Initiative on Rare and Undiagnosed Diseases (IRUD):
Towards integrative diagnosis network for universal healthcare system

G2MC: Implementing Genomic Medicine Globally
April 27, 2017

Takeya Adachi M.D., Ph.D.
Japan Agency for Medical Research and Development (AMED)
Nan-Byo
Since 1972

Rare
Causes and pathogenesis unclassified
Effective treatment unestablished
Long-term care required

Nan = difficult / hard to handle
Byo = diseases / illness
SUBACUTE MYELO-OPTICO-NEUROPATHY (S.M.O.N.) IN JAPAN
A Community Survey
KIMIHIRO NAKAE
SHUN-ICHI YAMAMOTO
AKIHIRO IGATA

Department of Epidemiology, University of Tokyo
School of Health Sciences, and
Department of Clinical Neurology,
Brain Research Institute, University of Tokyo, Japan
Patients under unidentified conditions

Relatively Rare & Diagnosed

Subsidies & Research Projects

Nan-Byo Since 1972

Ultra-Rare & Undiagnosed

What is overlooked by Nan-Byo
Relatively Rare & Diagnosed

IRUD

Ultra-Rare & Undiagnosed

Nan-Byo Since 1972

Diagnosis
Initiative on Rare and Undiagnosed Diseases
IRUD since 2015

- Diagnosis
- Analysis
- Data Network
Diagnosis network utilizing *Nan-Byo* measures

Upon Japanese Universal Healthcare System

**Clinical Centers**

**Outpatient** department-based

**Collaboration with *Nan-Byo* researchers**

1. Undiagnosed for >6 months; AND,
2-1. **Multiple organ** symptoms; OR
2-2. Genetic disorders suspected
Field Survey for potential target of IRUD

Diagnosis

National Universities
- ALL

Private Universities
- ALL

Local Clinics
- 300

Clinical Centers
- At most 30+

Collaborating Hospitals
- At most 150+
IRUD Regional Alliance Hospital Network includes **200** hospitals in Japan

**ToMMo** (Tohoku Univ.) provides rare variants of **2,000+** healthy Japanese sequence data as the controls

2,230 patients (5,674 trio samples) registered and received WES in 1.5 year
500 physicians & 50 coordinators

-Multidisciplinary Diagnostic Approach

- Medical Geneticists
- Neurologists
- Cardiologists
- Dermatologists
- Pediatricians
- Nephrologists
- Immunologists
- Genetic Counselors
- Hemato-Oncologists
- Pulmonologists
- Pulmonologists
- Gastro-enterologists
- Endocrinologists
- Allergologists
- Orthopedists
- Ophthalmologists
Diagnosis

- Whole Exome Sequence (WES)
- Patient matching via Patient Archives and MatchMaker Exchange
- Screening of candidate variants
- Whole Genome Sequence (WGS)

Diagnosed

- 22.1%
- 77.9%

n = 15
Aug. 2016
~25% of patients received the results within 6 months

n = 15
Aug. 2016

n = 4
Novel Diseases in collaboration with US, Europe, and Asia

Suggested Novel Diseases (Candidate genes < 5)

“N-of-2”
||
6

“N-of-1”
||
83
What is overlooked by NGS?

-WGS
-Other Omics
Transcriptomics
Metabolomics
Proteomics
Glycomics
Lipidomics

Further patient matching

60.1% Undiagnosed
Accommodate information about the use of resources in discovery and/or access scenarios

FINAL (15 December 2016)

Automatable Discovery and Access Matrix ("ADA-M") v1.0

GUIDANCE DOCUMENT

Global Alliance for Genomics & Health (GA4GH)
International Rare Disease Research Consortium (IRDiRC)
IRUD Beyond

- Diagnosis
- Analysis
- Data Network
- Treatment
- Improved Diagnosis

for ALL Rare & Undiagnosed Patients