Published in final edited form as:

J Allergy Clin Immunol Pract. 2020 May ; 8(5): 1778. doi:10.1016/j.jaip.2020.02.019.

Supplementation of the ESID registry working definitions for the clinical diagnosis of inborn errors of immunity with encoded human phenotype ontology (HPO) terms

Lukas M. Gasteiger, Cand med[a], **Peter N. Robinson, MD**[b], **Julia Pazmandi, MSc**[c,d,e], **Kaan Boztug, MD**[c,d,e], **Mikko R. J. Seppänen, MD**[f,g,h], **Markus G. Seidel, MD**[a], **Registry Working Party of the European Society for Immunodeficiencies (ESID)**

[a)]Research Unit for Pediatric Hematology and Immunology, Division of Pediatric Hemato-Oncology, Department of Pediatrics and Adolescent Medicine, Medical University Graz, Graz, Austria

[b)]The Jackson Laboratory for Genomic Medicine, Farmington, Conn

[c)]Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases (LBI-RUD), Vienna,Austria

[d)]St. Anna Children's Cancer Research Institute (CCRI), Vienna, Austria

[e)]CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria

[f)]Rare Diseases Center and Pediatric Research Center, Children and Adolescents, University of Helsinki and HUS Helsinki University Hospital, Helsinki, Finland

[g)]Adult Immunodeficiency Unit, Inflammation Center, University of Helsinki and HUS Helsinki University Hospital, Helsinki, Finland

[h)]Translational Immunology, Research Programs Unit and Clinicum, University of Helsinki, Helsinki, Finland.

Current technological developments in precision medicine increasingly rely on large-scale computational integration of laboratory data with clinical information. However, disease-associated clinical and laboratory features, and anatomical and functional phenotypes are often ill-defined in medical reports, being described with varying specificity and quality, mixing lay terms with professional jargon, using different languages across the world and a disease classification that is designed for billing purposes rather than for detailed phenotype definitions. The interpretation of results obtained from next-generation panel, whole exome, or whole genome sequencing (NGS) and other omics analyses used in the differential diagnostic workup of a patient or for research purposes apply algorithm-based filtering of called variants to distinguish potentially disease-relevant from irrelevant changes.

Corresponding author: Markus G. Seidel, MD, Division of Pediatric Hematology-Oncology, Department of Pediatrics and Adolescent Medicine, Medical University, Graz, Auenbruggerplatz 38, 8036 Graz, Austria. markus.seidel@medunigraz.at; and Peter N. Robinson, MD, The Jackson Laboratory for Genomic Medicine, Farmington, CT. peter.robinson@jax.org.

MGS and the Research Unit for Pediatric Hematology and Immunology are in part financed by the Styrian Children's Cancer Aid foundation (Steirische Kinderkrebshilfe).

Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

These algorithms are, not least, based on the available clinical information. The human phenotype ontology (HPO) is widely used in the diagnostic genomics community for “deep phenotyping” to inform NGS-based diagnostics.1,2 HPO-based algorithms help to narrow down candidate genes and variants by assessing the phenotypic similarity of associated diseases with the phenotypic features of the patients being sequenced, which can increase the yield of phenotype-driven computer-assisted data interpretation.

The European Society for Immunodeficiencies (ESID) registry contains data of more than 30,000 patients with inborn errors of immunity (IEI). Together with collaborating experts, the ESID registry working group has developed working definitions for the clinical diagnosis of primary immunodeficiencies to assure correct patient classification and data quality.3 To further increase the practical value of this catalogue, we now added HPO terms derived from the Orphanet (www.orpha.net) rare disease ontology (ORDO) database that uses HPO terminology via the HOOM (HPO and ORDO Ontological Module) file platform4 (see the new version of the ESID registry working definitions for the clinical diagnosis of IEI in Online Repository at www.jaci-inpractice.org or at the ESID registry Web site5). The HPO terms are attached to every IEI of the ESID registry working definitions for the clinical diagnosis, ordered according to their frequency with reference and date. They should enable a standardized phenotypic description of each patient entered into the ESID registry. Furthermore, Orphanet identifiers were added to each IEI.

Although not available in the current form of the ESID registry’s basic dataset, it could be envisioned that in the future, each clinical criterion and each HPO term the patient fulfills at the time point of data acquisition is recorded to obtain longitudinal information of the disease course. Ultimately, the annotation of all known IEI that are included in the classification of the international union of immunological societies6 with existing or newly created HPO terms will improve the computability of phenotype data for a multiplicity of clinical domains to maximize clinical and translational interoperability.

Acknowledgments

The authors thank Dr G. Kindle and the IT team in Freiburg for continuous maintenance and improvement of the ESID registry database and web platform.

References

1. Kohler S, Carmody L, Vasilevsky N, Jacobsen JOB, Danis D, Gourdine JP, et al. Expansion of the Human Phenotype Ontology (HPO) knowledge base and resources.Nucleic Acids Res. 2019; 47: D1018–D1027 [PubMed: 30476213]
2. Robinson PN, Kohler S, Bauer S, Seelow D, Horn D, Mundlos S. The Human Phenotype Ontology: a tool for annotating and analyzing human hereditary disease. Am J Hum Genet. 2008; 83: 610–615 [PubMed: 18950739]
3. Seidel MG, Kindle G, Gathmann B, Quinti I, Buckland M, van Montfrans J, et al. The European Society for Immunodeficiencies (ESID) Registry working definitions for the clinical diagnosis of inborn errors of Immunity. J Allergy Clin Immunol Pract. 2019; 7: 1763–1770 [PubMed: 30776527]
4. Maiella S, Olry A, Hanauer M, Lanneau V, Lourghi H, Donadille B, et al. Harmonising phenomics information for a better interoperability in the rare disease field. Eur J Med Genet. 2018; 61: 706–714 [PubMed: 29425702]

5. European Society for Immunodeficiencies Registry Working Party Diagnosis criteria. (Available from:) https://esid.org/Working-Parties/Registry-Working-Party/Diagnosis-criteria (Accessed March 11, 2020)

6. Tangye SG, Al-Herz W, Bousfiha A, Chatila T, Cunningham-Rundles C, Etzioni A, et al. Human inborn errors of immunity: 2019 update on the classification from the International Union of Immunological Societies Expert Committee. J Clin Immunol. 2020; 40: 24–64 [PubMed: 31953710]