



Features of Biobank

- 19,355 cases of pathological frozen tissue, 37,570 cases of withdrawn blood for analysis (as of end-December, 2015) = the nation's largest cancer tissue bank
- Pathologist removes tissues based on an accurate diagnosis and maintains high quality through rapid freezing
- Collect all possible samples to meet the needs of a variety of studies
- Generate a high-quality database for clinicopathological information, which can interface with in-hospital cancer registry information, etc.
- More convenient samples, obtained with informed consent for sample transfer to outside researchers, including companies, for genome-wide analysis and to establish cell lines

Historical performance and achievements

- Availability of pathological tissue (the number of cases used / the number of cases collected [2015]) is 92%. NCC Biobank is a bank for both storage and use of samples!
- Published 354 studies in English (the total impact factor is 1831.289 points, the total number of citations is 5,630.
- Of the total sample utilization studies, 63% involve joint research performed by providing detailed clinicopathological information to an external institution (21% is joint research with private companies)
- Used for nationwide clinical research derivations and many patent filings, such as The International Cancer Genome Consortium and The International Human Epigenome Consortium (ICGC, IHEC), Integrative Disease Omics Database construction, SCRUM-Japan, etc.
- Knowledge on how to manage high quality maintenance, as described in "Pathology organization sample handling rules and regulations for genome studies" by the Japanese Society of Pathology and meets Japan standards.

Future prospects

- To further improve the coefficient of utilization of completely collected samples and to pursue possible contributions to the All-Japan One Stop Service concept
- To consider the formulation of pipelines for sample transfer to companies, etc., without joint research with NCC
- To establish a "next-generation biobank", which collects samples on demand from companies; to improve the connectivity between biobanks as disorder cohorts and molecular information databases obtained by clinical sequencing, etc.; to promote industry-academia-government cooperation within all of Japan; and to contribute to the realization of genomic medicine

Discovery of a new cancer treatment target and application to clinical next-generation sequencing analysis with biobank samples

New Therapeutic Target Discovery

Pulmonary cancer: *RET* gene fusion
CREBBP gene variant
Biliary tract cancer: *FGFR2* gene fusion

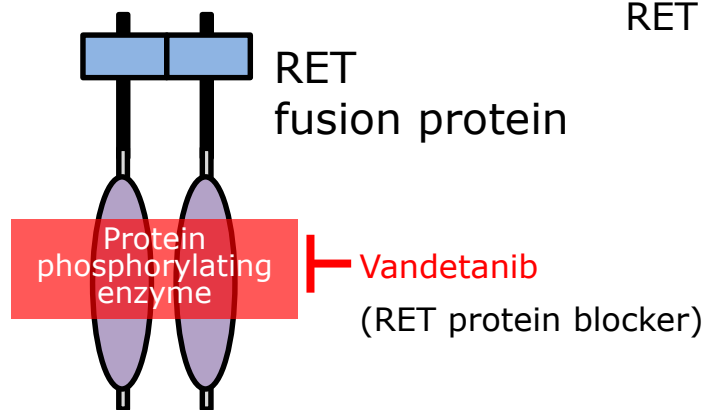
Disease mechanisms of cancer initiation in Japan

Liver cancer
ATL: adult T-cell leukemia-lymphoma
Ampullary carcinoma, etc.

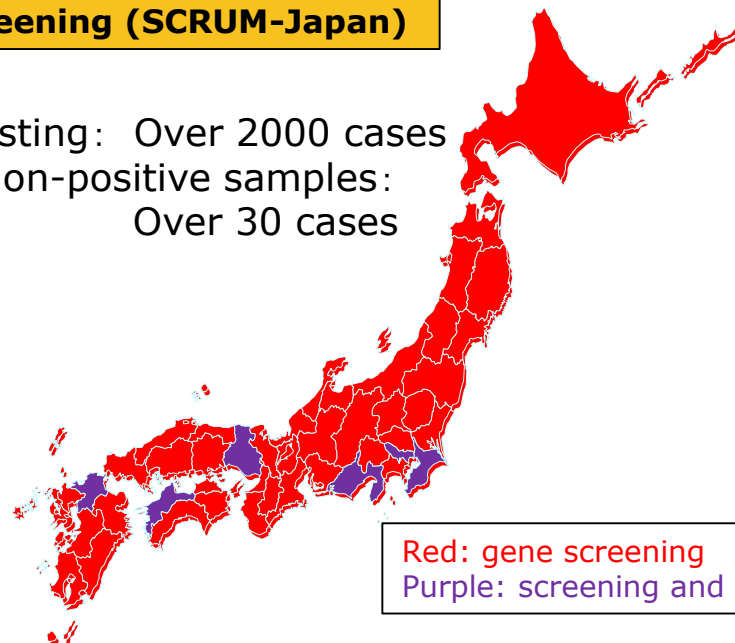
Kohno et al., Nat Med, 2012
Alexandrov et al., Nature, 2013
George et al., Nature, 2015
Nakamura et al., Nat Genet, 2015

Fujimoto et al., Nat Genet, 2012
Totoki, Nat Genet, 2014
Kataoka et al., Nat Genet, 2015
Yachida et al., Cancer Cell, 2016

Clinical trial of inhibitors based on nationwide screening (SCRUM-Japan)



Gene testing: Over 2000 cases
RET fusion-positive samples:
Over 30 cases



Red: gene screening
Purple: screening and treatment



Features of Biobank

《Collected samples》

- Blood samples from patients who visited NCVC
- Clinical residual samples
- Surgical pathology samples
- Autopsy tissue samples
- Deposited samples from researchers inside and outside NCVC, research institutes, etc.

《Numbers of samples collected》

Serum	5,673
Plasma	5,516
Living cells	5,661
DNA for transfer	5,268

*As of July 2016

《Accompanying information》

- National Center Biobank Network (NCBN) shared interviews sheet
- Health-related quality of life (QOL) survey
- Clinical data collected through the Data Warehouse (DWH) from electronic medical records and various section systems

Historical performance and achievements

- Analysis of pathogenic mechanisms of myocardial infarction, brain infarction, etc., using surgical pathology samples or autopsy tissues
- Analysis of causative genes or prognosis using genome and clinical information for genetic disorders (particularly cardiac dysrhythmia or hypercholesterinemia)

《 Specific example 》

- 1) Archiving of carotid endarterectomy specimens and comparison with MRI
- 2) Identification of a genetic mutation in CALMODULIN 2 as the cause of long QT syndrome and catechol-aminergic polymorphic ventricular tachycardia
- 3) Clarification of the risk of coronary artery disease in families with hypercholesterolemia by using genomic and clinical information

Future prospects

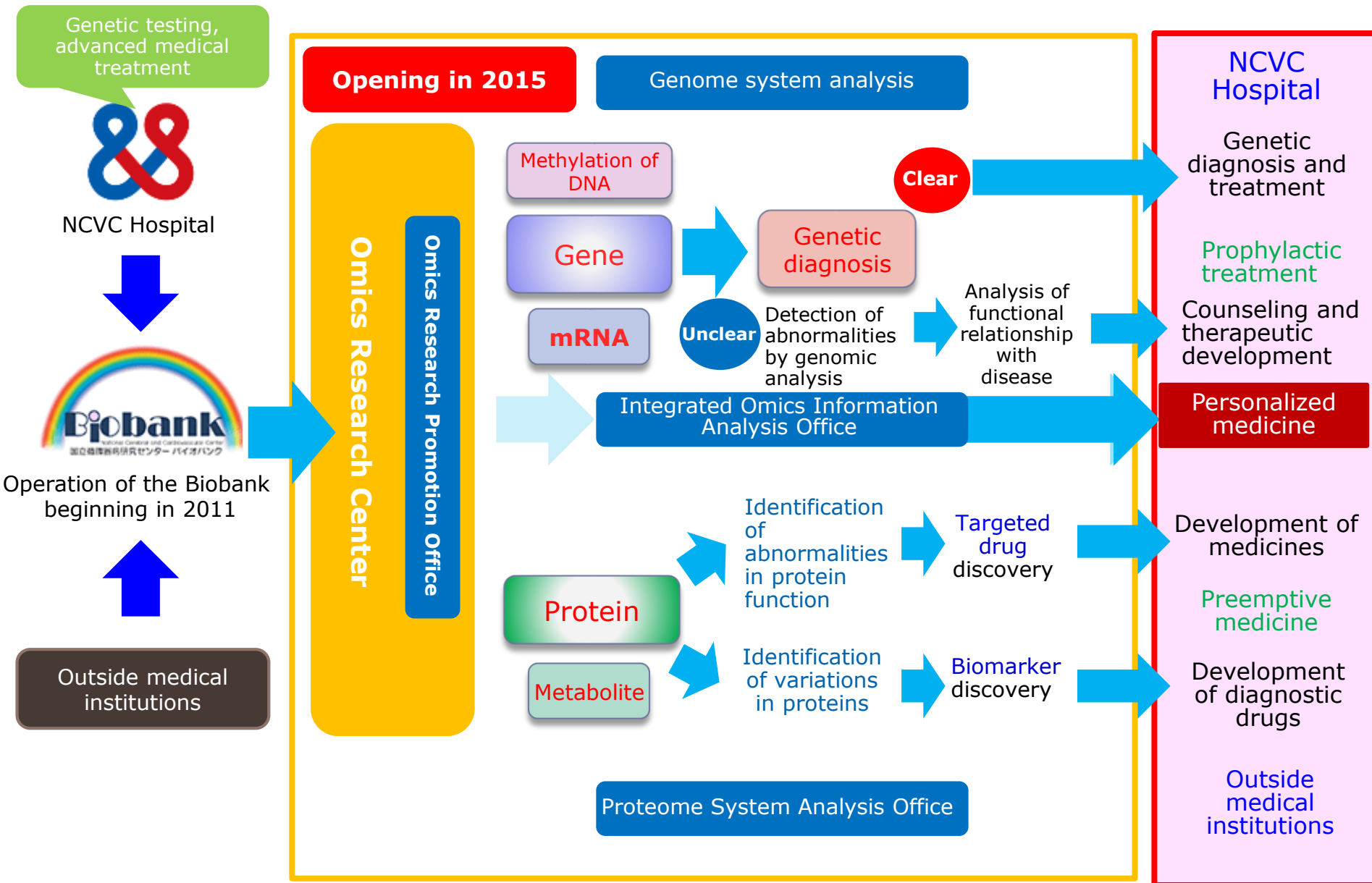
Securing of sample resources and promotion

Obtaining biobank consent from all of inpatients principle

Centralized administrative control over research materials

For management of “Human rights protection of subjects” or “Accelerating medical research”, all research materials held by NCVC should be managed by the biobank.

Need for and Role of the Biobank/Omics Research Center in NCVV





National Center of Neurology and Psychiatry (NCNP) - Bioresource

High-value-added bioresources available for use in studies of psychiatric, neurological, and muscular diseases

Features of Biobank

- Collection of "hard to get" samples
 - Frozen skeletal muscle samples: approx. 16000
 - Fibroblasts: more than 1700
 - Spinal fluid: more than 2500
 - Brain tissues: more than 550
- Samples to meet various research needs
 - Frozen tissues (including muscles and brain tissues)
 - Cultured cells (lymphoblasts, Fibroblasts, iPSCs, etc.)
- High-quality clinical information, including accurate diagnosis by specialists and PET/MRI images
- Ethical procedures for cooperation with industry, government, and academia

Historical performance and achievements

- In muscle diseases, more than 400 papers in leading journals, including Nature and Science, have been published, including identification of the intracellular location of dystrophin (Nature, 1988) and identification of the etiology of MELAS (Nature, 1990)
 - ⇒ Led to novel treatments or clinical trials, including exon skipping and taurine treatment
- Identification of biomarkers for subtypes of psychiatric disorders
 - ⇒ Fibrinogen, ethanolamine, etc.
- Identification of new causal genes for developmental disorders and neurological disorders
- Establishment of Biobank Utilization Committee

Future prospects

- Function as a core institution for large research projects focused on development of genomic medicine, intractable disease, undiagnosed diagnosis, etc.
 - ⇒ Implementation and cooperation to provide effective control of genomic information (genomic medicine)
- Develop new medical treatments and preventive measures by actively providing samples and information for research studies
- Delivery of specific bioresources according to the needs of researchers at the researcher's request
- For neurological disorders, samples, such as DNA, plasma, and spinal fluid, will be available for researchers

Blood samples for the researches of psychiatric and neurological diseases

Also possible for transfer: Now we can offer contracts that do not require results or intellectual property rights of the biobank. In this case, compensation for sample collection would be required.

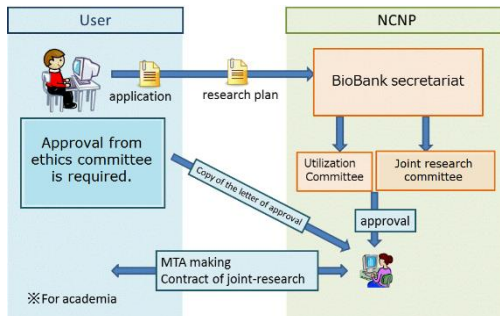
Plasma/DNA samples available

Disease	Number
Schizophrenia	293
Bipolar disorder	151
Major depressive disorder	188
Dementia	291
Parkinson disease	110
Multiple sclerosis	263
Healthy controls	180
• • • •	
Total (2016.8)	2979

Clinical information available

- 6NC shared interview sheet (Post history, family history, lifestyle habit, etc.)
- Psychiatric diagnosis interview (MINI)
- Assessment of symptoms HAM-D, MADRS (depression), YMRS (manic state), PANSS (Schizophrenia), MMSE (dementia)
- Treatment information
- Test results, such as images, may be available by consultation

How to utilize



After the inquiry and consultation, an application form and an approval from ethics committee of your institution are required. The Utilization Committee and the Joint Research Committee evaluate these documents.

[Applications and inquiries]
Utilization Committee
contact
biobank@ncnp.go.jp

Human muscle repository

The world's largest number of skeletal muscle samples

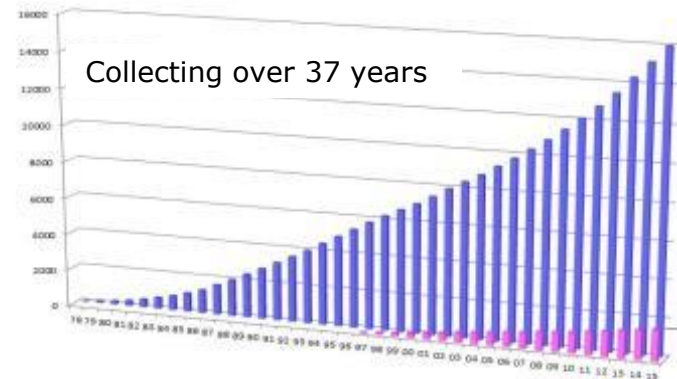
Frozen muscle tissues: more than 16,000
Fibroblasts: more than 1600

As of July 31, 2016

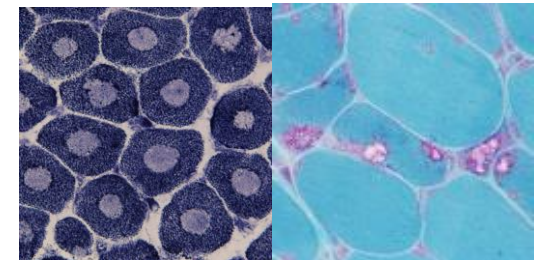


Sample number in muscle repository

As of December 31, 2015



Frozen muscle samples
16591



→ A worldwide hub for providing various myopathic bioresources

National Center for Global Health and Medicine (NCGM) - Biobank



National Center focused on internationally important diseases,
such as infectious diseases and lifestyle diseases

Features of Biobank

- Collect and add precise medical information in cooperation with the individual department for studies of **diabetes or other disease** and collect and analyze information on blood, DNA, microRNA, urine, and feces from patients.
- Utilize samples and information collected by the **liver disease network** and during liver biopsy.
- Medical care for 17% of cases of domestic **HIV infection** and collection of more than 1000 blood samples (ACC)
- Collect blood samples **from patients with malaria, influenza, and dengue fever** and maintain an appropriate database (DCC).

Historical performance and achievements

- Search and identify new serum and urinary biomarkers reflecting clinical conditions of lifestyle diseases, such as diabetes.
- Develop test drugs and diagnostic products for infectious diseases (e.g., viruses).
 - Provide samples for standardization of HBs antigen or *IL28B* gene testing.
 - Establish a drug-resistant variant for genetic testing against anti-HIV drugs (in conjunction with the National Institute of Infectious Diseases).
 - Development of and clinical trials for a novel influenza rapid diagnostic kit
- Identify drug susceptibility and disease susceptibility loci by genome-wide association analysis in a major joint study.

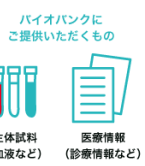
Future prospects

- **Promote international partnerships and network maintenance** and consolidate and promote the use of blood samples from participating institutions.
- Support the clinical use of **microRNA** as a biomarker.
- Promote integrated projects on **complex clinical conditions**.
 - Complications of diabetes and cancer
 - Progression to cancer from infectious disease (*Helicobacter pylori* or hepatitis virus)
- Promote the cross-cutting project 6NC for investigation of **the microbiome** (intestinal flora)
 - Target diseases are lifestyle diseases, such as cancer, arteriosclerosis, inflammatory bowel disease/allergies, and depression.

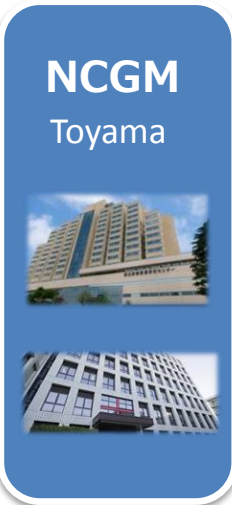


National Center for Global Health and Medicine

System to store samples and information for research (NCGM biobank)

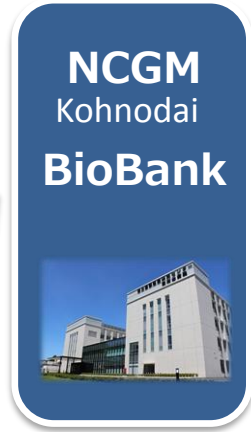
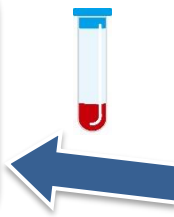


ナショナルセンター
バイオバンク・
ネットワーク
(NCBN)



NCGM Toyama

- Collect blood, DNA, microRNA, urine, and feces
- Collect biological samples and medical information on patients with diabetes
- Collect blood samples from patients with HIV infection (ACC)
- Collect blood samples from patients with influenza and dengue fever (DCC).



NCGM Kohnodai BioBank

- Collect biological samples and medical information through the liver disease network/liver biopsy.

Results of prior studies and achievements

- (1) Genome-wide association analysis in major joint studies ⇒ identification of drug susceptibility and disease susceptibility loci
- (2) Search and identification of new serum and urinary biomarkers reflecting the clinical conditions of lifestyle diseases such as diabetes
- (3) Develop test drugs and diagnostic products for infectious diseases (e.g., those caused by viruses):
 - Provide samples for standardization of HBs antigen or IL28B gene testing.
 - Establish a drug-resistant variant for genetic testing against anti-HIV drugs (in conjunction with the National Institute of Infectious Diseases).
 - Development of and clinical trials for a novel influenza rapid diagnostic kit



Novel influenza: negative

Novel influenza: positive



Future prospects

- 1 International partnerships and network maintenance Biobank
- 2 Clinical use of microRNA as a biomarker
- 3 Promotion of integrated projects on complex clinical conditions, such as diabetes and cancer
- 4 Promotion of the cross-cutting project 6NC focusing on the microbiome





National Center for Child Health and Development (NCCHD) - Biobank

The largest National Center for pediatric and obstetric research in Japan

Features of Biobank

- Various types of samples from pediatric patients with rare intractable diseases
- Samples from patients with obstetric complications (including cord blood and placenta)
- Eutocia samples from pregnant women
- Samples with a high degree of clinical information and examination findings
- The Japanese study group for comprehensive and accurate diagnosis of intractable diseases
- Cooperation with Initiative on Rare and Undiagnosed diseases in Pediatrics (IRUD-P)
- Semipermanent storage of materials, such as ES cells, based on regenerative medicine law

Historical performance and achievements

- Published a database of gene polymorphisms in Japanese individuals (multicenter joint research).
- Published data on gene polymorphisms associated with eutocia in a pregnant Japanese woman.
- Identify the causal genetic elements of rare diseases and intractable diseases.
- Discovery of a new disease concept - Kagami-Ogata syndrome.
- Development of a genetic diagnosis panel optimized to Japanese patients.

Cooperate with next-generation gene analysis

Future prospects

- Cooperate with cohort studies and epidemiological studies.
- Maintain and publish standard data essential for the analysis of perinatal medicine and pediatrics.
- Facilitate research on microbiomes, such as the intestinal flora.
- Search for biomarkers in samples from pediatric patients, which are hard to collect.
- Identify new causal genetic elements of rare diseases and intractable diseases. (Kawasaki disease, inflammatory bowel disease, obstetric complications, etc.)

Infrastructure development for research on life diseases

- Identification of the causes of intractable diseases
- Therapeutic development
- Provision of drug development seeds


NCCHD Biobank – Main Results and Achievements

Discovery of the new disease concept of disease groups that are difficult to treat and have remained undiagnosed.



Store samples of undiagnosed diseases transferred by national local medical institutions

For undiagnosed children and families



Save children who manifest symptoms of an unknown etiology prior to medical treatment.

Project to identify diseases or disease etiologies by whole genome analysis
Initiative on Rare and Undiagnosed Diseases in Pediatrics
It's starting.

Initiative on Rare and Undiagnosed Diseases in Pediatrics (IRUD-P)



IRUD-P
Initiative on Rare and Undiagnosed Diseases in Pediatrics

IRUD-P@ncchd.go.jp irud@skip.med.keio.ac.jp
TEL 03-5361-2117 TEL 03-5361-2306
916-2arob@ncchd.go.jp TEL 03-5361-7593

Certified by the International Genetic database (OMIM)

#608149

KAGAMI-OGATA SYNDROME

Alternative titles; symbols

UNIPARENTAL DISOMY, PATERNAL,
CHROMOSOME 14

➔ Significantly improve patient care and prognosis

➔ From etiological clarification to therapeutic development



National Center for Geriatrics and Gerontology (NCGG) – Biobank

Biobank

The largest Biobank for bioresources of dementia in Japan

Features of Biobank

- ◆ Biobanking of biological samples and clinical records focusing on the geriatric diseases including dementia and joint diseases.
 - Bioresources: DNA, serum, plasma, tissue, CSF, etc.
 - NCGG Biobank offers storage at -80C and in liquid nitrogen tanks.
 - No. of biobank participants: >5,000
 - No. of samples: approx. 85,000
- ◆ Support of the research groups using biobank samples and data.

Historical performance and achievements

- ◆ Approx.10,000 samples have been distributed to scientists and numerous outcomes have been generated as below.
 - Vitamin D deficiency, a risk for white matter hyperintensity in Alzheimer's Disease (AD) patients.
 - Insulin resistance in AD patients with diabetes.
 - White matter hyperintensity associated with urinary incontinence.
 - Identification of blood microRNA biomarkers for AD
 - Identification of pathological molecules of lumbar spinal canal stenosis.
- ◆ Development of the original sample management system, *Biora*®.

Future prospects

- ◆ Promote of genomic analysis for Japanese patients with dementia.
- ◆ Construction of whole exome sequence data base to which scientists can access.
- ◆ Cooperation with geriatric cohort studies.
 - Storage and distribution of samples and data
- ◆ Collection of omics data of biobank samples and linkage to clinical records.

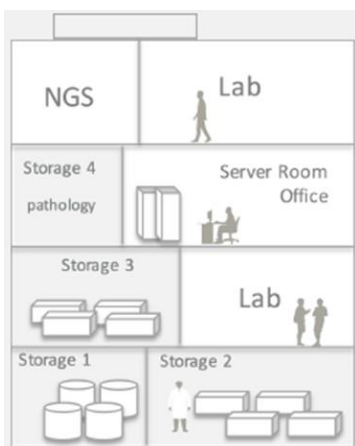


NCGG Biobank

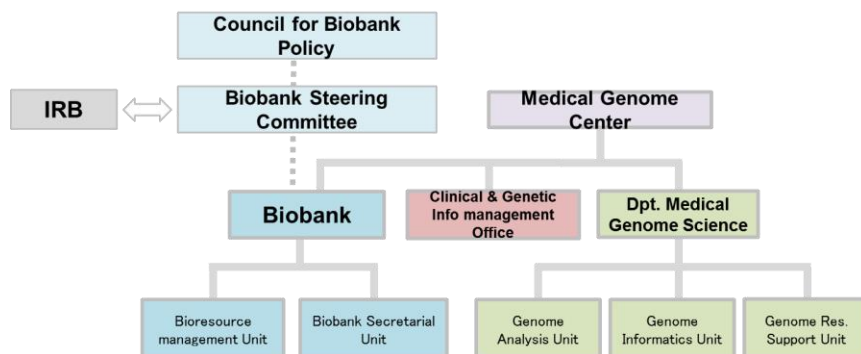
The largest Biobank for bioresources of dementia in Japan

Biobank

NCGG Biobank is a part of the Medical Genome Center (MGC) of NCGG, which administers the genome cohort studies of elderly people. Biobank has two functional units, Bioresource management unit and Biobank secretarial unit. The coordination of biobank activities is reviewed by Council for Biobank Policy and Biobank Steering Committee. Clinical information associated with the biological samples are managed by the Clinical and Genetic Information Management Office of MGC.



NCGG Biobank Organogram



Scientists can access our biobank, and have the possibility to link information about biological samples in the biobank with the large amount of clinical information in the MGC registries. MGC supports genetic studies using the biological samples in NCGG Biobank.

