ORIGINAL RESEARCH

The 2015 IUIS Phenotypic Classification for Primary Immunodeficiencies

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Abstract There are now nearly 300 single-gene inborn errors of immunity underlying phenotypes as diverse as infection, malignancy, allergy, auto-immunity, and auto-inflammation. For each of these five categories, a growing variety of phenotypes are ascribed to Primary Immunodeficiency Diseases (PID), making PIDs a rapidly expanding field of medicine. The International Union of Immunological Societies (IUIS) PID expert committee (EC) has published every
other year a classification of these disorders into tables, defined by shared pathogenesis and/or clinical consequences. In 2013, the IUIS committee also proposed a more user-friendly, phenotypic classification, based on the selection of key phenotypes at the bedside. We herein propose the revised figures, based on the accompanying 2015 IUIS PID EC classification.

**Keywords**  Primary immunodeficiencies · classification · IUIS PID expert committee

**Abbreviations**

αFP A fetoprotein
Ab Antibody
AD Autosomal dominant inheritance
ADA Adenosine deaminase
Adp Adenopathy
ALPS Autoimmune lymphoproliferative syndrome
AML Acute myeloid leukemia
Anti PPS Anti- pneumococcus antibody
AR Autosomal recessive inheritance
BCG Bacilli Calmette-Guerin
BL B lymphocyte
CANDLES CARD14 mediated psoriasis
CANDLE Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature syndrome
CAPS Cryopyrin-associated periodic syndromes
CBC Complete blood count
CD Cluster of differentiation
CDG-IIb Congenital disorder of glycosylation, type IIb
CGD Chronic granulomatous disease
CID Combined immunodeficiency
CINCA Chronic infantile neurologic cutaneous and articular syndrome
CMC Chronic mucocutaneous candidiasis
CMF Flow cytometry available
CMV Cytomegalovirus
CMML Chronic myelomonocytic leukemia
CNS Central nervous system
CSF Cerebrospinal fluid
CT Computed tomography
CTL Cytotoxic T-lymphocyte
DA Duration of attacks
Def Deficiency
DHR DiHydroRhodamine
Dip Diphtheria
DITRA Deficiency of interleukin 36 receptor antagonist
EBV Epstein-Barr virus
EDA Anhidrotic ectodermal dysplasia
EDA-ID Anhidrotic ectodermal dysplasia with immuno deficiency
EO Eosinophils
FA Frequency of attacks
FCAS Familial cold autoinflammatory syndrome
FILS Facial dysmorphism, immuno deficiency, livedo, and short stature
FISH Fluorescence in situ hybridization
GI Gastrointestinal
GOF Gain-of-function
HHV8 Human herpes virus type 8
Hib Haemophilus influenzae serotype b
HIDS Hyper IgD syndrome
HIPEG Hyper IgE syndrome
HIGM Hyper Ig M syndrome
HLA Human leukocyte antigen
HLH Hemophagocytic lymphohistiocytosis
HPV Human papilloma virus
HSM Hepatosplenomegaly
HSV Herpes simplex virus
HUS Hemolytic uremic syndrome
Hx Medical history
IBD Inflammatory bowel disease
IFNG Interferon gamma
Ig Immunoglobulin
IL Interleukin
IUGR Intrauterine growth retard
LAD Leukocyte adhesion deficiency
LOF Loss-of-function
MC Molluscum contagiosum
MKD Mevalonate kinase deficiency
MSMD Mendelian susceptibility to mycobacterial disease
MWS Muckle-wells syndrome
N Normal, not low
NK Natural killer
NKT Natural killer T cell
NN Neonatal
NP Neutropenia
PAPA Pyogenic sterile arthritis, pyoderma gangrenosum, acne syndrome
PMN Neutrophils
SCID Severe combined immuno deficiency
Sd Syndrome
SLE Systemic lupus erythematosus
SPM Splenomegaly
Staph Staphylococcus sp.
Introduction

Human Primary Immunodeficiency Diseases (PID) comprise at least 300 genetically-defined single-gene inborn errors of immunity [1]. Long considered as rare diseases, recent studies tend to show that they are more common than generally thought, if only by their rapidly increasing number [2]. They may be even more common, if we consider the emerging monogenic determinants leading to common infectious diseases, such as severe influenza [3]; autoimmune diseases, such as systemic lupus erythematosus [4], and auto-inflammatory diseases, such as Crohn’s disease [5]. The International Union of Immunological Societies (IUIS) PID expert committee has

### I. Immunodeficiencies affecting cellular and humoral immunity

**Lymphopenia (by CBC) or T cell lymphopenia (by lymphocyte immunophenotyping)**?

| Yes = SCID | No = CID |
|------------|----------|
| CD19 ↓ : SCID T-B- | CD19 N : SCID T- B+ |

**Distinctive clinical features?**

- **Yes**
  - **CD4 low**
  - **CD8 low**
  - **HLA-DR very low**
  - **MHC-II def**
  - **EBV**

- **No**
  - **CD8 very low**
  - **CD8 low**
  - **HLA-DR N**
  - **MHC-II def**

**Others**

- **TCR low**
- **CD3 def (CD3δ)**
- **DOCK2 def (DOCK2)**
- **P. jiroveci pneumonia, bacterial infections CARD11 def (CARD11)**
- **Bacterial, viral and Cryptosporidium infections. Low NK and Ig levels, NIK def (MAP3K14)**
- **Recurrent bacterial, viral and fungal infections; clinical phenotype of SCID KIR3DL1 def (KIR3DL1)**

**HPV Human papilloma virus, IBD Inflammatory bowel disease, Ig Immunoglobulin, MC Molluscum contagiosum, N Normal, not low, NK Natural Killer, NN Neonatal, NP Neutropenia, SCID Severe Combined Immunodeficiency, Staph Staphylococcus sp., TCR T-Cell Receptor, XL X-Linked**

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Fig. 1 Immunodeficiencies affecting cellular and humoral immunity. *ADA* Adenosine Deaminase, *Adp* adenopathy, *AR* Autosomal Recessive inheritance, *CBC* Complete Blood Count, *CD* Cluster of Differentiation, *CID* Combined Immunodeficiency, *EBV* Epstein-Barr Virus, *EO* Eosinophilia, *HHV8* Human Herpes virus type 8, *HIGM* Hyper IgM syndrome, *HLA* Human Leukocyte Antigen, *HSM* Hepatosplenomegaly, *HPV* Human papilloma virus, *IBD* Inflammatory bowel disease, *Ig* Immunoglobulin, *MC* Molluscum contagiosum, *N* Normal, not low, *NK* Natural Killer, *NN* Neonatal, *NP* Neutropenia, *SCID* Severe Combined Immunodeficiency, *Staph* Staphylococcus sp., *TCR* T-Cell Receptor, *XL* X-Linked
Fig. 2 CID with associated or syndromic features. These syndromes are generally associated with T-cell immunodeficiency. αFP alpha-fetoprotein, AD Autosomal Dominant inheritance, AR Autosomal Recessive inheritance, CMF Flow cytometry available, EDA Anhidrotic ectodermal dysplasia, EDA-ID Anhidrotic Ectodermal Dysplasia with Immunodeficiency, FILS Facial dysmorphism, immunodeficiency, livedo, and short stature, FISH Fluorescence in situ Hybridization, HSM Hepatosplenomegaly, HSV Herpes simplex virus, Ig Immunoglobulin, VZV Varicella Zoster virus, WAS Wiskott-Aldrich syndrome, XL X-Linked inheritance.

![Table and Diagram](image-url)
III. Predominantly antibody deficiencies

Recurrent bacterial infections eg: Otitis, pneumonia, sinusitis, diarrhea, sepsis

Serum Immunoglobulin Assays: IgG, IgA, IgM

| IgG, IgA and/or IgM with \(|\) |
|---|
| Exclude 2nd causes: drugs [Hx], myeloma [bone marrow], Lymphoma. Ig loss (not hypogammaglobulinemia in urine, GI or skin) |

**B Lymphocyte (CD19+) enumeration (CMF)**

- B absent
- B > 1%

**X-Linked Agammaglobulinaemia (XLA)**
- AR Agammaglobulinaemias
  - AR heavy chain Def (IGHM)
  - IgA (CD79B)
  - BlNK (BLNK)
  - I5 (IGL1, PI3K91 def (PIK3R1))

**AD E47 transcription factor def (TCF3)**

**Congenital sideroblastic anemia, cleavage, developmental delay: TRNT1 def (TRNT1)**

**Trichothiodystrophy TCTC3 def (TTC37)**

**Dysmorphic facial features, hypotonia, neurologic disorder, severe hypogammaglobulinemia, CDG-IId (MOG5)**

**Common Variable Immunodeficiency Disorders (CVI)**
- Very rare AR disorders: TACI, BAF15, CD40, CD8, CD21, TWEAK, NFkB2

**Thymoma with Immunodeficiency**
- Bacterial opportunistic infections, autoimmunity

**Myeloproliferative with hypogammaglobulinemia**
- Monoallelic 7, triallelic 8 or DKO, GATA2

**Growth retardation EBV, CMV viremia. PIK3R1 loss-of-function (PIK3R1)**

**Congenital B cell lymphocytopenia**

- AD, SPM, Adp.
- Bacterial and viral infections, EBV chronic infection, Autoimmune cytopenia

**CARD11 gain of function mutations (CARD11)**

**IgG2 Low + impaired response to PPS and hib:**
- Bronchiectasis, autoimmunity, chronic EBV, CMV infection
- Activated PI3K-δ (PIK3CD, p110)

**IgG subclasses +/- IgA, absent IgE, asymptomatic:**
- Ig heavy chain mutations or deletion (mutation or chromosomal deletion 14q32)

**All have lambda chain, asymptomatic K chain def (IGKC)**

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**Fig. 3** Predominantly Antibody deficiencies. **Ab** Antibody, **Adp** adenopathy, **Anti PPS** Anti-pneumococcus Antibody, **AR** Autosomal Recessive inheritance, **CD** Cluster of Differentiation, **CDG-IId** Congenital disorder of glycosylation, type IId, **CMV** Cytomegalovirus, **CT** Computed Tomography, **EBV** Epstein-Barr Virus, **Dip** Diphtheria, **GI** Gastrointestinal, **Hib** Haemophilus influenzae serotype b, **Hx** medical history, **Ig** Immunoglobulin, **SPM** Splenomegaly, **subcl** subclass, **Tet** Tetanus, **XL** X-Linked inheritance
### IV. Diseases of immune dysregulation

| Hemophagocytic Lymphohistiocytosis (HLH) | Syndromes with Autoimmunity | Immune dysregulation with colitis | Type 1 Interferonopathies |
|------------------------------------------|-----------------------------|---------------------------------|--------------------------|
| **Hypogammaglobulinemia**                | **X-linked agamaglobulinemia** | **Inflammatory bowel disease**   | **+** Sinusitis, mouth ulcers, arthropathy |
| Specific hair shaft anomaly              | **HLH**                     | **Infantile hypogammaglobulinemia** | **SAMD1** |
| Neutropenia                              | **FHL2**                    | **SAA**                          | **AGS5 (SAMD1)** |
| Increased bleeding                       | **FHL1**                    |                                 |                          |
| Low degranulation (T, NK)                | **FHL3**                    |                                 |                          |
| **Heremansky-Pudlo syndrome**            | Primary neurological disease |                                 |                          |
| Giant lymphocytes in Leukocytes on blood smear | **HLH** |                                 |                          |
| Specific hair shaft anomaly              | **HLH**                     |                                 |                          |
| Low degranulation (T, NK)                | **HLH**                     |                                 |                          |
| **CD 151 deficiency**                    | **MUC13-4 deficiency**      |                                 |                          |
| **CD 16**                                | **FHL3**                    |                                 |                          |
| **Inflammatory bowel disease**           | **MUC18-2 deficiency**      |                                 |                          |
| **HLH**                                  | **FHL5**                    |                                 |                          |
| **Immunodeficiency, impaired T-cell function** | **CD8 deficiency** |                                 |                          |
| **Heremansky-Pudlo syndrome**            | **FHL5**                    |                                 |                          |
| **HLH**                                  | **FHL4**                    |                                 |                          |
| **Synaptotagmin 11 deficiency**          | **CD8 deficiency**          |                                 |                          |
| **HLH**                                  | **HLH**                     |                                 |                          |
| **CD 151 deficiency**                    | **FHL5**                    |                                 |                          |
| **Immunodeficiency, impaired T-cell function** | **CD8 deficiency** |                                 |                          |
| **Heremansky-Pudlo syndrome**            | **FHL5**                    |                                 |                          |
| **HLH**                                  | **FHL4**                    |                                 |                          |

#### Fig. 4 Diseases of Immune Dysregulation

- **AD** Autosomal Dominant inheritance, **ALS** Autoimmune lymphoproliferative syndrome, **AR** Autosomal Recessive inheritance, **CD** Cluster of Differentiation, **CMF** Flow cytometry available, **CSF** Cerebrospinal fluid, **CTL** Cytotoxic T-Lymphocyte, **EBV** Epstein-Barr Virus, **GOF** Gain-of-function, **HLH** Hemophagocytic lymphohistiocytosis, **HSM** Hepatosplenomegaly, **IBD** Inflammatory bowel disease, **IFN** Interferon gamma, **Ig** Immunoglobulin, **IL** interleukin, **Inflamm** Inflammation, **NK** Natural Killer, **NKT** Natural Killer T cell, **T** T lymphocyte, **XL** X-Linked inheritance

### Key Terms
- **AD** Autosomal Dominant inheritance
- **AR** Autosomal Recessive inheritance
- **CD** Cluster of Differentiation
- **CMF** Flow cytometry available
- **CSF** Cerebrospinal fluid
- **CTL** Cytotoxic T-Lymphocyte
- **EBV** Epstein-Barr Virus
- **GOF** Gain-of-function
- **HLH** Hemophagocytic lymphohistiocytosis
- **HSM** Hepatosplenomegaly
- **IBD** Inflammatory bowel disease
- **IFN** Interferon gamma
- **Ig** Immunoglobulin
- **IL** interleukin
- **Inflamm** Inflammation
- **NK** Natural Killer
- **NKT** Natural Killer T cell
- **T** T lymphocyte
- **XL** X-Linked inheritance

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V. Congenital defects of phagocyte number, function, or both

| Syndromic                                                                                 | Neutropenia ? | Abnormal |
|-------------------------------------------------------------------------------------------|---------------|----------|
| Yes (without anti-PMN)                                                                     |               |          |
| No syndromic                                                                              |               |          |
| Yes : Cyclic neutropenia (ELANE)                                                           |               |          |
| Yes : Cyclic neutropenia (SN)                                                              |               |          |
| XBC (or XCGD)                                                                              |               |          |
| Structural heart defects, urogenital abnormalities, and venous angiectasias of trunks and limbs |               |          |
| Extramedullary hematopoiesis, bone marrow fibrosis, nephroangiosis: SCNS, VPS45            |               |          |
| Fasting hypoglycemia, lactic acidosis, hyperlipidemia, Hepatomegaly: Glycogen storage disease type 1b (GSPT1) |               |          |
| Retinopathy, developmental delay, facial dysmorphism : Cohen syndrome (VPS32A)             |               |          |
| Cardio-myopathy, growth retardation, XL-Barth syndrome (TAA)                              |               |          |
| Polikidderma, myeloiddysplasia : Polikidderma with neutropenia (C16orf57)                 |               |          |
| Failure to thrive, partial Albinism, Hypogammaglobulinemia : P14/LAMTOR2 def (ROBLOD/LAMTOR2) |               |          |
| Microcephaly, hypoglycemia, hypotonia, ataxia, seizures, cataracts, IUGR, 3-methylglutaconic aciduria, type VII (CLBP) |               |          |
| Symptomatic                                                                                |               |          |
| Asymptomatic                                                                               |               |          |
| J CBC Twice Weekly x4 Cyclic variations                                                   |               |          |
| Transient NP of infancy                                                                    |               |          |
| Virus induced NP                                                                          |               |          |
| Periodontitis, palmoplantar Hyperkeratosis, Papillon-Lefevre (CTSC)                        |               |          |
| Poor wound Healing Leukocytosis, DHR assay negative to FMLP stimulation, Rac 2 def (RAC2) |               |          |
| Bilobed nuclei, Specific granule deficiency (GCS/EPBD)                                     |               |          |
| Alveolar macrophages, Pulmonary alveolar proteinosis (CSF2RA)                              |               |          |
| Periodontitis only Localized juvenile periodontitis (FPR1)                                |               |          |
| Failure to thrive, mental retardation: β-Actin (ACTB)                                     |               |          |

CD Cluster of Differentiation, CGD Chronic Granulomatous Disease, CML Chronic Myelogenous Leukemia, DHR DiHydroRhodamine, IUGR Intrauterine growth retard, LAD Leukocyte Adhesion Deficiency, NP Neutropenia, PNN Neutrophils, SCN Severe congenital neutropenia, WBC White Blood Cells, XL X-Linked inheritance
### VI. Defects in Intrinsec and Innate Immunity

| Predominant Susceptibility to invasive infections with pyogenic bacteria |
| Bacteremia (encapsulated bacteria) | Predominant susceptibility to viral infection |
| No spleen | Herpes simplex Encephalitis |
| Isolated congenital aplasia (RPSA) | Dominant clinical phenotype is herpes simplex encephalitis (HSE) during primary infection with herpes simplex virus type 1 (HSV1), usually between 3 months and 6 years of age. Routine screening tests are normal. Specific tests examining the TRIM pathway marked decrease in the ability of patient's fibroblasts to produce IFN-B/α in response to HSV1 infection. |
| IRAK4 del (IRA4) | MyD88 del (MYD88) |

| Parasitic infections and fungal diseases |
| Trypanosomiasis |
| AD: APOB1 |
| Warts, Hypogammaglobulinemia, infections, Myelokathexis |
| CMC Chronic mucocutaneous candidiasis |
| AD: STAT1 (gain of function) IL17F |
| AR: IL17RA IL17RC |
| Viral infections |
| STAT1 del |
| STAT2 deficiency |
| Severe viral infections |
| CD16 del |
| Severe influenza |
| disease IRF7 del |
| Blepharitis, Folliculitis and macroglia |
| ACT1 del (ACT1) |

| Susceptibility to Mycobacteria |
| MSMD Mendelian Susceptibility to Mycobacterial Disease |
| AD IFNGR1 (mycobacterial osteomyelitis) |
| Complete AR IFNAR1 and AR IFNAR2 (Serious disseminated BCG and environmental mycobacteria infections (soft tissue, bone marrow, lungs, skin, bone and lymph nodes), Salmonella spp., Listeria monocytogenes and viruses |
| Partial STAT1 LOF (AD), Partial IFNAR1, partial IL-12Rβ1, complete IL-12Rβ1, complete IL-12B, complete ISG15, XL CYBB, IRF8, Tyk2, XL NEMO usually less severe |

Fig. 6 Defects in Intrinsec and Innate Immunity. AD Autosomal Dominant inheritance, AR Autosomal Recessive inheritance, BCG Bacilli Calmette-Guérin, BL B lymphocyte, CMC Chronic mucocutaneous candidiasis, HSV Herpes simplex virus, IFN-γ Interferon gamma, Ig Immunoglobulin, IL interleukin, LOF Loss-of-function, MSMD Mendelian Susceptibility to Mycobacterial Disease, PMN Neutrophils, XL X-Linked inheritance
### VII. Auto-inflammatory disorders

| Recurrent inflammation | Systemic inflammation with urticaria rash | Sterile inflammation (skin / bone / joints) | Others |
|------------------------|------------------------------------------|-------------------------------------------|--------|
| **Autoinflammatory Disorders** | **Autoinflammatory Disorders** | **Autoinflammatory Disorders** | **Autoinflammatory Disorders** |
| **AD** | **AD** | **AD** | **AD** |
| **DA** | **DA** | **DA** | **DA** |
| **FA** | **FA** | **FA** | **FA** |
| **Frequency of Attacks** | **Duration of Attacks** | **Frequency of Attacks** | **Frequency of Attacks** |
| **Characteristics** | **Characteristics** | **Characteristics** | **Characteristics** |
| **Genetics** | **Genetics** | **Genetics** | **Genetics** |
| **Clinical Manifestations** | **Clinical Manifestations** | **Clinical Manifestations** | **Clinical Manifestations** |
| **Diagnostic Tests** | **Diagnostic Tests** | **Diagnostic Tests** | **Diagnostic Tests** |

**Fig. 7** Autoinflammatory Disorders. *AD* Autosomal Dominant inheritance, *AR* Autosomal Recessive inheritance, *CAMPS* CARD14 mediated psoriasis, *CANDLE* Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature syndrome, *CAPS* Cryopyrin-Associated Periodic syndromes, *CINCA* Chronic Infantile Neurologic Cutaneous and Articular syndrome, *DA* Duration of Attacks, *DIRA* deficiency of interleukin 36 Receptor antagonist, *FA* Frequency of Attacks, *HIDS* Hyper IgD syndrome, *Ig* Immunoglobulin, *IL* interleukin, *MKD* Mevalonate Kinase deficiency, *MWS* Muckle-Wells syndrome, *NOMID* Neonatal Onset Multisystem Inflammatory Disease, *PA* Pyogenic sterile Arthritis, Pyoderma gangrenosum, Acne syndrome, *SPM* Splenomegaly, *TNF* Tumor Necrosis Factor, *TRAPS* TNF Receptor-Associated Periodic Syndrome
Fig. 8  Complement deficiencies.  *AD*  Autosomal Dominant inheritance,  *GOF*  Gain-of-function,  *LOF*  Loss-of-function,  *LAD*  Leukocyte Adhesion Deficiency,  *SLE*  Systemic Lupus Erythematosus
Fig. 9 Phenocopies of primary immunodeficiencies. *Ab* Antibody, ALPS Autoimmune lymphoproliferative syndrome, CMC Chronic mucocutaneous candidiasis, CID Combined Immunodeficiency, HUS Hemolytic uremic syndrome, IFNγ Interferon gamma, IL Interleukin, MSMD Mendelian Susceptibility to Mycobacteria Disease, VZV Varicella Zoster virus

### IX. Phenocopies of PID

| Associated with Somatic Mutations                                                                 | Associated with Auto-Antibodies                             |
|-------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| Sporadic;                                                                                        | CMC AutoAb to IL-17 and/or IL-22                           |
| Defective lymphocyte apoptosis after IL-2 withdrawal                                             | Mycobacterial, fungal, salmonella                            |
| ALPS-SFAS (somatic mutations in TNFRSF6)                                                        | VZV infections / MSMD or CID                                |
| Activating N-RAS defect,                                                                           | Adult-onset immunodeficiency (AutoAb to IFN gamma)         |
| Activating K-RAS defect                                                                           | Staphylococcal infections / STAT3 deficiency                |
| (somatic mutations of NRAS or KRAS)                                                              | Recurrent skin infection (AutoAb to IL-6)                   |
| Urticaria-like rash,                                                                               | Pulmonary alveolar proteinosis / CSF2RA deficiency          |
| arthropathy, neurological symptoms                                                                | Pulmonary alveolar proteinosis (AutoAb to GM-CSF)           |
| Cryopyrinopathy (somatic mutations of NLRP3)                                                      | Angioedema /C1 INH deficiency                               |
|                                                                                                  | Acquired angioedema (AutoAb to C1Inhibitor)                 |
|                                                                                                  | Atypical HUS                                                 |
|                                                                                                  | aHUS (AutoAb to Factor H)                                   |
proposed a PID classification [1], which facilitates clinical research and comparative studies world-wide; it is updated every other year to include new disorders or disease-causing genes. This classification is organized in tables, each of which groups PIDs that share a given pathogenesis. As this classification may be cumbersome for use by the clinician at the bedside, the IUIS PID expert committee recently proposed a phenotypic complement to its classification [6]. As the number of PIDs is quickly increasing, and at an even faster pace since the advent of next-generation sequencing, the phenotypic classification from 2013 became outdated and requires revision at the same pace as the classical IUIS classification. Our original phenotypic classification proved successful, which placed it in the 96th percentile for citation rank in Springer journals [7]. Given the success of our user-friendly classification of PIDs, providing a tree-based decision-making process based on the observation of clinical and biological phenotypes, we present here an update of these figures, based on the accompanying 2015 PID classification.

Methodology

We included all diseases included in the 2015 update of the IUIS PID classification [1], keeping the nine major categories unchanged. In addition, we considered other articles proposing a PID classification published recently [8, 9]. An algorithm was assigned to each of the nine main groups of the classification and the same color was used for each group of similar conditions. Disease names are presented in red and genes in bold. In addition, we classed diseases or genes from most common to less common, at the best of our knowledge [10, 11]. These algorithms were first established by a small committee; then validated by one or two experts for each figure.

Results

An update of our classification, validated by the IUIS PID expert committee, is presented in Figs. 1, 2, 3, 4, 5, 6, 7, 8 and 9.

Discussion

Since our 2013 study, 70 new diseases have been included in the 2015 classification. Four disorders have been removed, as the reports concerning associated immunodeficiency or genetic base were not confirmed. We also eliminated duplication of a disease in more than one figure and profoundly revised some figures, following the 2015 IUIS classification.

Conclusion

The IUIS PID expert committee developed this phenotypic classification in order to help clinicians at the bedside to diagnose PIDs but also to promote collaboration with national and international research centers. Needless to say, the expert committee encourages the development of other types of PID classification. Indeed, given the success encountered by the two current IUIS classifications, others classifications are likely to be useful and complementary.

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