APPENDIX: PARTICIPANTS IN THE PLANNING PHASE OF THE ICGC
(NOV 2007 – MARCH 2008)

INTERNATIONAL CANCER GENOME CONSORTIUM (ICGC) WORKING GROUPS

Clinical and Pathology Issues	Quality Standards of Samples	Genome Analyses	Informed Consent and Privacy Protections	Sample Size/Study Design	Data Management/ Databases and Coordination	Data Release, Data Tiers, Intellectual Property, and Publications
Lynda Chin	**Peter Lichter**	**Mike Stratton**	**Bartha Knoppers**	**Eric Lander**	**Lincoln Stein**	**Mark Guyer**
Jean-Yves Blay	Carolyn Compton	Olli Kallioniemi	Martin Bobrow	Ron DePinho	Cameron Brennan	Daniela Gerhard
William Dalton	Andy Futreal	Ed Liu	Wylie Burke	Doug Easton	Arul Chinnaiyan	Karen Kennedy
Tony Green	Youyong Lu	Marco Marra	Kazuto Kato	Gadi Getz	Peter Good	Brad Ozenberger
Stan Hamilton	Miguel Angel Pita	John McPherson	Karen Kennedy	Partha P. Majumder	Joe Gray	
Timothy Ley		Brad Ozenberger	Brad Ozenberger		J Gowrishankar	
Ed Liu		Henk Stunnenberg	Daniel Tan		David Haussler	
Paul Mischel		Daniel Tan	Susan Wallace		David Housman	
Kenneth Pienta		Brandon Wainwright	Henry Yang		Tim Hubbard	
Rajiv Sarin		Rick Wilson			Bartha Madhavan	
Daniel Tan					Paul Spellman	

Core Bioethical Elements that need to be complied by ICGC members. (1)

For prospective research, ICGC members should convey to potential participants, that:

- The ICGC is a coordinated effort among related scientific research projects being carried on around the world.
- Participation in the ICGC and its component projects is voluntary.
- Samples and data collected will be used for cancer research, which may include whole genome sequencing.
- The patient's care will not be affected by their decision regarding participation.
- The samples collected will be in limited quantities; access to them will be tightly controlled and will depend on the policy and practices of the ICGC-member project. **At least** a small percentage of the samples may be shared with international laboratories for the purposes of performing quality control studies.

Samples may be shared.

- Data derived from the samples collected and data generated by the ICGC members will be made accessible to ICGC members and other international researchers through either an open or a controlled access database under terms and conditions that will maximize participant confidentiality.

Data will be shared. The ICGC will adopt "two-tier access system".

Two level data access system is currently used in human genome databases.

Risks for the privacy of participants.
(through re-identification etc.)

⇩

■To avoid social and ethical problems, dbGaP and WTCCC split their research data into open-access data and controlled-access data (that includes individual genotype and phenotype data).

■Controlled-access data are distributed to only qualified researchers. (after a review by the Data Access Committee)

They established detailed mechanisms to ensure that controlled-access data is properly used.

Core Bioethical Elements that need to be complied by ICGC members. (2)

- Those accessing data and samples will be required to affirm that they will not attempt to re-identify participants.
- There is a remote risk of being identified from data available on the databases.

Risk of identification.

- Once data is placed in open databases, that data cannot be withdrawn later.
- In controlled access databases the links to (local) data that can identify an individual will be destroyed upon withdrawal. Data previously distributed will continue to be used.
- ICGC members agree not to make claims to possible IP derived from primary data.

No IP with primary data.

- No profit from eventual commercial products will be returned to subjects donating samples.

ICGC-member projects will be responsible for carrying out these policies and guidelines. Nevertheless, ICGC acknowledges that the informed consent process used by ICGC members will necessarily differ according to local, socio-cultural and legal requirements.

ICGC guidelines for information that should be provided to participants regarding prospective research (1)

•ICGC administration, oversight, funding, duration, ethics and scientific approvals and contact persons.

• Who will be recruited and the approach.

• Procedures involved in participation, including any physical and psychological 'risks.'

• Information on the kinds of samples and data that will be collected.

• Protections in place 'locally' to ensure the confidentiality of samples and data.

• Research uses of data (ICGC members are encouraged to seek the broadest level of consent that is appropriate at the local level; e.g.. "cancer and related research; cancer and other disease-related research").

Broad, but not blanket consent.

• Whether access to samples will be available for purposes such as validation, quality control, research, etc.
• Whether access to medical/administrative health records will be sought.

ICGC guidelines for information that should be provided to participants regarding prospective research (2)

• Whether information regarding participation will be included in medical records.

• Provided it is agreed at recruitment, if clinically important and validated findings emerge during the initial recruitment and screening phase, or in the early research, attempts will be made to pass this information back via the clinician, by whatever mechanism may be agreed at the local level.

Possibility of returning results to participants.

• Information on whether or not compensation/reimbursement is available.
• Withdrawal procedures, such as sample retrieval and/or destruction and data coding and anonymization procedures.
• Ownership of samples.
• Prospects for third-party commercialization and intellectual property procedures.
• Purposes for which the uses of data and samples will not be allowed (if required to be named by country).

• How information on the general results of the research will be disseminated.
• Who participants can contact regarding their concerns.

From: International Cancer Genome Consortium (ICGC) Goals, Structure, Policies and Guidelines (http://icgc.org/files/ICGC_April_29_2008.pdf)

Current status of ICGC

In addition to the coordination of actual experimental procedures;

- Details for data access are being finalized.
  Formation of IDAC (International Data Access Committee).
  and other mechanisms are needed.
- Sample collection and analysis has been started in some of the Projects.
- Research protocols of other projects are under review by IRBs in their countries.
- Procedures for the use of retrospective samples need to be finalized.

4 working groups plus International Steering Committee are working on various issues.

Issues that need to be considered in Japan and other Asian countries

1. More effective collaboration between scientists and experts on ethics and public policy. (Example: Establishing an ethics and policy group within a large research project like ICGC.)
2. Stronger network of those who work in the field of ethics and public policy is necessary to share information and exchange opinions. (Newly created journal, *Asian Bioethics Reviews*, and efforts by Centre for Law and Genetics of University of Tasmania will facilitate networking, but we need more activities.)
3. Empirical research on:
   1) the governing systems of various projects.
      (What kind of issues do researchers face?)
   2) the opinions of the public and experts (scientists and researchers on ethics and public policy).

Result of the Questionnaire on the Japanese Guidelines on Genomic/Genetic Research - with a proposal of amendments –

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Comparative Law Center / Kyoto University
Leader of the Research Project on "Ethical Issues on New Medicine Using Genomic information
Grant-in-Aid for Scientific Research, Ministry of Health, Labour and Welfare

Objectives of the Questionnaire

Questionnaire on the Experiences and the Expectation of Researchers for the Reform of the Guidelines on Genomic/Genetic Research
(Common Guidelines of Three Ministries)

Background

- Gap between the advancement of genomic/genetic research and the provisions of Guidelines

  The Guidelines cannot catch up the advancement ?
- Possibility of new developments (especially, Human Whole Genome Re-sequencing)
- To offer a basis for discussion for the reform of the Guidelines
- To aim at making a new guidelines for clinical use of genomic information

Questionnaire - Method

- Questionnaire on 8 important issues in the Guidelines

  Ask researchers problems encountered in the experiences

  multiple choice + free written answer

  Aim at clarifying the current situation and the problems which researchers face in their research

  Try to avoid statistic data processing in order to clarify concrete situations
- Ask opinions on the Guidelines

  1. Necessity of matching the provisions of the Guidelines : On which points?

  2. Difficulties encountered in the research in the application of the Guidelines

  3. Examples of useful concepts / provisions

  4. Other opinions and suggestions

Outline of the Answers

- Addressees : Researchers in genomic and genetic research in Japan (Names are picked up from different sources and covers leading researchers
- Response : 212 / 942 22.2 %
- Types of research

  1) Multifactorial diseases (57.1)

  2) Monogenic disorders (36.8)

  3) Side effects (27.8)

  4) Tracking research (21.7)
- Insufficiency of the Guidelines (Q.4-1) : 12.7
- Difficulties in Informed Consent Procedure : 12.7
- Disclosure of personal genetic information : 32.5 (from participant 91.3, family 37.7)
- Difficulties in Ethical Review Procedure : 11.3
- Difficulties in Joint research : 83.0 (with abroad 35.2)
- Difficulties in Genetic Counseling : 25.5 (with aprticipant 85.2、blood relatives 64.8)
- Issues relating to and necessity of provisions on Bank / Data base:

  Protection of samples and genetic information 66.0、

  Management and use 62.3、Collection of samples 47.2

Insufficiency of the Guidelines

A. Limited scope of the Guidelines to research

⇒ Need of the guidelines for clinical use of genetic information

B. Insufficient response to "genetic business"

C. Excessively rigid provisions

= Need of attention to promote research

D. Coordination with other relevant guidelines

E. Insufficient response to pharmaco-genomics

F. Too narrow discretion of the researchers

Points for reform

- Informed Consent Procedure
- Treatment of samples and data
- Joint research with foreign institutions
- Ethical review system
- New Types of research = biobank and database

Informed Consent

Prior, informed and free consent
Current procedure
= One sample, one research, one informed consent
No multiple use, no deposit after research
New possibility
= general / blank / broad consent
conditions : sufficient information should be given on future possibilities of research
No easy use of blank consent = risk of abuse

Samples and Data

1) Linked anonymisation as principle
So far, unlinkable anonymisation has been the principle, linkable anonymisation as exception
2) Safety of storage of samples and data
3) Quality control of samples and data
4) Renewable system of collection
This point relates to the biobank issue.

Joint Research

Current Guidelines requirement

Application of stricter rules among rules applicable in the relevant countries

However, such requirement is not realistic, so that we may propose that each research team of each country should apply the rules applicable to that country, regardless of the degree of strictness of rules.

Ethical Review System

The most important issue

= knowledge and ability of the members of IRB

Often members of the IRB are not truly aware what is the ethical review.

The quality of discussion is not assured.

⇒ Training system of the members of the IRB may be needed.

biobank and database

Current situation in Japan

- No national regulation on biobank so far.
  Each so-called biobank has or has not it's own regulation.
- Size, objective, scope of use and accessibility are diversified.
- Cooperation is not always assured among researchers. Small size biobank is in many cases closed to the third party researchers.

Elements to be included in the biobank regulation

- **Informed Consent Procedure**
  Broad consent
  good understanding on what is the biobank
- **Linkable Anomysation of samples**
  Protection of samples and personal information
- **Samples and Data collection**
  Quality control needed
- **Accessibility to samples and data**
  Openness is required. However, the data quality should be universally (nationally) uniform.
- **Governance system more than ethical review system**
  Size, substantial elements and social impact are so important that traditional ethical review system may not be adequate or sufficient.

平成 20 年度

公開国際シンポジウム「バイオバンクとゲノム医療

—ゲノム医療の生命倫理—」

資料

International Symposium
Biobank and Genomic Research
-Bioethics of Genomic Medicine -
10:00 –13:00 22nd March, 2009
Kyoto University Clock Tower
International Exchange Hall III

Biobank Japan and its Ethical Framework

Kaori MUTO, Ph.D.
Dpt. of Public Policy
Institute of Medical Science
The University of Tokyo

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Topics

- What is Biobank Japan?
- Ethical Framework?—Then and now
- Based on the critique "Governance by stealth" by Triendl and Gottweis
  - incld in "Biobanks—Governance in Comparative Perspective", edited by H. Gottweis and A. Peterson, Routledge, 2008
  - Muto used to be a member of Bioethics Committee (Committee for ELSI) and a leader of the Ethics and Governance Working Group in the project.

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Biobank Japan Project

By any definition, Biobank Japan is among the world's largest and best-funded efforts to build a large-scale biorepository linking biological materials, DNA samples, and data on genetic variation and clinical information taken from actual patients. At the same time, Biobank Japan is one of the least debated or controversial of the large biobank projects currently being developed. [...] Biobank Japan stands out in terms of its size, overall budget, investment in fascilities, and perhaps also the sheer speed [...]

(Triendl and Gottweis, 2008)

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Biobank Japan Project

- 5 yr-project launched in June 2003 (First Term)
- Extended 5 more yrs in April 2008 (Second Term)
- Headed by Yusuke Nakamura (IMSUT)
- Supported by Ministry of Education, Culture, Sports and Technology (MEXT)

文部科学省 リーディングプロジェクト
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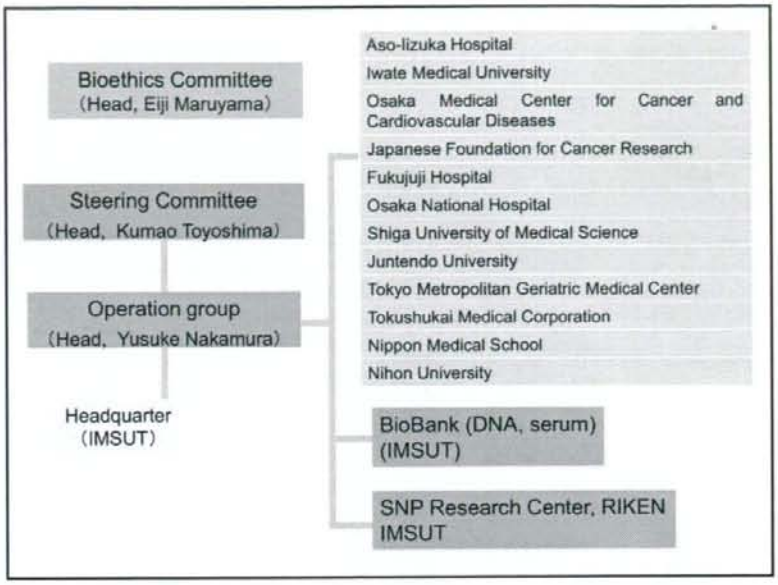
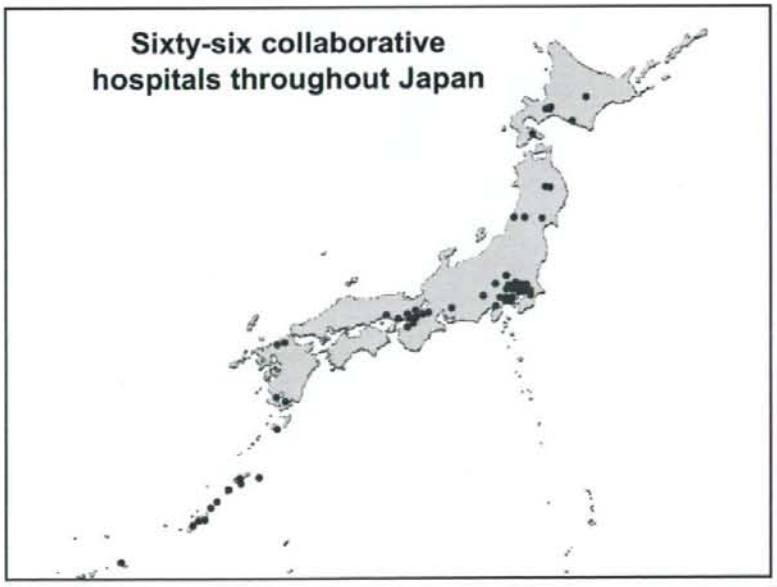
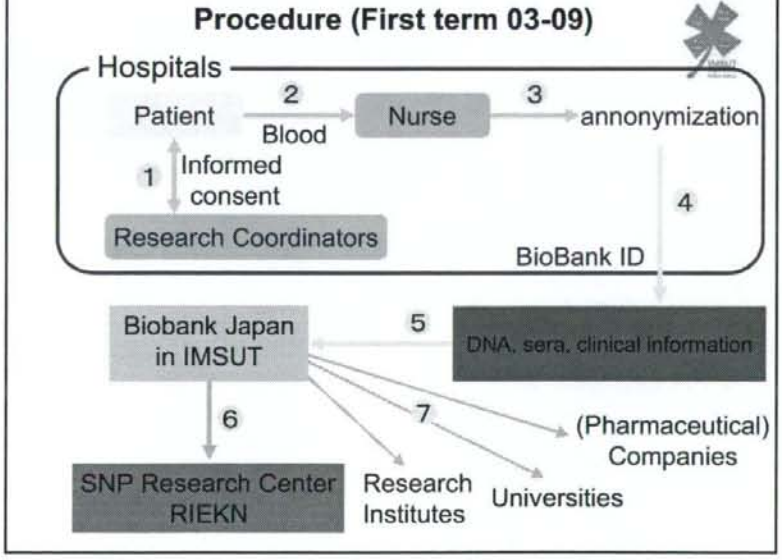

Bioethics Committee
(Head, Eiji Maruyama)
Steering Committee
(Head, Kumao Toyoshima)
Operation group
(Head, Yusuke Nakamura)
Headquarter
(IMSUT)
Aso-Iizuka Hospital
Iwate Medical University
Osaka Medical Center for Cancer and Cardiovascular Diseases
Japanese Foundation for Cancer Research
Fukujuji Hospital
Osaka National Hospital
Shiga University of Medical Science
Juntendo University
Tokyo Metropolitan Geriatric Medical Center
Tokushukai Medical Corporation
Nippon Medical School
Nihon University
BioBank (DNA, serum)
(IMSUT)
SNP Research Center, RIKEN
IMSUT


Sixty-six collaborative hospitals throughout Japan

Registered diseases (47 common diseases)

Diabetes mellitus	Bronchial asthma	Hysteromyoma
Hyperlipidemia	Pulmonary fibrosis	Endometriosis
Cataract	Pollinosis	Uterine cancer
Glaucoma	Drug induced eruption	Ovarian cancer
Myocardial infarction	Tuberculosis	Breast cancer
Unstable angina	Atopic dermatitis	Esophageal cancer
Angina pectoris	Hepatitis B	Gastric adenocarcinoma
Arrhythmias	Hepatitis C	Colorectal cancer
Congestive heart failure	Liver cirrhosis	Prostatic carcinoma
ASO	Ureterolith	Hepatocellular carcinoma
Febrile convulsion	Nephrotic syndrome	Cholangiocarcinoma
Epilepsy	Basedow's disease	Pancreatic cancer
Cerebral infarction	Rheumatoid arthritis	Myeloproliferative diseases
Cerebral aneurysm	Keloid	Lung cancer
ALS	Periodontosis	
COPD	Osteoporosis	

Procedure (First term 03-09)



Biobank Japan Project

- First Term (2003-08)
  - Building basic structures: banking, anonymization, security and database
  - Collection of DNA, sera, and clinical information in four years from 199,742 patients with 47 common diseases (Recruitment period: 4.5 yrs)
  - Systematic genomics (mainly SNP analysis)
  - Identification of genes with medical importance

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Biobank Japan Project

- Second Term (2008-12)
  - Collection of sera and clinical information from some amounts of participants once a year
  - Systematic genomics (mainly SNP analysis) and proteomics analysis on cancer and heart diseases with broader research community.
  - Data cleaning of clinical information
  - Prognosis survey from all participants

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Biobank Japan Project

- Not designed as epidemiological cohort study based on community population.
- Neither an isolated project nor a national biobank.
- Built into the larger research infrastructure in genomics, followed by SNPs research at the IMSUT, in which MEXT had already invested.
- Thus, BBJP is also defined as an aspect of a large PGx project rather than a provider of biological resources to other scientists.

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Public consultation

Biobank Japan remains largely unknown to the Japanese public and [...] even to the country's medical and biological research community. [...] None of the ministry's advisory bodies had been consulted on the subject of the project, virtually no debate took place. [...] [It] was eventually selected by the finance ministry from around 40 "Leading Projects" at the MEXT.

(Triendl and Gottweis, 2008)

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Public consultation

- Very short preparation period after budget compilation
- No public consultation before launch
- Independent and ethical advisory board (Bioethics Committee) was established for the project, funded by the MEXT
- The committee's main agenda: monitoring of sample collection process

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Biobank Newsletter and Café Sciantifique

- "Biobank Newsletter" (2007-) is quarterly newsletter for participants, coordinators and the public since 2007.
- Summary of latest scientific articles using samples and data from BBJ, voices from participants and commentary.
- We're planning to have a Café Scientifique this summer.

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Bioethics Committee and Biobank Japan

In many ways, the [Bioethics Committee's] reports read almost like summaries of a site review or an inspection. [...] [T]he issues raised by the committee are somewhat superficial and rather removed from some of the key questions facing a large biobank project. [...] While arguing the Bioethics Committee has followed a somewhat 'bureaucratic agenda' and is only limited use to the project, Nakamura also points out that individual members of the committee have helped considerably to finetune the sample collection process.

(Triendl and Gottweis, 2008)

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Bioethics committee and Biobank Japan

- The Bioethics Committee was inflicted with "information asymmetry", which made the committee concentrate on the sample collection process.
- Little attention has been paid to issues of management, use, transfer and ownership of the resources collected for future change.
- Recently, project leader asks consultation on specific theme to the Bioethics Committee.

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Standard consent process of the BBJP

1. Physicians ask patients whether they are interested in details about the BBJP after their regular consultation.
2. If patients were interested in details, research coordinators show the DVD (10 minutes) and explain the overviews of the BBJP using special pamphlets.
3. Patients are asked whether to donate their DNA as well as sera and clinical information once a year.
4. They are also required to give consent to several conditions such that their personal genotyped data won't be disclosed, IP issues, rights to withdraw consent and so on.
5. They can give consent and blood right after this explanation; otherwise they can take time to think twice at home.
6. In total, it takes about 30 minutes in average.

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Questionnaire survey to participants

- We conducted self-reported questionnaire (4 pages) survey to research participants at one hospital of the BBJ project. This study was approved by the IRB of the IMSUT.
- Study period: 2007.10.23-2008.10.22
- Male 792 : Female 584
- 1,378 samples
- Respond Rate=70.2%

figure(1) agegroups