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INTERNATIONAL CONGRESS ON RESEARCH
OF RARE AND ORPHAN DISEASES

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



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Undiagnosed
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First Conference of Undiagnosed Diseases Network International
29-30 September 2014, Rome



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Requirements for Online Application

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First International Conference

ISS, 29-30 Sept, 2014 Rome

2015



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Format: Abstract

Mol Genet Metab. 2015 Dec;116(4):223-5. doi: 10.1016/j.ymgme.2015.11.003. Epub 2015 Nov 5.

Undiagnosed Diseases Network International (UDNI): White paper for global actions to meet patient needs.

Taruscio D¹, Groft SC², Cederroth H³, Melegh B⁴, Lasko P⁵, Kosaki K⁶, Baynam G⁷, McCray A⁸, Gahl WA⁹.

+ Author information



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

Australia

Austria

Belgium

Canada

France

Germany

Hungary

Israel

India

Italy

Japan

Korea

Spain

Sri Lanka

Sweden

Thailand

The Netherlands

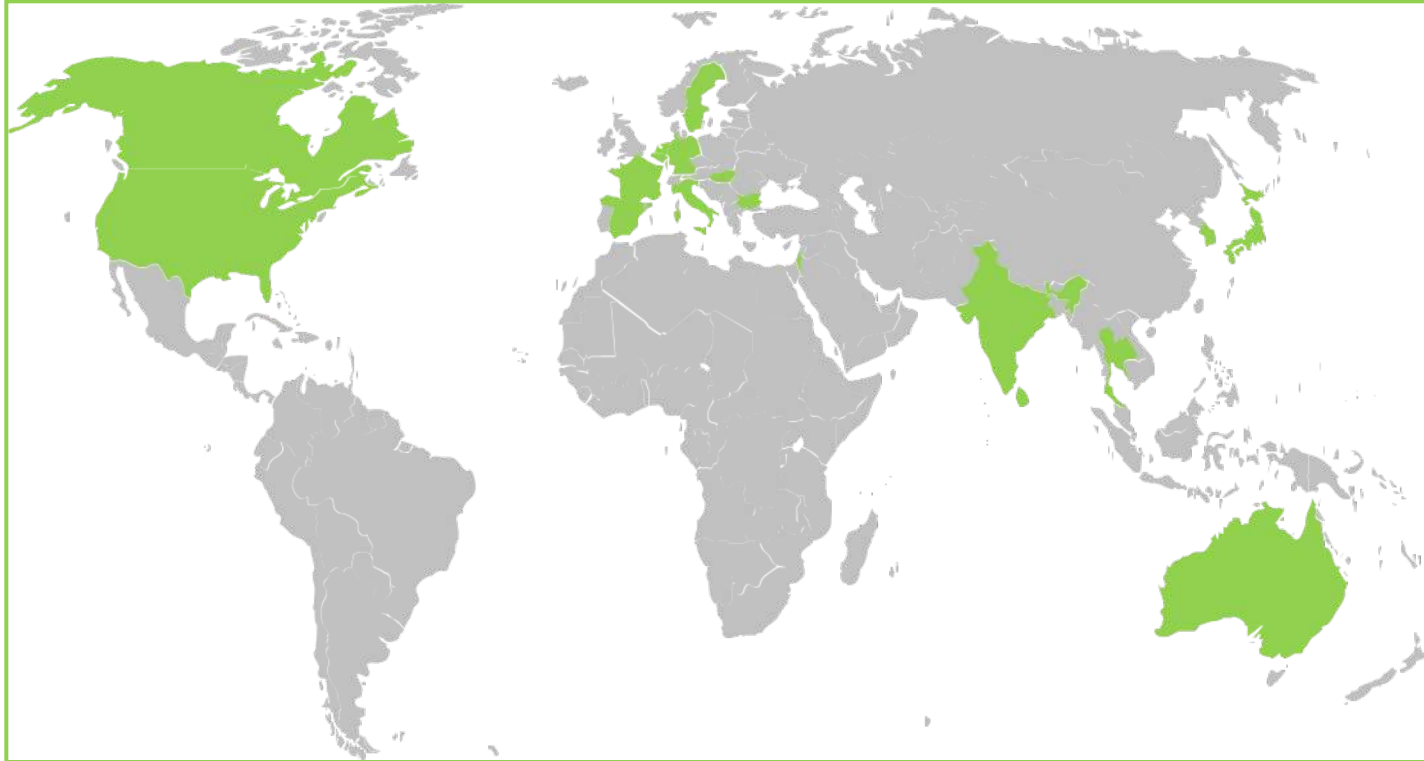
United States




Turkey, Cina: starting!



UDNI Update: Membership



- In **GREEN**: Countries with at least one UDN **Program**
- **Membership requests are increasing**



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Members

Membership

Membership will be open to clinical investigators who serve undiagnosed disease patients from all countries.

Members agree to adhere to the principles mentioned in the "General Description"

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Concise information about project objectives and participants

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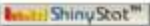
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Membership:

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

ISTITUTO SUPERIORE DI SANITÀ



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



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6th CONFERENCE OF UNDIAGNOSED DISEASES NETWORK INTERNATIONAL,
19-21 JUNE 2018, NAPLES, ITALY

Program in Progress



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UDNI Countries

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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 lessen 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.

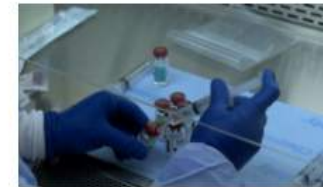
We hope the various activities of UDNI as well as the new initiatives and research studies will be realised at the highest level and will significantly contribute to the development and implementation of efficacious strategies to help persons and their families who have waited for a certain diagnosis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



UDNI: an international effort to address rare and undiagnosed diseases

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About undiagnosed diseases

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Conference "Undiagnosed Rare Diseases: a joint Italy-USA Project"

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"The Undiagnosed"

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UDNI Workshop at RE(AC)T Congress

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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. Roccato, 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

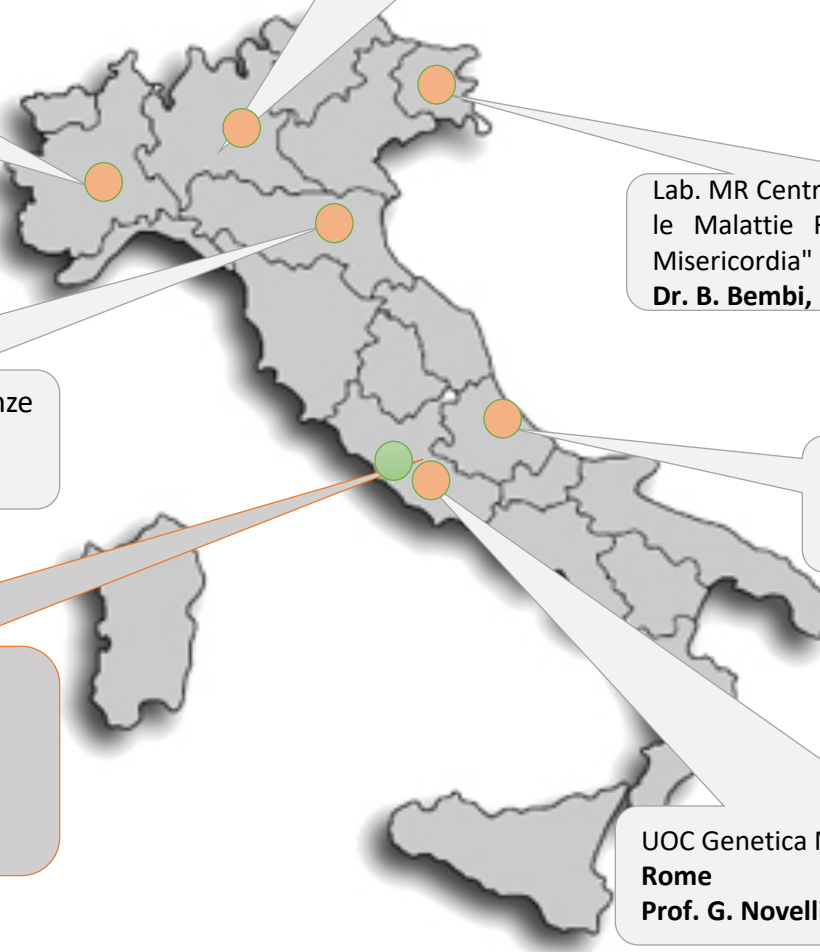
Lab. MR Centro Regionale di Coordinamento per le Malattie Rare A.O.U. "Santa Maria della Misericordia" di Udine, **Udine**
Dr. B. Bembi, Dr. R. Dariol

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)**

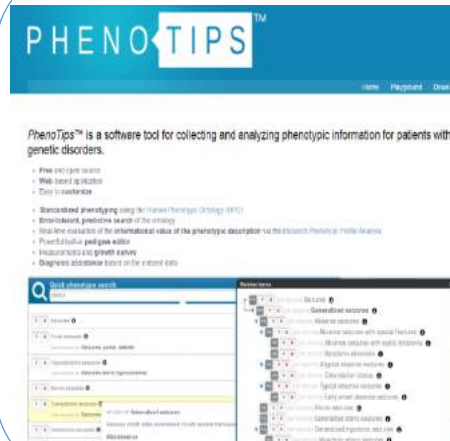
172 Centres



**Italian National
Rare Diseases
Registry**



**Data collection
in the Italian
UDN database**



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Undiagnosed
Diseases Network

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*
 - *Workshop (Rome: March 2016, Turin: January 2017; Turin: January 2018)*
- ✓ **Italian UDNP web site:** description of the project, participants and expected outcomes

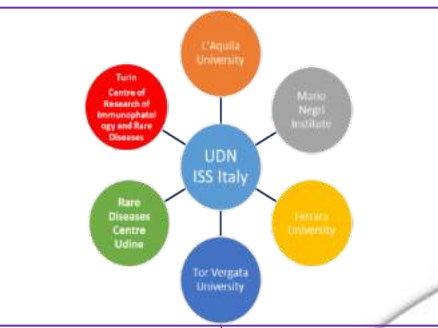


Inclusion criteria: NEW!

- 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: Connected Nodes

<http://www.matchmakerexchange.org>



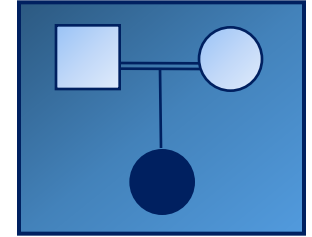
Matchmaker Exchange

-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



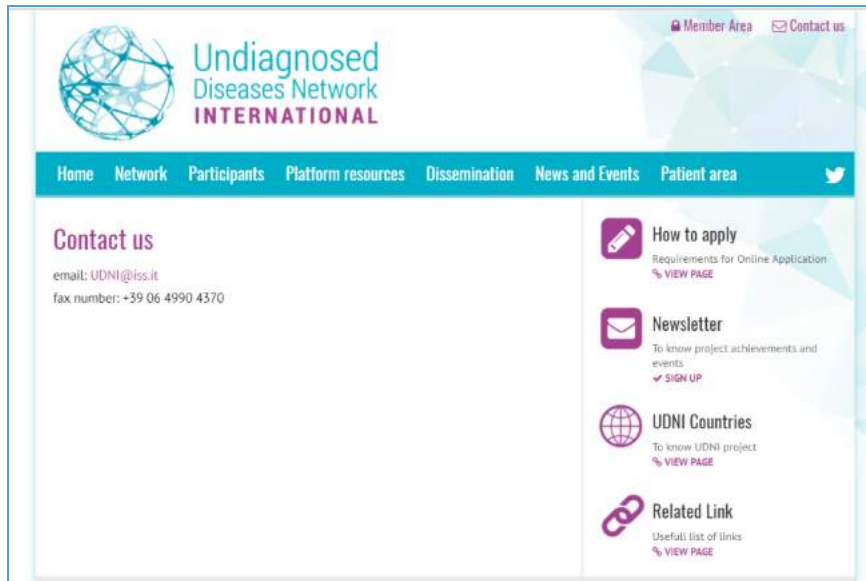
Number of cases entered: 10

- 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)

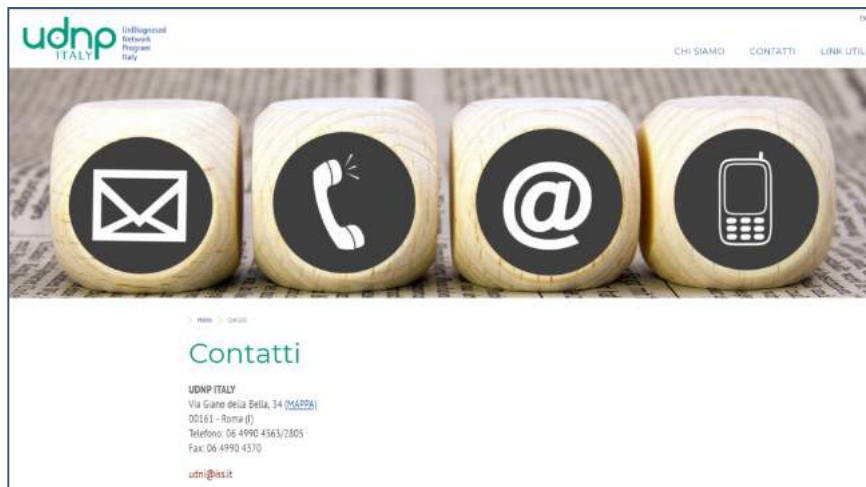
Each of the cases is shared (fully accessible) with UDNI Work Group on PhenomeCentral



Contact us:



<http://www.udninternational.org/>



<http://www.udnpitaly.com/>