*CD81*	1701	ENSG00000110651
	TACI deficiency	Normal or decreased		Decrease in IgG and IgA; IgM might be normal	Variable clinical expression, Recurrent bacterial infections	AR	Mutationsin *TNFRSF13C* (BAFF-R)	604907	*TNFRSF13C*	17755	ENSG00000159958
	BAFF receptor deficiency	Normal or decreased		Decrease in IgG and IgM	Variable clinical expression, Recurrent bacterial infections	AD	Mutations in *TNFRSF13B* (TACI)	606269	*TNFRSF13B*	18153	ENSG00000240505
C	**X-linked lymphoproliferative syndrome 1**[III]	Normal		All isotypes may be low	Some patients have antibody deficiency, although most present with fulminant EBV infection or lymphoma	XL	Mutations in *SH2D1A*				
3.	**Severe reduction in serum IgG and IgA with increased IgM and normal numbers of B cells**										
A	**CD40L deficiency**[IV] **Hyper IgM syndrome 1**	Normal or increased		IgG and IgA decreased; IgM increased or normal	Neutropenia, thrombocytopenia, hemolytic anemia and other autoimmune diseases, opportunistic infections, sclerosing cholangitis caused by cryptosporidiosis	XL	Mutations in *CD40L*	300386	*CD40LG*	11935	ENSG00000102245
B	**CD40 deficiency**[IV] **Hyper IgM syndrome 3**	Normal		IgG and IgA decreased; IgM increased or normal	Neutropenia, gastrointestinal and liver disease, opportunistic infections	AR	Mutations in *CD40*	109535	*CD40*	11919	ENSG00000101017
C	**AID deficiency**[V] **Hyper IgM syndrome type 2**	Normal		IgG and IgA decreased; IgM increased	Enlarged lymph nodes and germinal centers	AR or AD	Mutation in *AICDA.* Defect BER	605257	*AICDA*	13203	ENSG00000111732
D	**UNG deficiency**[V] **Hyper IgM syndrome type 5**	Normal		IgG and IgA decreased; IgM increased	Enlarged lymph nodes and germinal centers	AR	Mutation in *UNG.* Defect BER	191525	*UNG*	12572	ENSG00000076248
4.	**Isotype or light chain deficiencies with normal numbers of B cells**										
A	**Ig heavy chain deletions**	Normal		IgG1, IgG2, or IgG4 absent; IgA1 and IgE can be absent	May be asymptomatic	AR	Chromosomal deletion at 14q32				
B	**κ Chain deficiency**	Normal		All immunoglobulins have lambda light chain	Asymptomatic or recurrent viral-bacterial infections	AR	Mutation in Kappa constant gene	147200	*IGKC*	5716	ENSG00000211592
C	**Isolated IgG subclass deficiency**	Normal		Reduction in one or more IgG subclass	Recurrent bacterial infections	Variable	Unknown				

D	**IgA with IgG subclass deficiency**	Normal		Reduced IgA, decrease in one or more IgG subclass;	Asymptomatic or recurrent infections with or without poor antibody response to carbohydrate antigens, allergies or autoimmune disease	Variable	Unknown				
E	**Selective IgA deficiency**	Normal		IgA decreased	Some cases progress to CVID, others coexist with CVID in the same family	Variable	Mutation in TACI or MSH5 in few cases	606269 603382	*TNFRSF13B*	18153,	ENSG00000240505
5.	**Specific antibody deficiency with normal Ig concentrations and numbers of B cells**	Normal		Normal	Inability to make antibodies to specific antigens	Variable	Unknown				
6.	Transient hypogammaglobulinemia of infancy	Normal		IgG and IgA decreased	Recurrent moderate bacterial infections	Variable	Unknown				

L, X-linked inheritance; *AR*, autosomal recessive inheritance; *Btk*, Burton tyrosine kinase; *BLNK*, B-cell linker protein; *AD*, autosomal dominant inheritance; *TACI*, transmembrane activator and calcium-modulator and cyclophilin ligand interactor; *BAFFR*, B-cell activating factor receptor; *Msh5*, homolog of *E.coli* MutS; *ICOS*, inducible costimulator; *AID*, activation-induced cytidine deaminase; BER, Base excicion repair of DNA single strand breaks, *UNG*, uracil-DNA glycosylase; *Ig(κ)*, immunoglobulin of κ light-chain type.

[I]Common variable immunodeficiency: there are several different clinical phenotypes, probably representing distinguishable diseases with differing immunopathogeneses

[II]Alterations in *TACI*, *BAFFR* and *Msh5* sequences represent contributing polymorphism or disease-modifying alterations. A disease-causing effect has been identified for homozygous C140R, S144X, and A181E *TACI* mutations.

[III]XLP1 (X-linked lymphoproliferative syndrome) is also included in Supplemental Table V.

[IV]CD40L deficiency (X-linked hyper IgM syndrome 1) and CD40 deficiency are also included in Supplemental Table I.

[V]Deficiency of activation-induced cytidine deaminse or uracil-DNA glycosylase present as forms of the HIGM syndrome but differ from CD40 ligand and CD40 deficiencies in that the patients have large lymph nodes with germinal centers and are not susceptible to opportunistic infections.