Country: Spain

Organization: Institute of Rare Diseases Research (IIER), Institute of health Carlos III (ISCIII)

Program/Project: SpainUDP is the acronym of the Spanish Undiagnosed Rare Diseases Program, which has been implemented by the Institute of Rare Disease Research, IIER, ISCIII. The Institute of Health Carlos III is the governmental organization for health research, acting also as a Funding Agency for Health Research at the National Health System and it is a full member of IRDiRC.

After a pilot phase (because IIER had identified the need for this program earlier), in 2015, SpainUDP became fully established and an agreement was signed between IIER-ISCIII and the Foundation for Biomedical Research of the University Hospital Puerta de Hierro, Madrid (HUPH) for supporting detailed clinical examination and to perform the needed complementary studies in very complex undiagnosed cases. At the same time, and after many years collaborating in different aspects (also in undiagnosed cases) a closer collaboration with the Spanish Federation of Rare Diseases patients (FEDER) was established through their help line, namely the Information and Orientation System (SIO), which provides help to rare diseases patients.

SpainUDP aims to offer a multidisciplinary approach to those patients who have long sought a diagnosis without any success. It is linked to other IIER's national programs such as: the National Biobank of Rare Diseases (BioNER), which is a founder of EuroBioBank; the Spanish National Rare Diseases Registry – SpainRDR; and the Spanish National Mutations Database (SpainMDB). IIER is also a full member of RD-CONNECT since its inception, and they are contributing with their undiagnosed cases to the platform of this project, fulfilling all the international standards for these purposes.

In a first phase of the study, cases sent to the program by FEDER, any clinician and/or by themselves or their families are required to provide all clinical information available. Also patients entering the Spanish National Rare Diseases Registry without a definite diagnosis are invited to be evaluated in SpainUDP. All documents for each patient are carefully reviewed by IIER's professionals (a multidisciplinary group of clinicians, geneticists, bioinformatics and researchers), who constitute the

Coordinating team. If the case is accepted and some documentation is lacking, it is requested. In addition, a close collaboration with local healthcare services is established.

If actions carried out during the first phase are not enough to achieve a diagnosis, the most appropriate genetic analyses are performed. On the other hand, when necessary, a plan for up to a full week of inpatient clinical testing is organized. Specific meetings to discuss how to understand the clinical phenotype of complex cases between IIER's experts and hospital experts are organized in order to program all of the complementary tests to be performed (with administration for sedation if necessary), and needed to complete the clinical diagnosis.

IIER centralizes data management by means of a new informatics, secure application based on SharePoint 2013, which has been specifically implemented to share, store and manage clinical data collected, as well as laboratory tests, images, etc.

In addition, the "Phenotips" software is used to store an accurate and standardized description of patients' phenotype (through HPO—Human Phenotype Ontology). Also, "Phenome Central" allows communicating specific case details within larger shared international networks.

Finally, the genotype-phenotype correlation is managed by using the RD-CONNECT platform.

SpainUDP aims to make appropriate diagnoses in rare diseases patients who still have not had a confirmed diagnosis, usually for a long time. At the same time, this multidisciplinary program, linked to a research institute, aims to foster the discovery of new diseases through a translational approach.

Director of IIER and SpainUDP: Manuel Posada, MD, PhD

Website of ISCIII: http://www.isciii.es