GLOBAL LEADERS IN GENOMIC MEDICINE
January 8-9, 2014
National Academy of Sciences Building
2101 Constitution Avenue, NW
Washington, DC 20001

New initiative for the implementation of Genomic Medicine in Japan

1) Office of Healthcare Policy, Cabinet Secretariat
2) Center for Integrative Medical Science, RIKEN
3) The Institute of Medical Science, The University of Tokyo

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Structure of the Headquarters of Healthcare Policy

provisional translation

Headquarters of Healthcare Policy (HHP)

Director-General of HHP : Prime Minister
Vice Director-General of HHP : Chief Cabinet Secretary
Members of HHP : Ministers of State other than Prime Minister and Chief Cabinet Secretary

< functions>

- Promotion of the implementation of the Health and Medical Strategy
- The headquarters of medical R&D (“Japanese version of NIH”)

The HHP shall

- develop a comprehensive plan for promotion of medical R&D.
- integrate medical R&D budget requests of relevant ministries.

Advice of Policy Issues

Advisors on Health and Medical Strategy

consist of superior expertise belonging to pharmaceutical and medical equipment industry, and medical institution, etc.

advise the HHP on :

- Promotion of implementation of the Health and Medical Strategy
- Promotion of industrialization , etc.

Technical Advice

Special Committee on Medical Research and Development

consists of superior researchers in a medical field.

advises the HHP on scientific matters required for development of a comprehensive plan for promotion of medical R&D.

Promotion Council for Health and Medical Strategy

Chairperson : Chief Cabinet Secretary
Acting Chairpersons : Deputy Chief Cabinet Secretaries (belonging to the House of Representatives and the House of Councilors)
Deputy Chairperson : Director-General of the Office of Healthcare Policy
Members : Director-Generals of relevant ministries

Task Force for Global Reach of Japanese-style Medical Technology and Services

Chairperson : Director-General of the Office of Healthcare Policy
Members: Director-Generals of relevant ministries
Officer of Organization concerned

Committee of the Academia-Industry-Government Network for Drug Discovery Research

Chairperson : Director-General of the Office of Healthcare Policy
Members: Director-Generals of relevant ministries
Officer of Organization concerned

Secretariat

Office of Healthcare Policy,
Cabinet Secretariat

1. Functions of Headquarters（HQ）of Healthcare Policy

provisional translation

- Strategically integrating medical R&D budget requests of the government to allocate the budget upon priority projects, and developing a comprehensive plan for promotion of medical R&D early next year, the HQ shall determine prioritizing research fields and targets.
- The HQ shall establish two panels for the above purposes;

The panel of advisors, superior researchers in a medical field, to the HQ

The panel of advisors, superior researchers in a medical field, to the HQ is responsible for submitting an opinion about the HQ's comprehensive plan for promotion of medical R&D.

The panel of advisors, eminent persons from industry, government, and academia, to the HQ

The panel of advisors, eminent persons from industry, government, and academia, to the HQ is responsible for submitting an opinion about the promotion of implementation of the Health and Medical Strategy and the promotion of industrialization, etc..

2. The HQ's integration of medical R&D budget requests of the government

- The HQ shall integrate medical R&D budget requests in order strategically to concentrate the budget upon priority projects under a strong leadership of State Ministers from each ministry's budget demand forward.
- The following measures shall be taken to integrate medical R&D budget requests of relevant ministries prior to budget demands:.
  - The HQ shall formulate a basic policy for the medical R&D budget demands.
  - Each ministry shall submit total rough estimate of their medical R&D budget to the cabinet secretariat in accordance with the basic policy.
  - Each ministry shall obtain consent of the cabinet secretariat to their rough estimate
- Specifically;
  - The cabinet secretariat shall adjust each ministry's estimate to a comprehensive plan for promotion of medical R&D and if necessarily require each ministry to make an amendment to their estimate.
  - Each ministry shall make an amendment to their estimate in accordance with a requirement of the cabinet secretariat and report details of amendment to the cabinet secretariat.
  - Each ministry shall submit their budget demands obtained cabinet secretariat's consent to the ministry of finance in collaboration with the cabinet secretariat.

3. The new independent administrative agency's functions; Grants and funding for medical R&D in an integrated fashion

- Instead each ministry implements, the new independent administrative agency shall centrally allocate grants to researchers/institutions in order to continue nation's R&D projects that cover phases from basic research to development of practical use without an interval.
- Promoting medical R&D more efficiently and effectively, the agency shall also implement the budget for infrastructure development (ex. a subsidiary for development of core hospital for clinical research/trial) in an integrated fashion.

4. Allocation on Special Coordination funds for the promotion of Medical R&D

- The HQ shall allocate on special coordination funds for the promotion of medical R&D across the ministries in order flexibly and efficiently to respond to advance in medical R&D projects and adoption of application for medical R&D subsidies etc..
- Special Coordination funds shall be appropriated from a part of scientific and technological innovation promotion funds (tentative name) entered in the budget of the Cabinet Office.

provisional translation

The new system of implementation of the Health and Medical Strategy

Headquarters of Healthcare Policy(HHP)

The HQ shall

- develop a comprehensive plan for promotion of medical R&D.
- integrate medical R&D budget requests of relevant ministries.
- strategically and intensively decide allocating promotional adjustment funds .

Adopt agenda based on the comprehensive plan for promotion of medical R&D

Manage and integrate both allocated grants to researchers/scientists and institutions, and funding

※ Integrate the budget for infrastructure development into a new agency

Integration of medical R&D budget requests

Researchers' bottom-up Scientific Research

Grant-in-Aid for Scientific Research (KAKENHI)

Smoothly transit discovered seeds

Nation's top-down scientific/clinical R&D

- The government will allocate about \100 billion for grant and funding into a new agency.
- management nation's top-down project s by Program Directors and Program Officers belonging the new agency

Infrastructure development

Core hospital for clinical research/trial etc.

Steadily implement the clinical research/trial based on the extra-international standard

Funds for individual Research

※ Universities, Institutions, Researchers/ Scientists

Intramural research

National Institutions

Measure on source of revenue for Institutions

※ National Center for Global Health and Medicine, RIKEN, National Institute of Advanced Industrial Science and Technology, National Institute of Infectious Diseases etc.

Implement researches based on the comprehensive plan for promotion of medical R&D

Budget Bill for Medical Research in FY 2014

1$ = 100yen

	FY 2014		FY 2013
New Agency	121.5 billion yen (MEXT57.0、MHLW47.6、METI16.9)	+20.3 billion yen +20.1%	101.2 billion yen (MEXT44.7、MHLW40.2、METI16.3)
Related Resarch Institutes	74.0 billion yen (MEXT20.0、MHLW45.5、METI8.5)	+ 2.7 billion yen + 3.7%	71.3 billion yen (MEXT15.5、MHLW47.6、METI8.1)

MEXT: Ministry of Education, Culture, Sports, Science and Technology
MHLW: Ministry of Health, Labor and Welfare
METI: Ministry of Economy, Trade and Industry

Cooperation Project among Related Ministries

For Development of New Medicine and Medical Devices

- Medicine 25.4 billion yen
- Medical Devices 11.2 billion yen

For Novel Medical Technologies

- Regenerative Medicine (iPS cells, ES cells etc.,) 15.1 billion yen
- Genomic Medicine 7.0 billion yen

For Clinical Study and Clinical Trial

12.1 billion yen

For Specific Diseases

- Cancer 17.2 billion yen
- Mental Diseases and Neurologic Diseases 7.1 billion yen
- Emerging and Re-emerging Infectious Diseases 5.3 billion yen
- Rare Diseases 9.3 billion yen

5. Implementation of Genomic Medicine Project

Nation's top-down funds	Intramural funds
FY2014 budget : \ 5,5B (FY2013 supplementary budget : \ 3,0 B)	FY2014 budget : \ 1,6 B (FY2013 supplementary budget : \ 0,8 B)

To improve medical care and health care for common diseases including cancer and lifestyle-related diseases, MEXT and MHLW cooperate for the implementation of Genomic Medicine project.

Base on the "Health and Medical Strategy" by Japanese government in June 2013, this project promotes clinical application of genomic research findings for aiming at the return to the public quickly, in parallel with the strengthening of genomic research infrastructure.

[Goals to be achieved by 2015]

- Construct biobank network
- Establish Central Genome Center (CGC) and Medical Genome Center (MGC)
- Construct Japanese reference genome sequence (Japanese RefSeq)
- Build comprehensive genomic variation DB linked to clinical phenotypes

[Goals to be achieved by 2020–30]

- Improvements for the medical and health care of lifestyle diseases
- Establish predictive diagnostics for cancer incidence and severe ADR
- Start clinical genomic research for depression and dementia
- Clarify the pathogenesis of neurological diseases, etc.

Development of research infrastructure → **Clinical application**

Biobank Network construction → ***Central Genome Center installation*** → ***Medical Genome Center installation*** → ***Implementation of Genomic Medicine for all generations***

[Taylor-made medical treatment program]
Budget : ¥ 1,8 B
(supplementary budget : ¥ 3,0 B)

BioBank Japan

BBJ
(IMSUT & RIKEN)
Disease-oriented biobank
(200,000 patients)

National Center Biobank Network
(Budget intramural : ¥ 1,1 B)

NCBN
(NCC, NCNP, NCVC, NCGM, NCCHD, NCGG)
Disease-oriented biobank
cooperated with 6 national center

[Tohoku Medical Megabank Program]
(Budget : ¥ 3,6 B)

Tohoku Medical Megabank Project

TMMB
(Tohoku Univ. & Iwate Med Univ.)
Population-based biobank
(150,000 local residents planned)

Central Genome Center

CGC
(RIKEN & IMSUT)

Large-scale genomic research
Strengthening of Genomic Research infrastructure

Coordination secretariat

Coordinate Biobanks, CGC and MGC
Management and quality control of samples and information

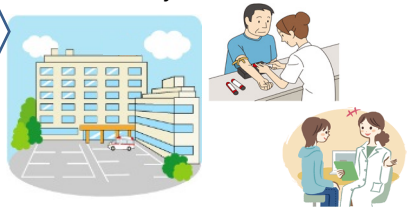
Long-term survey of disaster residents
- Local-resident cohort (80,000 people)
- Three-generation cohort (70,000 people)

Universities
Studies for disease mechanisms

Medical Genome Center
Budget : ¥ 0,4 B
(supplementary budget : ¥ 0,8 B)

MGC

Clinical application of genomic information
Strengthening of clinical research by use of highly-specialized hospital functions



Based on high quality evidence from genomic research, MGC establish
- optimized treatment through prediction of drug responses
- optimized **predictive diagnostics**
- optimized **preventive health care** for disease

(Examples)

Childhood diseases
- **Autism**
- **Cancer**

Epilepsy

Depression

Lifestyle diseases
- **Stroke**
- **CHD**
- **Diabetes**

etc.

Cancer
- **Lung ca.**
- **Breast ca.**
- **Prostate ca.**

etc.

Drug side effects

Dementia
DM nephropathy

Realize optimized diagnosis, treatment, and prevention

Extend healthy life expectancy

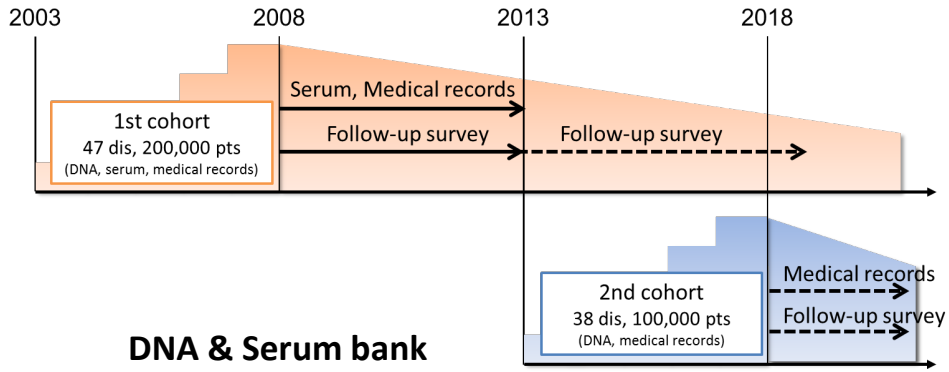
Taylor-made medical treatment program (The Biobank Japan Project)

FY2014 budget: \ 1,8B
(suppl. budget: \ 3,0B)

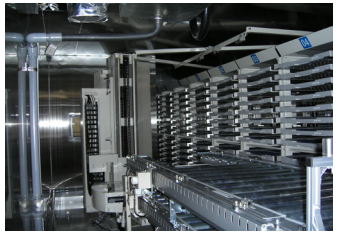
Overview

- Taylor-made medical treatment program was started in 2003 as a Leading Project of MEXT for the implementation of personalized medicine
- In the 1st period (2003-2007), this program constructed a large disease-oriented biobank (BioBank Japan) in collaboration with 66 hospitals in all areas of Japan.
- In the 2nd period (2008-2012), this program performed large-scale GWAS using the samples collected in the BioBank Japan and identified >260 novel susceptibility genes or loci for various diseases and drug responses.
- In the 3rd period (2013-2017), this program expands biobank infrastructure, further promote genomic research and move forward to apply findings into clinical research in collaboration with other national projects.

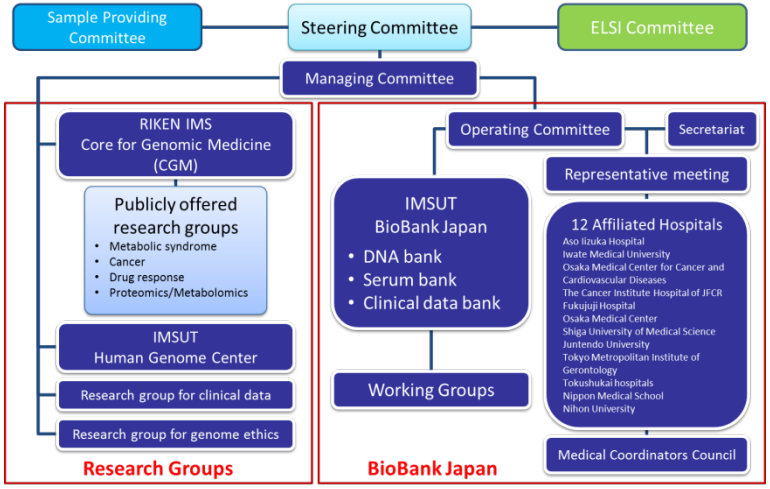
Research infrastructure of the BioBank Japan



DNA & Serum bank



Organization



BioBank Japan samples in the 1st cohort
(199,998 patients, 340,298 cases)

Disease	N	Disease	N	Disease	N
Hyperlipidemia	53,863	Hay fever	6,282	Hepatitis B	1,508
Diabetes	44,346	Glaucoma	6,135	Hematological cancer	1,478
Cataract	26,067	Prostate cancer	5,694	Esophageal cancer	1,453
Brain infarction	18,862	Unstable angina	5,286	Uterine cervical cancer	1,258
Arrhythmia	19,037	Rheumatoid arthritis	4,449	Nephrotic synd.	1,180
Stable angina	17,655	Lung cancer	4,396	ILD	1,158
Myocardial infarction	13,988	Periodontitis	3,958	Uterine corpus cancer	1,087
Heart failure	10,063	ASO	3,824	Pulmonary tbc	1,011
Bronchial asthma	9,561	COPD	3,504	Ovarian cancer	928
Osteoporosis	8,376	Liver cirrhosis	3,348	Keloid	896
Colorectal cancer	7,638	Atopic dermatitis	3,002	ALS	785
Gastric cancer	7,166	Brain aneurythm	2,999	Drug eruption	740
Urolithiasis	7,028	Epilepsy	2,727	Pancreas cancer	569
Breast cancer	6,629	Basedow disease	2,494	Gallbladder cancer	504
Hepatitis C	6,392	Liver cancer	2,509	Febrile seizure	341
Uterine fibroid	6,217	Endometriosis	1,907		(as of Oct. 2013)

NCBN: National Center Biobank Network by Integrated Research Institutes & Hospitals for Specific Diseases

Geriatric diseases

Neurology and psychiatry

Child health & development

Biobank and detailed clinico-pathological info

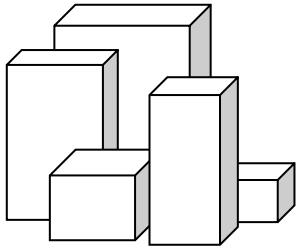
Cerebral & cardiovascular dis.

Biobank inventory data
Limited clinico-pathological info

Infectious dis.
Metabolic syndrome
Autoimmune dis.

Cancer

Research at NCs



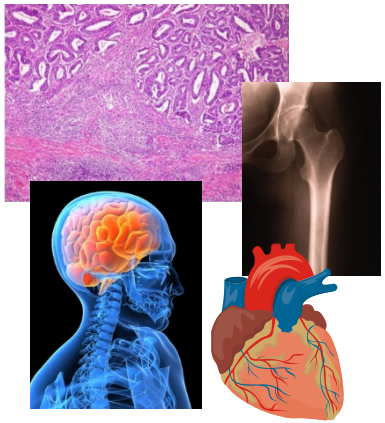
Drug R&D, etc

Academias, industries

Drug development & personalized medicine

Catalog DB
for One-stop access
Since Dec 2013

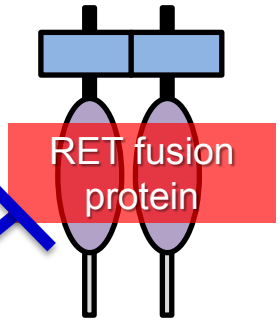
Germline DNA	13,429
Plasma/serum	21,112
Tissues	75,824
etc.	



One recent example (cancer)

RNA sequencing of lung cancer tissues

RET kinase inhibitors



Novel driver mutation

(Kohno T, et al. Nat Med 2012)

Multi-center IIT for rare subtypes

東北メディカル・メガバンク機構
TOHOKU MEDICAL MEGABANK ORGANIZATION

Tohoku Medical Megabank Project

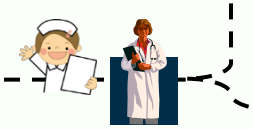
FY2014：\ 3,6 B
（FY2013：\ 4,2 B）

Objective: Revitalization of medical care in disaster-hit area of massive quake and tsunami of March 11, 2011 (Great East Japan earthquake) and develop infrastructure for next-generation medicine through a large-scale cohort study in the disaster-hit areas.

- Revitalization of local medicine through health check-up and medical services to eliminate health concerns of the affected residents
- Construct biobank for next-generation medicine through a large cohort study with genomic information

Concept: To create new innovative industries such as drug discovery and genomic medicine, this plan conducts genomic research through construction of biobank of 150,000 residents by the health survey in Miyagi and Iwate prefecture where massive earthquake and tsunami suffered many people.

Affected residents of Great East Japan earthquake (150,000)



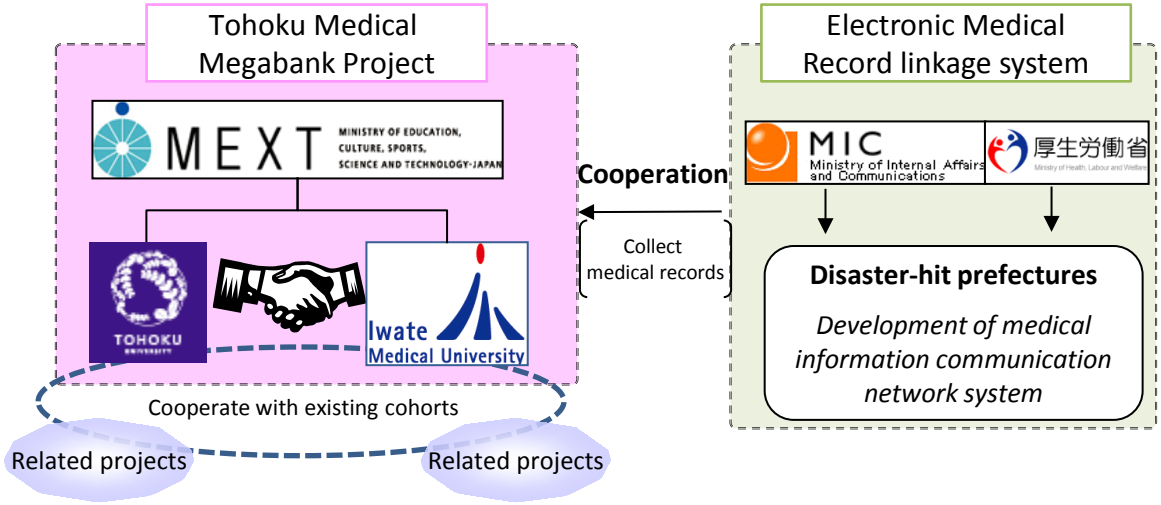
Highly motivated medical personnel conduct health survey in the affected areas

Health records
biological samples

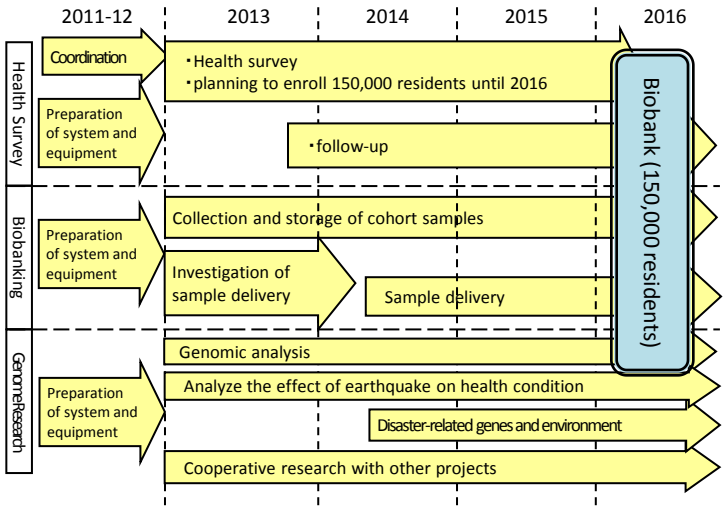
Construct biobank by collecting health records and biological samples through the survey

Analyze disaster-related diseases (CHD, stroke, neuropsychiatric disorders etc.) for the drug discovery or personalized medicine

Organization



Roadmap



Practice of Genomic Medicine @ The Institute of Medical Science, The University of Tokyo (IMSUT)
- From Supercomputer to Research Hospital -

1000 people are working in this campus

Genomic Medicine @ IMSUT

Organization

Departments

- Department of Microbiology and Immunology
- Department of Cancer Biology
- Department of Basic Medical Sciences

Research Centers

- Human Genome Center
- Center for Experimental Medicine
- Advanced Clinical Research Center
- Center for Stem Cell and Regenerative Medicine
- International Research Center for Infectious Diseases

Research Hospital (135 beds)

Supercomputer System

- Budget: $10M/Year
- Performance: 225 TFLOPS
- Storage: 3 PB (Lustre) + 2 PB (Nearline)

Genomic Medicine @ IMSUT Research Hospital

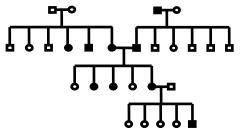
Since 2001

GM Organization

Hospital

Clinical Departments

Team Genomic Medicine (TGM)



Clinical Laboratory

Genetic Laboratory

Human Genome Center

Laboratory of DNA Information Analysis

Laboratory of Sequence Analysis

Advanced Clinical Research Center

Division of Clinical Genome Research

Division of Molecular Therapy

Japanese Association of Hospitals for Genetic Medicine

Tokyo Genetic Counseling Network

Staff Members

- Doctors and Nurses
- Genetic counselors
- Clinical psychologists
- Genome scientists

Patients and Clients

- Cancer
- Hereditary diseases
- Common diseases
- Genetic issues

Businesses and Studies

- Genetic test for neoplasms: ~ 400 /year
- Genetic counseling: 30-40 cases/year
- Genetic Dx of hereditary tumors: ~10 /year
- Development of personalized medicine

Extension to Whole Genome Sequencing, and More@IMSUT

Since 2013

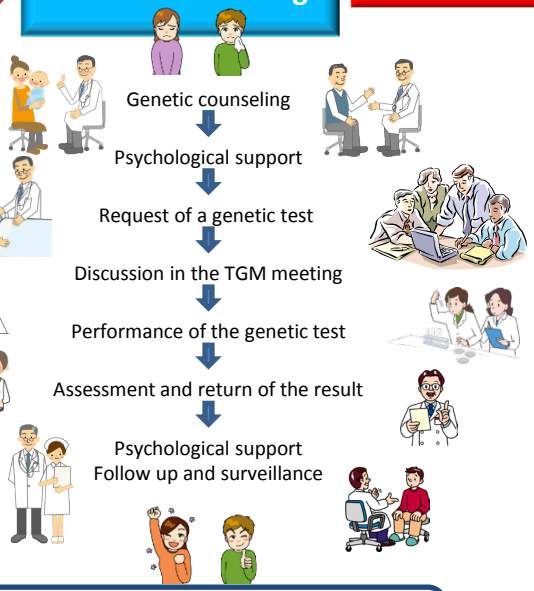
Patient

Specimen

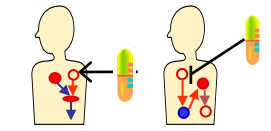
GCT@IMSUT
Yoichi Furukawa, MD, PhD

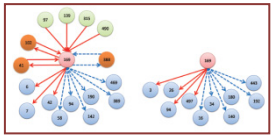
ELSI Team@IMSUT
Kaori Muto, PhD

Genetic Counseling



Prediction of Medical Intervention





Decision Support System (not yet)

- Optimizing therapeutics
- Avoiding adverse reactions by anticancer drugs
- Personalized medical examination/ Surveillance

Leukemia
Lymphoma
Gastrointestinal Cancer

Extension to

Whole Genome Sequence
Exome Analysis
Transcriptome Analysis
Epigenome Analysis (not yet)

Personal Genomes and Omics Data

NGS Facility
Nanopore Sequencer (not yet)

Data Analysis and Interpretation

Sequencing and Data Analysis Facilities & Management

Satoru Miyano, PhD

Human Genome Center

Yoichi Furukawa, MD, PhD
Arinobu Tojo, MD, PhD

Advanced Clinical Research Center
Research Hospital

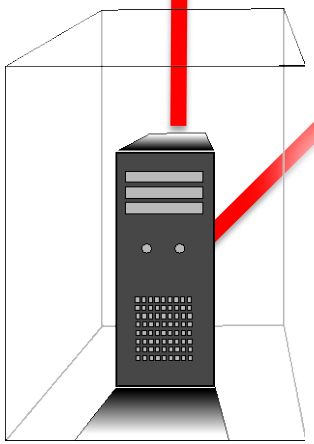
Sequencing and Data Analysis Facilities & Management @ IMSUT

Closed Network

Separated from medical record

Being expanded

Clinical Sequence Laboratory



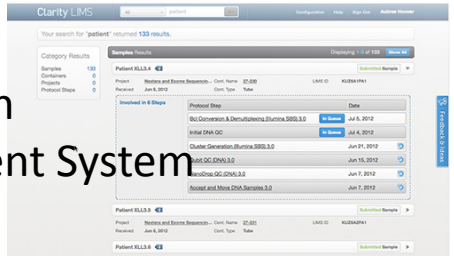
Highly Secured Supercomputer System for Clinical Sequence

Computation nodes: 3,840 CPU cores

Storage: Lustre file system (642TB)

All logs from input to output are automatically recorded with software versions, parameters, who did, etc.

Laboratory Information Management System (LIMS)



Data Analysis Rooms

VPN connected to Clinician's office

Control Room

U TOKYO is founding "*Int'l Genomic Medicine Research Organization*"

(IMSUT, Graduate School of Medicine, RCAST, Graduate School of Frontier Science)

東京大学 THE UNIVERSITY OF TOKYO

Innovation for therapy and prevention

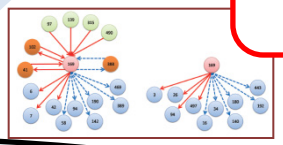
- Optimizing therapeutics
- Avoiding adverse reactions
- Personalized medical examination/ Surveillance
- Pesonalized Prevention

U Tokyo Hospital (1500 beds) & IMSUT Research Hospital

Implementing Genomic Medicine

NGS

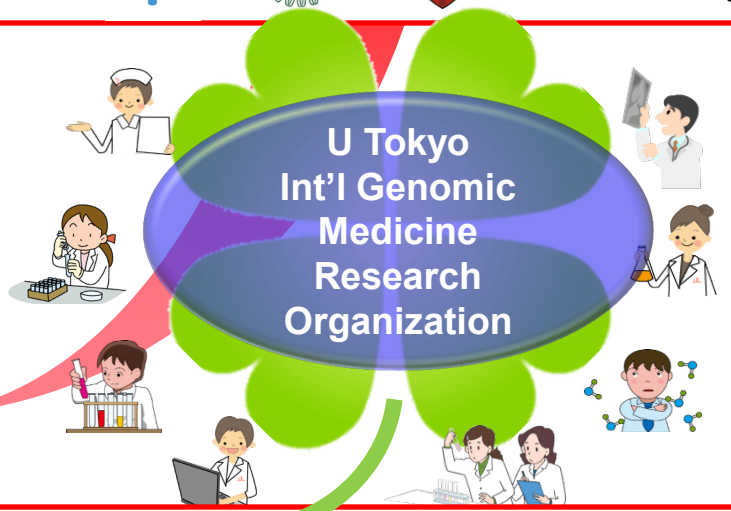
EMR



Medical Informatics for Genomic Medicine

GSFS IMS GSM

Research Center for Advanced Science and Technology



Biomedical Big Data

Human Genome Center
Institute of Medical Science, University of Tokyo

Supercomputer System with Large Storage

- Whole Genome
- Transcriptome
- Epigenome

+

- Familial/lifestyle data
- Diagnosis/therapy data
- Progress after treatment

Foster specialists in genomic medicine