Rare Disease Policy in Japan

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Today's Topics

① Introduction

② Research on the treatment of rare diseases with support of medical expenses

③ Research projects for “NANBYO”

④ Challenges of research projects
① Introduction
Organization
Health Service Bureau

- The Aim: Overcome Diseases and Enhance Health
- Divisions
  - General Affairs Division
  - Specific Disease Control Division
  - Tuberculosis and Infectious Diseases Control Division
  - Environmental Health Division
  - Water Supply Division
Specific Disease Control Division

- **Members**
  - **Director**
    - Yamamoto M.D. PhD.
  - **Sub-Director**
    - Hagiwara
    - Araki M.D. PhD.
  - **Technical members**
    - Nakagawa M.D. PhD.
    - Mano M.D. PhD.
  - **Secretary members**
    - Takenouch
    - Mizoguch
    - Kayanuma
    - Nagai
Our Target

- Our target is called “NANBYO（難病）” in Japanese.
- We say Rare and Intractable Disease for “NANBYO” in English.

What is “NANBYO（難病）”??
- NAN (難) = something difficult or hard to do and worried about.
- BYO(病) = Disease, illness and syndrome.
Large outbreak SMON and After

- 1972: The Diet discussed about measures against “NANBYO” intensively.
- 1972: “Outline of the Measures against Intractable Disease (Nanbyo Taisaku Yoko)” was established.
  - Office for Specific Disease Control was established in Ministry of Healthcare and Welfare.
- The disease “NANBYO” was selected by Director General’s special consultative body.
- 2012: The 40th anniversary !!
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Definition of “NANBYO”
Written in Nanbyo Taisaku Yoko (1972～)

- unidentifiable cause
- without a clearly established treatment
- considerably high risk of disability
  - Heavy burden for patients & family financially and mentally (long term of care)
- Rarity (<50,000)

- However, disease covered by other programs are excluded.
  - Ex: Cancer, Brain Attack, Mental disorder...
support of medical expenses

- Research on the treatment of rare diseases (support of medical expenses)
  - Target 56/130 “NANBYO” (about 710,000 patients)
  - Budgets: about $1.45 billion
    - Government: about $0.35 billion
    - Local governments: about $1.1 billion
- USD 1 = JPY 80
Limits to monthly medical expenses in each hospital

- **Severe condition / stage**
  - Full support of medical expenses: $0 /month
- **Outpatient care**
  - $0 ~ $144.38 /month
  - Depends on the family income
- **Hospitalization**
  - $0 ~ $288.75 /month
  - Depends on the family income
The number of patients whom getting the support of medical expenses

- Top 3 diseases with highest number of patients
  - Ulcerative colitis 117,855
  - Parkinson disease and related diseases (progressive supranuclear palsy, corticobasal degeneration, Parkinson disease (Yahr's stage 3 - 5)) 106,637
  - Systemic lupus erythematosus (SLE) 56,254

- Top 3 diseases with lowest number of patients
  - Restrictive cardiomyopathy 18
  - Severe erythema multiforme (Acute Phase) 48
  - Subacute sclerosing panencephalitis (SSPE) 87
Trends of the number of "NANBYO" patients

Number of Patients

710 thousand patients (2011.3)

Ulcerative Colitis
117,855

Parkinson's disease
106,637

Systemic Lupus Erythematosus
56,254

scleroderma, dermatomyositis, or polymyositis
42,233
Challenges of support programs

- The burden of medical cost subsidy is very huge and increasing, according to the increase of patients and the patient’s aging.
  - Totally $1.45 billion ($1=¥80), 710,000 patients.
- It is very difficult for the government to designate new target diseases for medical cost subsidy, politically and budgetary.
- Limitation to support medical expenses by research grants.
- Insufficient support programs of employment and social welfare.
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Research projects for “NANBYO”

- Promoting survey and research activities
  - Total Budget for Research Teams: about $0.13 billion in 2011.
  - Today there are 277 research teams.
  - 130 “NANBYO” and 234 rare diseases next to “NANBYO”.
FY2011 Research projects for “NANBYO”

Budget: $ 0.13 billion

Research Projects
$ 0.1 billion

Utilizing clinical data of patients, registered in Project

Special Programmes
$ 0.03 billion

Clinical Research (130 diseases/syndromes)

Encouraged Research (newly added rare diseases)

<established in 2009>
- 2009: 177 diseases
- 2010: 214 diseases
- 2011: 234 diseases

Prioritized research
Develop innovative method for diagnosis/treatment
Budget (2011)/one team about $ 3.8 million
~ $ 6.3 million

Cross-cutting research

Designated research

Genomic Projects

Analyzing on rare/intractable diseases

Introducing Next Generation Sequencer

5 targeted aria
At 5 core institutes

※ Theses projects are all encouraged international collaboration
Projects for Study Group of Lysosomal Storage Disorders (LSD),

**Project 1**
- Take a Natural History of Patients with LSD
- Numbers and their Incidence of LSD
- QOL/ADL Evaluation in LSD patients

**Project 2**
1. Develop Screening Methods for Early Diagnosis by DNA Tech.
2. Screening by DBS and Tandem MS/MS for LSD patients.

**Project 3**
1. Studies for Pathogenesis of LSD
2. Genetic Diagnosis Procedure
3. Genotype to Phenotype Correlation
4. Generate iPS cells from LSD

**Project 4**
1) Evaluation of Efficacy by Enzyme Replacement Therapy
2) Develop Novel Treatment for LSD (Chaperon, Gene/Cell therapy)
Applications of iPS Cells

Disease-specific iPS cells may provide a new application tool in cell-gene therapy, and valuable experimental platforms to model rare human diseases.

- **Patient’s skin or blood**
- **4 or 3 factors**
- **iPS cells**
- **Differentiation**
  - Neural cells
  - Cardiac cells
  - Hepatocytes
  - β-cells

**Increase safety**

**Regenerative medicine** *(in vivo USE)*

**Diagnosis, Disease Mechanism**
**Disease Model**
**Toxicology, Drug Screening** *(in vitro USE)*
Clinical study of safe bridge-to-transplantation/recovery in DCM patients

- Bridge to Transplantation
  - Viability (−)
    - Implantable LVAD

- Bridge to Recovery (Study1)
  - LVAD+Myobalst Sheet

- Regenerative Therapy (Study2)
  - Myobalst Sheet

DCM

Viability (+)
Phase I Study of recombinant human HGF in ALS patients

HGF: hepatocyte growth factor

Subjects: ALS patients of severity 1 or 2 (within 2 years after the onset)

Study design:

Single dosing cohorts

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<tr>
<th>Cohort 1</th>
<th>Cohort 2</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
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<tbody>
<tr>
<td>Low dose</td>
<td>Middle dose</td>
<td>High dose</td>
<td>Repeated dosing</td>
</tr>
<tr>
<td>n=3</td>
<td>n=3</td>
<td>n=3</td>
<td>(5 times) n=3</td>
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Administration route: Intrathecal administration via the catheter connected with subcutaneously implanted port (2 hours infusion)

Clinical site: Tohoku University Hospital, Sendai

HGF extended survival rate of ALS rats

HGF protects motor neurons

HGF receptor

HGF: HGF extended survival rate of ALS rats

Control

Treatment

Days old

Survival (%)
Clinical Trial of wearable robot Hybrid Assistive Limb (HAL)

- For rare neuromuscular diseases
  - protect degenerative muscles, to maintain muscle function longer and to prevent atrophy in healthier muscles
  - Reduction of disease progression speed

Enhancement Technology for neuromuscular diseases
2012: Result announcement conference of “NANBYO” research projects

- 2012.1.14(sat) 13:00～16:10
- Osaka International Convention Center
- Title: Application to the rare disease of Regeneration technology and gene therapy technology.
- About 1,000 participants
  - Researchers, patients, family...
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Challenges of research projects

- Too many kinds of Rare diseases to research one by one.
- Rare patients / rare expertise in one country
- Insufficient patient registry
- Target is not clear → What disease? What technology?
- Few economical incentives
- iPS technology or Regeneration technology are so new and no valuation method
- Poor infrastructures for Gene Therapy
- Weak linkage between basic medical sciences and clinical medical sciences
Key points for our future

- **Connection**
  - If you connect with each other, we can gather and share many information
    - Patients, researchers, family, patient support organizations, hospital, laboratory, government
    - Epidemiology, mechanism of the disease, diagnostic method, DNA, target for treatment and ...

- **Collaboration**
  - Collaboration can make reduce the restrictions
    - Budget problem, lack of researchers, number of patients, ideas for treatment, management way of the disease and your life...

- **Creation**
  - Create innovation and solution for the problems
  - And HAPPY for all stake holders.

\[ C^3 : \text{Connection} + \text{Collaboration} = \text{Creation} \]
Thank you for your attention.