Undiagnosed Diseases

International Congress on Research of Rare and Orphan Diseases

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RE(ACT) Congress 2018
Undiagnosed Diseases
March 7, 2018
March 7-10, 2018
Bologna, Italy

Challenges and Strategic Needs – The Diagnostic Odyssey

- **National Commission on Orphan Diseases 1989**
- **Obtaining the Diagnosis**
  - **<1 year - 51% Diagnosed**
  - **>1 year but <5 Years – 31% Diagnosed**
  - **>5 years – 15% Diagnose**
  - **Reports of Average Time to Diagnosis of 3.9 – 7.6 years**
  - **~6% of Requests to GARD for Undiagnosed Diseases**
- **Expansion of Newborn Screening Programs Will Help**
- **Better Family Histories and More Accurate Information**
- **Increased Development of Genetic and Diagnostic Tests**
- **Need Appropriate Genetic Counseling Services**
- **Develop Better Diagnostic Criteria for Rare Diseases**
- **Expand Sequencing Capabilities and Interpretation of Results**

Challenges and Strategic Needs

The Diagnostic Odyssey

- **Undiagnosed Diseases Program at the NIH**
- **Undiagnosed Diseases Network**
- **Undiagnosed Diseases Network International**
- **European Commission's Horizon 2020 - Solve-RD Research Program at University of Tubingen, Radboud University Medical Center Nijmegen, and the University Of Leicester to Collaborate with 4 ERNs (Neurologic, Neuromuscular, congenital malformations and intellectual disability, and genetic tumor risk syndromes**
- **Shire Report**
  - **4.8 years from onset of symptoms to Accurate Diagnosis**
  - **7.3 Physicians seen before a diagnosis is made**
- **Shire – Microsoft – EURORDIS The Global Commission to End the Diagnostic Odyssey for Children**

Challenges and Strategic Needs – The Diagnostic Odyssey

- **NORD Experiences – Surveys and Providing Support to Meet Clinical Needs of patients applying to UDP/UDN**

- **EURORDIS Survey of Delay in Diagnosis of Patients with 8 diseases (Crohn's Disease, Cystic Fibrosis, Duchenne Muscular Dystrophy, Ehlers-Danlos Syndrome, Marfan Syndrome, Prader-Willi syndrome, Tuberous Sclerosis, Fragile X-Syndrome)**
  - **25% of Patients waited between 5 and 30 years for Diagnois**
  - **40% Received a Misdiagnosis**
  - **25% of Patients travelled to different region of country and 2% travelled to a different Country**
  - **25% did not receive information on genetic nature of Diseases**
  - **50% of Patients had Genetic Counselling available**

Undiagnosed Diseases Program

- Late 2007: Plans for launching a new Undiagnosed Diseases Program (UDP) are formulated
- Implemented on May 19, 2008
- Goals:
  - To assist patients with unknown disorders reach an accurate diagnosis
  - To discover new diseases that provide insight into human physiology and genetics
  - Establish New Research Protocols for the undiagnosed cases

Providing UDP Support

- Office of NIH Director: Allowed ORD to loan 3 FTEs to NHGRI (Dr. William Gahl)
- Office of Rare Diseases: $280K annually for salaries of 2 NPs + 1 scheduler (4-year commitment)
- Clinical Center: 1 office, clinic/bed availability, Call Center & PR support, Medical Board Room
- NHGRI: Administrative & PR support, 1 CD, other OCD/Branch personnel, travel & testing funds
- NINDS: Detailed an Admin. Assistant (1 year)
- Other ICs: ~30 senior consultant volunteers for chart review; patients seen in existing clinics

UDP Operations

- Applicants submit medical records
- Referring physician sends summary letter
- UDP Director triages submitted records
- NIH senior consultants review records
- UDP Director synthesizes recommendations and makes final disposition
- Patients/referring physicians are informed
- Accepted patients come to CC for 1 week
- Weekly UDP Teaching Rounds
- Special Pediatrics Meeting q2 weeks

NIH Biospecimens Interest Group Presents:

Mystery Diagnosis

The Undiagnosed Diseases Program

Wednesday, September 16, 2009
1:00PM
Masur Auditorium/Building 10

Featuring:

Dr. Steve Groft, Director of the Office of Rare Disease Research (ORDR)

Dr. William Gahl, Clinical Director of NHGRI and the ORDR Intramural Research Program

Dr. John I. Gallin, Clinical Center Director

For additional information, please contact:

Yaffa Rubinstein, 301-402-4338, rubinsty@od.nih.gov
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Sign language interpreter will be provided.

Office of Rare Diseases Research

OBBR Office of Biorepositories and Biospecimen Research

National Institutes of Health

Undiagnosed Diseases Network

Seven clinical sites, a coordinating center, two DNA sequencing cores, a metabolomics core, a model organisms screening center, and a central biorepository

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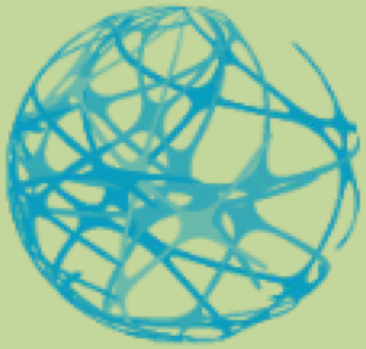
www.udninternational.org



Undiagnosed Diseases Network INTERNATIONAL

(1) Improve the level of diagnosis and care for patients with undiagnosed diseases through the development of common protocols designed by a large community of investigators.

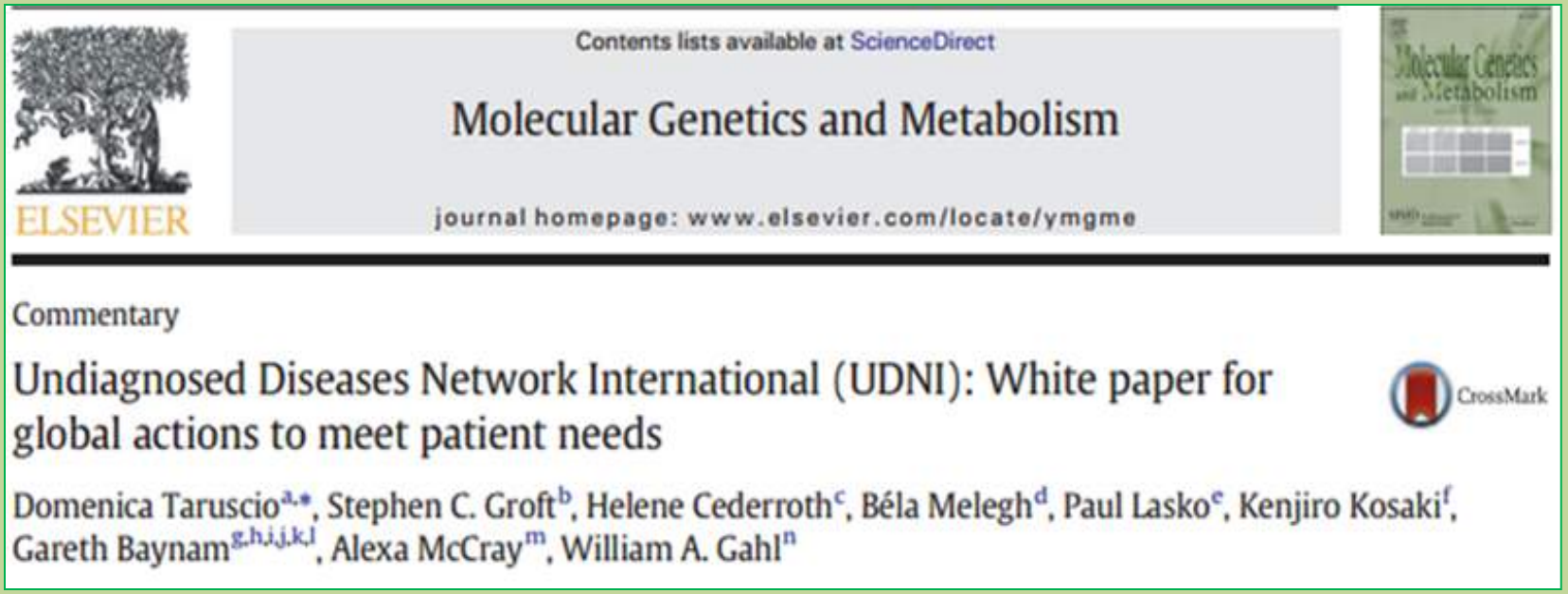
(2) Facilitate research into the etiology of undiagnosed diseases, by collecting and sharing standardized, high-quality clinical and laboratory data, including genotyping, phenotyping, and documentation of environmental exposures.

(3) 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.

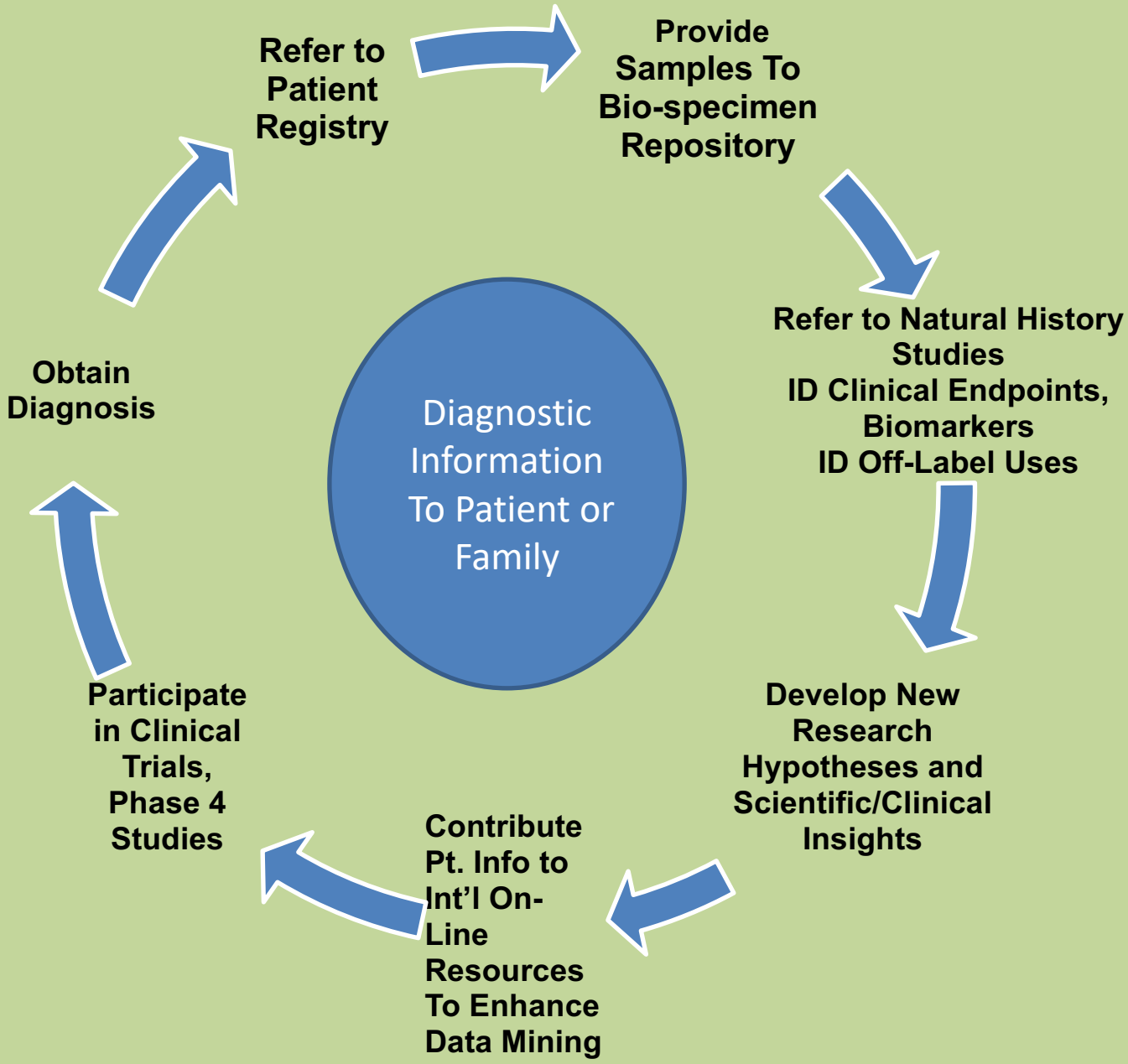
Website:

www.udninternational.org

Published Sept 2015



Possible Next Steps After the Diagnosis



Future Needs and Directions of Undiagnosed Diseases

- Establish Comprehensive Global Data Access, Data Entry and Data Sharing Procedures and Oversights for Shared Genotype and Phenotype Information, Best Practices, and Study Protocols for All Practitioners and Research Teams
- Develop Dedicated Multidisciplinary, Team Approach to Undiagnosed Diseases at National and Local Levels to Address Physical, Mental, and Psycho-Social Needs of Patients and Families – Living with Uncertainty, Isolation from Mainstream Medicine, Stigmatization
- Integrate Undiagnosed Diseases Patients and Programs into Existing Research, Training, and Treatment Programs at Medical Centers and Local Hospitals

Future Needs and Directions of Undiagnosed Diseases

- Role of Telemedicine in Isolated and Rural Areas with Referral Capability
- Provide Sufficient Financial and Personnel Resources to Expand and Sustain Programs and Initiatives such as Matchmaker Exchange, Phenome Central, DECIPHER, Patient Archive
- Maintain Confidentiality of Patients and Families with Transition Back to Referring Source
- Support Collaborative Patient-Centric Organizations dedicated to Undiagnosed Rare and Common Diseases
- Publicize Existence and Location of Participating Centers

Undiagnosed Diseases Network INTERNATIONAL

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM