Undiagnosed Rare Diseases: a bilateral project between

Italy (Istituto Superiore di Sanità) and
USA (NIH)

Domenica Taruscio & Marco Salvatore
National Centre for Rare Diseases
Istituto Superiore di Sanità, Rome – Italy
The Undiagnosed Diseases Network International: The first meeting
First International Conference
ISS, 29-30 Sept, 2014 Rome

Board members:
G. Baynam (Australia), H. Cederroth (Sweden), W. Gahl (USA), S. Groft (USA), K. Kosaki (Japan), P. Lasko (Canada), B. Melegh (Hungary), D. Taruscio (Italy)
AIMS of UDNI:

- **Improve the level of diagnosis and care** for patients with UND through the development of common protocols designed by a large community of investigators.

- Facilitate research into the etiology of undiagnosed diseases, **by collecting and sharing standardized, high-quality clinical and laboratory data, including genotyping, phenotyping, and documentation of environmental exposures.**

- **Create an integrated and collaborative community across multiple Countries** and among laboratory and clinical investigators prepared to investigate the pathophysiology of these newly recognized and rare diseases.

- **TO SHARE:** Best practices, protocols, consents, phenotypes, genomic data, functional analyses and models, knowledge management tools.
UDNI Website (management by CNMR, Istituto Superiore di Sanità)

- UDNI Information (background, principles, practices, membership application form)
- Dissemination of UDNI activities
- UDNI Programs of participating Countries
- NEWSLETTER
Membership List, ordered alphabetically by Country name

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Turkey, Cina: starting!
UDNI Update: Membership

- In **GREEN**: Countries with at least one UDN Program
- Membership requests are increasing
Membership:
Clinical investigators serving undiagnosed disease from all countries.

*New proposal (Stockholm Conference; to be agreed on June conference)*
Clinical, Non-Clinical, Institutional, Patient Advocacy/Engagement
Past Conferences

I International Conference on Rare and Undiagnosed Diseases
29-30 September 2014, Rome

II International Conference on Rare and Undiagnosed Diseases
26-27 June 2015, Budapest

III International Conference on Rare and Undiagnosed Diseases
18 February 2016, Wien

IV International Conference on Rare and Undiagnosed Diseases
16-17 November 2016, Tokyo
Past Conference

V International Conference on Rare and Undiagnosed Diseases
30-31 August 2017, Stockholm - Sweden
V International Conference on Rare and Undiagnosed Diseases
30-31 August 2017, Stockholm - Sweden
VI International Conference, 19-21 June 2018, Naples (Italy)
Letter from the Communication Group of the UDNI

In 2008, the National Institutes of Health’s headed a successful Program on Undiagnosed Diseases to obtain diagnosis for individuals who had long sought one without success. A few years later, as a result of two international conferences held respectively in Rome (2014) and in Budapest (2015), sponsored by the Office of the NIH Director and the Wilhelm Foundation in Sweden, the International Network on Undiagnosed Diseases (UDNI) was founded and sustained thanks to the collective and powerful vision of a group of specialised experts from different countries.

Undiagnosed diseases are a global health issue, a challenging task requiring much skill and effort from the global scientific and healthcare community together with a multidisciplinary commitment and dedicated patient involvement at the national and international levels. To merge and drive ideas, approaches and lessons concerns among members, the UDNI has built a consensus framework of principles, best practices and governance; the Board of Directors reflects its international character including experts from Australia, Sweden, Canada, Hungary, Italy, Japan and the USA. Currently, the UDNI encompasses centres with internationally recognized multi-professional and outstanding expertise on rare diseases, for ensuring the scientific quality to face undiagnosed conditions. Certainly, many others clinical and research centres will be part of this wide research community in the future.

We hope the various activities of UDNI as well as the new initiatives and research studies will be realised at the highest level and will significantly contribute to the development and implementation of efficacious strategies to help persons and their families who have waited for a certain diagnosis for a long time.

Driven by motivation and enthusiasm, as indivisible parts of all our past and future activities, we want this newsletter to represent a quick and easy/informal way to update readers on many topics re undiagnosed and rare diseases and to help disseminate results of the ongoing research activities of the UDNI.
UDN Program Italy

Undiagnosed Rare Diseases: a joint Italy – USA project

Bilateral Project: Italy- USA
Short ID card

Funded by the Italian Ministry of Foreign Affairs and International Collaborations (2016-18)
Coordinated by National Center Rare Diseases, Istituto Superiore di Sanità, Italy (Dr. D. Taruscio)
6 Clinical Italian Centres: Turin, Bergamo, Udine, Ferrara, L’Aquila, Rome
USA Partner: National Human Genome Research Institute, NIH (Dr. W.A. Gahl)
Undiagnosed Rare Diseases: a joint Italy – USA project

AIMS

➢ to collect & characterize patients with undiagnosed diseases, from the Italian Network for Rare Diseases (Italian law 279/2001), sharing common standards and terminologies for URD classification;

➢ to establish a National database, interoperable at International level;

➢ to perform genetic molecular analysis in selected cases;

➢ to strengthen International collaborations

to define a diagnosis for patients
Undiagnosed Rare Diseases: a joint Italy – USA project

Pilot phase of the project:

1 Coordinating Centre: Istituto Superiore di Sanità

6 clinical participating centres

Centro Multidisciplinare di immunopatologia e documentazione su malattie rare, Torino
Prof. D. Roccatello, Dr. S. Baldovino; Dr. S. Sciascia, E. Menegatti

IRCCS - Istituto di Ricerche Farmacologiche "Mario Negri", Centro di Ricerche Cliniche per le Malattie Rare, Bergamo
Dr. E. Daina, Prof G. Remuzzi, Dr. P. Iatropoulos, Dr. E. Bresin

Lab. MR Centro Regionale di Coordinamento per le Malattie Rare A.O.U. "Santa Maria della Misericordia" di Udine, Udine
Dr. B. Bembi, Dr. R. Dariol

U.O. Logistica Genetica Medica, Dip. Scienze Mediche, Università Ferrara, Ferrara
Prof. A. Ferlini, Dr. M. Neri

Genetica Medica, Università degli Studi de L’Aquila, L’Aquila
Prof. F. Brancati

COORDINATION: National Center for Rare Diseases, Istituto Superiore di Sanità, Rome
Dr. D. Taruscio, Dr. M. Salvatore, Dr. MC de Stefano, Dr. Federica Censi, Dr. G. Floridia

UOC Genetica Medica, Policlinico Tor Vergata, Rome
Prof. G. Novelli, Prof F. Sangiuolo, F. Brancati
UDN P ITALY “Undiagnosed Rare Diseases a joint Italy – USA project”

National Network for Rare diseases (DM 279/2001)
172 Centres

Data collection in the Italian UDN database

Italian National Rare Diseases Registry

UDN Diseases Network INTERNATIONAL

UDN P ITALY

“Instituto Superiore di Sanità”

Farnesina

NIH

PHENOTIPS

“PhenoTips” is a software tool for collecting and analyzing phenotypic information for patients with genetic disorders.

UDN: Undiagnosed Diseases Network

Undiagnosed Diseases Network International

Phenotypic information for patients with genetic disorders.

UDN: Undiagnosed Diseases Network

PhenoTips: Phenotypic information software tool

UDN P ITALY

“Undiagnosed Rare Diseases a joint Italy – USA project”

Italian National Rare Diseases Registry

UDN Diseases Network INTERNATIONAL

UDN P ITALY

“Instituto Superiore di Sanità”

Farnesina

NIH

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UDN: Undiagnosed Diseases Network

Undiagnosed Diseases Network International

Phenotypic information for patients with genetic disorders.

UDN: Undiagnosed Diseases Network

PhenoTips: Phenotypic information software tool

UDN P ITALY

“Undiagnosed Rare Diseases a joint Italy – USA project”
Undiagnosed Rare Diseases: a joint Italy – USA project

✓ Methodologies and criteria for inclusion of clinic cases in the ISS database are shared with the participating centres by:

- Call Conferences
- Meetings

✓ Italian UDNP web site: description of the project, participants and expected outcomes
Inclusion criteria: NEW!

- Deep-phenotyping: Patients who remain without a clear clinical diagnosis although extensively and thoroughly investigated;
- Patient phenotypes must be expressed using Human Phenotype Ontology (HPO) terms in order to ensure comparability with other patients both within and outside of the Network;
- HPO terms should be defined and shared among participants;
- Any age: both adult and paediatric patients;
- No molecular diagnosis: no hypothesized cause-effect relationship over known genotype-phenotype correlation;
- Any inheritance: Familiar, sporadic cases, ethnic isolates
Matchmaker Exchange - project launched in October 2013

- involves a large number of teams and projects working towards a federated platform (Exchange)

- to facilitate the matching of cases with similar phenotypic and genotypic profiles (matchmaking) through standardized application programming interfaces (APIs) and procedural conventions.

CASES in the ISS database: 60 (progressively increasing)

Selected cases in ISS PhenoTips Database:
Ferrara and Bergamo will present some of the cases included into the database

1. Deep sequencing (WES/WGS of family and trios)

2. Contribution of cases to data display and matching framework of PhenomeCentral (UDNI; 10 cases)
PhenomeCentral: cases entered by UDN ISS Italy

Number of cases entered: 10

- Data types submitted (HPO terminology):
  - Patient information
  - Family history and pedigree
  - Prenatal and perinatal history
  - Medical history
  - Clinical symptoms and physical findings
  - List of genes (candidate and/or previously tested, unlikely causative)

Each of the cases is shared (fully accessible) with UDNI Work Group on PhenomeCentral
Contact us:

http://www.udninternational.org/

http://www.udnpitaly.com/