

**Table S1.** Diseases of immune dysregulation according to IUIS classification (2022). Accessed on 8th July 2022.

Category	Disease	Genetic Defect	Clinical Characteristics
Familial Hemophagocytic Lymphohistiocytosis (FHL syndromes)	Perforin deficiency (FHL2)	<i>PRF1</i>	Fever Hepatosplenomegaly Hemophagocytic lymphohistiocytosis Cytopenias
	UNC13D/Munc13-4 deficiency (FHL3)	<i>UNC13D</i>	Fever Hepatosplenomegaly
	Syntaxin 11 deficiency (FHL4)	<i>STX11</i>	Hemophagocytic lymphohistiocytosis
	STXBP2/ Munc18-2 deficiency (FHL5)	<i>STXBP2</i>	Cytopenias
	FAAP24 deficiency	<i>FAAP24</i>	EBV-driven lymphoproliferative disease
	SLC7A7 deficiency	<i>SLC7A7</i>	Lysinuric protein intolerance Bleeding tendency Alveolar proteinosis
	RHOG deficiency	<i>RHOG</i>	Hemophagocytosis Fever Hepatosplenomegaly Cytopenias Low haemoglobin Hypertriglyceridemia Elevated ferritin sCD25
FHL syndromes with hypopigmentation	Chediak-Higashi syndrome	<i>LYST</i>	Fever Hepatosplenomegaly Hemophagocytic lymphohistiocytosis Partial albinism Recurrent infections Progressive neurological dysfunction Cytopenias Neutropenia Bleeding tendency Giant lysosomes
	Griscelli syndrome type 2	<i>RAB27A</i>	Fever Hepatosplenomegaly Hemophagocytic lymphohistiocytosis Partial albinism Cytopenias
	Hermansky-Pudlak syndrome type 2	<i>AP3B1</i>	Hemophagocytic lymphohistiocytosis Partial albinism Recurrent infections Pulmonary fibrosis Neutropenia Bleeding tendency
	Hermansky-Pudlak syndrome type 10	<i>AP3D1</i>	Recurrent infections Oculocutaneous albinism Seizures Hearing loss Neurodevelopmental delay Neutropenia
	CEBPE neofunction	<i>CEBPE</i>	Recurrent abdominal pain Aseptic fever Systemic inflammation Abscesses Ulceration Infections Mild bleeding diathesis
Regulatory T cells defects	IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy X-linked)	<i>FOXP3</i>	Autoimmune enteropathy Early onset diabetes Thyroiditis Eczema Hemolytic anemia

			Thrombocytopenia ↑IgE, IgA Lack of CD4+CD25+FOXP3+ regulatory T cells (Tregs)
	CD25 deficiency	<i>IL2RA</i>	Lymphoproliferation Autoimmunity Impaired T cell proliferation in vitro
	CD122 deficiency	<i>IL2RB</i>	Recurrent viral infections Lymphoproliferation Hepatosplenomegaly Lymphadenopathy Enteropathy Dermatitis Autoimmune hemolytic anemia Hypergammaglobulinemia
	CTLA4 haploinsufficiency (ALPS-V)	<i>CTLA4</i>	Recurrent infections Enteropathy Interstitial lung disease Autoimmune cytopenias Extra-lymphoid lymphocytic infiltration
	LRBA deficiency	<i>LRBA</i>	Recurrent infections Autoimmunity Inflammatory bowel disease
	DEF6 deficiency	<i>DEF6</i>	Recurrent infections Enteropathy Cardiomyopathy Hepatosplenomegaly
	STAT3 GOF	<i>STAT3</i>	Recurrent infections Lymphoproliferation Solid organ autoimmunity
	BACH2 deficiency	<i>BACH2</i>	Sinopulmonary infections Lymphocytic colitis
	FERMT1 deficiency	<i>FERMT1</i>	Dermatosis Photosensitivity Skin atrophy Skin fragility Scaling
	IKAROS GOF	<i>IKZF1</i>	Recurrent infections Multiple autoimmune features: diabetes, colitis, thyroiditis Allergy Lymphoproliferation Plasma cell expansion Evans syndrome
	APECED (APS-1; autoimmune polyendocrinopathy with candidiasis and ectodermal dystrophy)	<i>AIRE</i>	Autoimmune diseases: hypoparathyroidism, hypothyroidism, adrenal insufficiency, diabetes, gonadal dysfunction and other Alopecia areata Enteropathy Dental enamel hypoplasia Pernicious anemia Chronic mucocutaneous candidiasis
	ITCH deficiency	<i>ITCH</i>	Autoimmunity (thyroiditis, diabetes type I, hepatitis, enteropathy) Early-onset chronic lung disease Failure to thrive Developmental delay Dysmorphic facial features
	Tripeptidyl-Peptidase II deficiency	<i>TPP2</i>	Recurrent infections Lymphoproliferation Severe autoimmune cytopenias Hypergammaglobulinemia
Autoimmunity with or without lymphoproliferation	JAK1 GOF	<i>JAK1</i>	Hepatosplenomegaly Viral infections Poor growth Thyroid disease Eosinophilic enteritis
	Prolidase deficiency	<i>PEPD</i>	Infections

Immune dysregulation with colitis			Eczema Chronic skin ulcers Autoantibodies
	SOCS1 haploinsufficiency	<i>SOCS1</i>	Recurrent bacterial infections Early onset severe multisystemic autoimmunity Arthritis, thyroiditis, hepatitis, psoriasis Hepatosplenomegaly Systemic lupus erythematosus Glomerulonephritis Cytopenias
	PD-1 deficiency	<i>PDCD1</i>	Hepatosplenomegaly Autoimmunity (type 1 diabetes, hypothyroidism, juvenile idiopathic arthritis) Fatal pulmonary autoimmunity Tuberculosis
	IL-10 deficiency	<i>IL10</i>	Recurrent respiratory diseases Folliculitis Arthritis Inflammatory bowel disease
	IL-10R deficiency	<i>IL10RA/ IL10RB</i>	Recurrent respiratory diseases Folliculitis Arthritis Inflammatory bowel disease Lymphoma
	NFAT5 haploinsufficiency	<i>NFAT5</i>	Inflammatory bowel disease Recurrent sinopulmonary infections
	TGFB1 deficiency	<i>TGFB1</i>	Inflammatory bowel disease Recurrent viral infections Microcephaly Encephalopathy
	RIPK1	<i>RIPK1</i>	Early onset inflammatory bowel disease Recurrent infections Progressive polyarthritis
	ELF4 deficiency	<i>ELF4</i>	Early onset inflammatory bowel disease/mucosal autoinflammation Fevers Ulcers
	ALPS-FAS	<i>TNFRSF6</i>	Splenomegaly Adenopathies Autoimmune cytopenias ↑ lymphoma risk ↑ serum FasL N/↑ IgG, IgA
Autoimmune Lymphoproliferative Syndrome (ALPS)	ALPS-FASLG	<i>TNFSF6</i>	Splenomegaly Adenopathies Autoimmune cytopenias SLE Soluble FasL is not elevated
	ALPS- Caspase 10	<i>CASP10</i>	Splenomegaly Adenopathies Autoimmunity
	ALPS- Caspase 8	<i>CASP8</i>	Splenomegaly Adenopathies Viral and bacterial infections Hypogammaglobulinemia
	FADD deficiency	<i>FADD</i>	Viral and bacterial infections Functional hyposplenism Recurrent episodes of encephalopathy and liver dysfunction
	SAP deficiency (XLP1)	<i>SH2D1A</i>	Clinical and immunologic features triggered by EBV infection: Hemophagocytic lymphohistiocytosis Lymphoproliferation Aplastic anemia Lymphoma Hypogammaglobulinemia
Susceptibility to EBV and lymphoproliferative conditions	XIAP deficiency (XLP2)	<i>XIAP</i>	EBV infection Lymphoproliferation

		Splenomegaly Hemophagocytic lymphohistiocytosis Colitis Inflammatory bowel disease Hepatitis
CD27 deficiency	<i>CD27</i>	Features triggered by EBV infection: Hemophagocytic lymphohistiocytosis Aplastic anemia B-Lymphoma
CD70 deficiency	<i>CD70</i>	EBV susceptibility Hodgkin lymphoma Autoimmunity
CTPS1 deficiency	<i>CTPS1</i>	Recurrent/chronic bacterial or viral infections EBV lymphoproliferation B-cell non-Hodgkin lymphoma
CD137 deficiency	<i>TNFRSF9</i>	EBV lymphoproliferation Chronic active EBV infection B-cell lymphoma ↓IgG, IgA
RASGRP1	<i>RASGRP1</i>	Recurrent pneumonia Herpesvirus infections EBV associated lymphoma ↓NK function
RLTPR deficiency	<i>CARMIL2</i>	Recurrent bacterial, fungal and mycobacterial infections Viral warts Malignancy Atopy
X-linked magnesium EBV and neoplasia (XMEN)	<i>MAGT1</i>	EBV infection Viral infection Respiratory and gastrointestinal infections Lymphoma Glycosylation defects
PRKCD deficiency	<i>PRKCD</i>	EBV chronic infection Recurrent infections Lymphoproliferation SLE-like autoimmunity Low IgG
TET2 deficiency	<i>TET2</i>	ALPS-like, recurrent viral infections EBV viremia Lymphadenopathy Hepatosplenomegaly Autoimmunity B-cell lymphoma Developmental delay