towards high-quality clinical trials and
implementation of genomic medicine

Medical Ethics and Personal Information Protection

Course : **ATLAS Training Program**

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[Educational background]

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Topics of today's lecture

1. Handling patient information

2. ELSI in cancer genomic medicine

(ELSI: Ethical, Legal, and Social Issues)

1. Handling patient information

Introduction

Handling patient information within time-honored ethics

- Hippocratic Oath (Ancient Greece): “Whatever I see or hear in the lives of my patients, whether in connection with my professional practice or not, which ought not to be spoken of outside, I will keep secret, as considering all such things to be private.”
- Recommendation for doctors engaged in biomedical research involving human subjects (commonly known as the Declaration of Helsinki, First Version 1964, Latest Version 2013): “Every precaution must be taken to protect the privacy of research subjects and confidentiality of their personal information” (Paragraph 24)

Japanese legislation on patient information

- Persons subject to confidentiality: Article 134 of the Penal Code: “When a physician, pharmacist, pharmaceuticals distributor, midwife, attorney, defense counsel, notary public or an individual engaged in a similar profession, without just cause, discloses another person's confidential information which has come to be known in the course of such profession, imprisonment for not more than 6 months or a fine of not more than 100,000 yen is imposed.”

  → Medical professionals are required to protect patient confidentiality to maintain a relationship of trust between the medical professional and patient. Private matters cannot be discussed with someone who does not respect confidentiality. Limited information provided by the patient is disadvantageous for ensuring appropriate medical care.

- Target of protection of personal information

  → Recently, compliance with the Act on the Protection of Personal Information has become required in various settings, including in medical care and medical research.

What is protection of personal information?

- Various types of information are handled in all areas of society, and some information may be personal information that can identify a specific individual
- The distribution of information has a role in societal development and enables people to have prosperous lives
- Personal information must be protected because it may harm the individual if it is misused

  Example 1. If your own profile is inaccurate, you may be judged based on this incorrect information

  Example 2. If you are elderly, unwell, and/or living alone, leaking your address and telephone number may pose a threat to your life and property

- Controlling one's own information is a right

⇒ The Act on the Protection of Personal Information is the law that addresses the two incompatible issues of "Proper and effective use of personal information" and "Protection of personal information"

⇒ The concepts presented in the Act on the Protection of Personal Information have been adopted as rules in research ethics.

Scope and definition of personal information
(Article 2, Paragraph 1 of the Act on the Protection of Personal Information)

Personal information is information that corresponds to any of the following:

a) A specific individual can be identified based on the information alone

   Example: An individual can be identified using information such as their name, facial image, photograph, combination of subject data.

b) A specific individual cannot be identified with the information alone but can be identified by matching the information with other information (information external to the research, such as medical records)

c) Items included under individual identification codes (Article 2, Paragraph 2 of the Act on the Protection of Personal Information):

   ① Biometric information (facial features, fingerprints, iris, voice quality, movement, genomic information, etc.)

   ② National identification number, health insurance number, etc.

Furthermore, personal information containing the patient's medical history falls under Special care-required personal information (Article 2, Paragraph 3 of the Act on the Protection of Personal Information).

Genomic information corresponding to individual identification codes

(Article 1 of the Cabinet Order on the Act on the Protection of Personal Information)

Base sequences that comprise the DNA collected from a cell: Genome data (character string notation of base sequences comprising the DNA collected from a cell), such as whole-genome sequencing data, whole-exome sequencing data, whole-genome single nucleotide polymorphism (SNP) data, sequencing data comprised from 40 or more individual SNPs, and short tandem repeats (STR), which enable authentication of the person using the genetic information.

Anonymously processed information = Creation of non-personal information

- Numerous approaches can be used to create anonymously processed information from personal information (Article 2, Paragraph 6 of the Act on the Protection of Personal Information) and handle the information as non-personal information
  - Delete all individual identification codes contained in the personal information
  - Delete specific descriptions

    Example: Delete medical history descriptions for conditions with very few cases
  - Top (bottom) coating: Summarize particularly large or small numbers contained in the personal information database subject to processing

    Example: For age-related data, compile numerical data for cases aged 80 years and older as data for “≥80 years”

⇒ These processing methods are not considered to be realistic in a medical care or medical research setting. Alternatively, if they were implemented, medical care would become infeasible. Therefore, patient information, particularly genomic information, must be considered as personal information.

Obligations when using special care-required personal information of patients

- Safe management of personal information: Omitted because it is unrelated to ELSI

- Acquisition and use of personal information with the person's consent in the following three scenarios:
  ① New acquisition of personal information
  ② Secondary use of personal information other than the initial purpose of use
  Example: Using information originally obtained for medical treatment for research
  ③ Provision of personal information to a third party
  Example: Exchanging personal information within a research group (analysis data, etc.)

Obligations of Japanese researchers conducting international joint research

- Explaining to the subject that the samples and information used in the research will be sent overseas and obtaining their consent

  ⇒ The explanation must include ① Outline of the research, ② Name of the foreign country, ③ Information on the system used to protect personal information in the respective country, and ④ Mechanism for protecting personal information adopted by the foreign research organization

- When confirming the intention of the individual regarding cooperation in the research using methods other than consent,

  ・It is necessary for the research to be conducted by an academic research organization for academic research purposes, and the scope of individuals using the samples/information for research must be clear

  ・The right of refusal by the research subjects is guaranteed by publishing the following information on the research organization's website: ① Outline of the research, ② Details of the samples/information to be sent, ③ Information on the overseas researchers, ④ How (background) the samples/information were acquired, ⑤ Research group principal investigator and affiliated organization, ⑥ Scope of people who will be using the research, ⑦ Supervisor managing the samples/information, ⑧ That use of the samples/information will be stopped at the request of the person subject to research, and ⑨ Methods for receipt of the request indicated in ⑧ Commonly known as Opt-out response

  ・Regular confirmation of information on the system used to protect personal information in the respective country, and the mechanism for protecting personal information adopted by the foreign research organization, even after providing samples/information

Foreign countries where Japan's Personal Information Protection Commission has ascertained the personal information protection system (as of July 2022)

United States, United Arab Emirates, Israel, India, Indonesia, Ukraine, Australia, Qatar, Canada, Cambodia, Costa Rica, Singapore, Switzerland, Thailand, Republic of Korea, Taiwan, People's Republic of China, Tunisia, Turkey, New Zealand, Panama, Philippines, Brazil , Vietnam, Peru, Hong Kong, Malaysia, South Africa, Myanmar, Mexico, Mongolia, Laos, Russia

(https: //www.ppc.go.jp/personalinfo/legal/kaiseihogohou/#gaikoku)

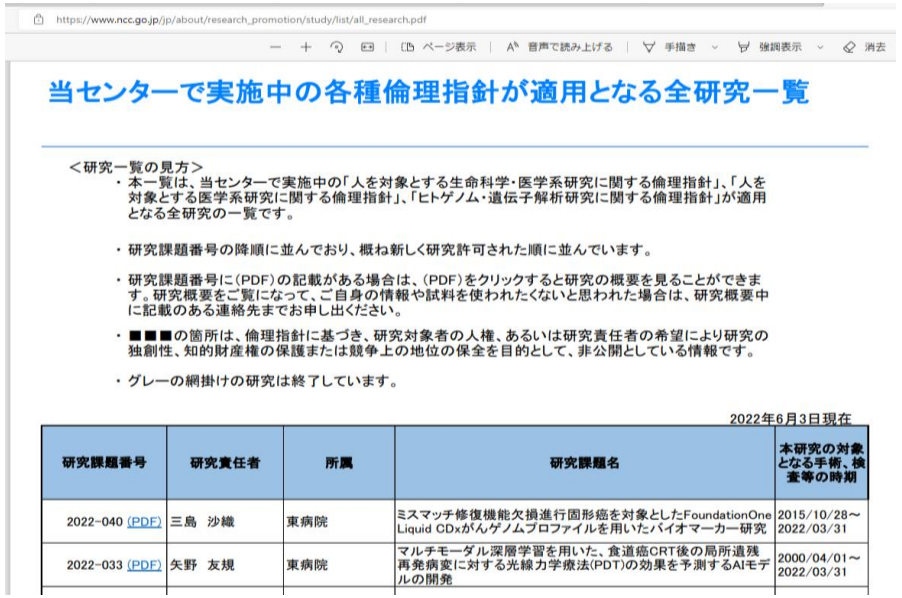
→ Japanese researchers must explain "Information on the system used for protection of personal information" to the research subjects based on this information

Opt-out response

1

2

3



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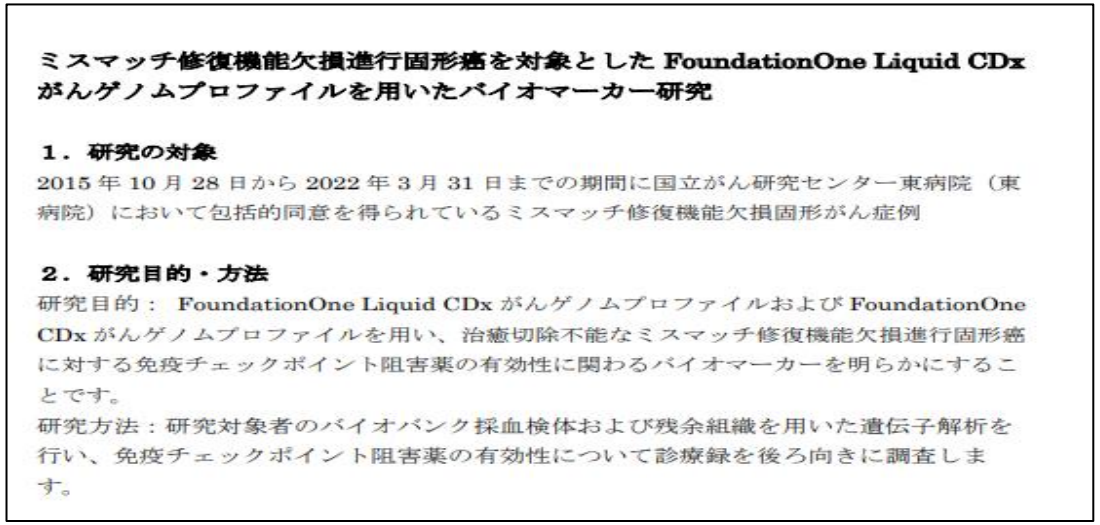

2. ELSI in cancer genomic medicine

Appropriate explanations to patients

- Both patients and society should be informed on patients who are eligible for cancer multi-gene panel testing. For example, at the Center for Cancer Genomics and Advanced Therapeutics, National Cancer Center (C-CAT), these patients are restricted to those “with solid cancers without standard treatment or patients with solid cancers with local progression or metastasis who have completed standard treatment.”

- The researchers should explain the possible outcomes of the test, and what the researchers know and do not know about the test, namely that even if a patient undergoes cancer multi-gene panel testing, gene mutations may not be detected or drugs may not be available for the patient. The researchers should not excessively raise the patient’s expectations.

Who is informed of the test results?

- Properties of genetic information inherited in germ cells
  - ① Immutability : Remains unchanged throughout a person's life
  - ② Predictability : Ability to predict future development of certain diseases
  - ③ Commonality : The same genes may be shared within a family

- Should test results (particularly positive test results) be communicated to persons other than the patient? What should be done if the patient refuses disclosure of the information to his or her family? And other relevant questions.
  - ⇒ These questions must be examined while considering matters such as the doctor's duty of confidentiality to the patient, relationship between the doctor and patient's family, and whether there is subsequent possible medical treatment.

Handling secondary findings of the test

- Multi-gene panel testing may incidentally reveal gene mutations as secondary findings to the primary purpose of the test, as these tests examine a wide range of genes and genes in both normal cells and tumor cells. These gene mutations may also be germ cell line mutations.

- The secondary findings may also be useful to the patient and their family; however, this information may also create a large psychological burden, particularly if no treatments are available (treatment and/or prevention)

⇒ Before the patient undergoes the test, it is essential to explain the possibility of discovering these secondary findings to the patient and ensure that they understand the implications of the results. Ask the patient's wishes beforehand regarding disclosure of the results; if mutations are found, respond to the patient after consultation with the attending physician.

Another school of thought on the disclosure of secondary findings is that "Disclosure of findings should be limited to findings that are definitely pathogenic variants, which are beneficial for management of the health of the patient and/or their family, and for which treatment and/or preventive measures are available. Results should not be disclosed if there are no clear benefits, if disclosure may create a psychological burden for the patient and/or their relatives, and/or may cause misunderstanding due to insufficient accuracy or reliability of the findings."

Handling genetic discrimination

- A Japanese survey (conducted in February 2017) showed that approximately 3% of respondents experienced discrimination or inappropriate treatment based on genetic information. Experiences included rejection of life insurance applications by an insurance company and increased insurance premiums.
  - Application rejected or increased insurance premiums set by the insurance company when applying for life insurance: 1.2%
  - Application rejected or increased insurance premiums set by the insurance company when applying for medical insurance: 1.2%
  - Application rejected or increased insurance premiums set by the insurance company when applying for education endowment insurance: 0.6%
  - Desire for legislation regarding the use of genetic information: 71%
- There are concerns that if people fear discriminatory treatment, they will not agree to the use of their genetic information or genomic information for research, which may slow new drug development and the introduction of genomic medicine.

Initiatives in Japan : Japan Medical Association and Japanese Association of Medical Sciences

The Japan Medical Association and Japanese Association of Medical Sciences' "Joint Statement on 'Prevention of Unfair Discrimination and Social Disadvantage due to Genetic Information/Genomic Information'" (April 2022)

1. The national government should urgently prepare legislation to prevent unfair discrimination and social disadvantage based on genetic/genomic information, and the relevant ministries should establish social and economic policies, including insurance and employment policies, to prevent inappropriate handling of an individual's genetic/genomic information. A committee should be established to investigate how the information should be used to promptly evaluate measures in line with the actual situation in Japan.

2. Competent authorities must build a mechanism of guidance and supervision to urgently encourage businesses and related organizations, such as insurance companies, which may handle genetic/genomic information, to adopt voluntary restraints related to the handling of this information and ensure that the contents of these measures are made available to consumers in an easy-to-understand and appropriate format.

3. Businesses and related organizations, such as insurance companies, which may handle genetic/genomic information, should hold open discussions on the handling of this information and promptly investigate and publish voluntary restraint measures.

Initiatives in Japan: The Life Insurance Association of Japan

The Life Insurance Association of Japan “Handling Genetic Information in Life Insurance Underwriting and Payment Practices” (May 2022)

○ In life insurance underwriting and payment practices, judgements are made objectively, rationally, and fairly based on information such as names of diseases, whether surgery is scheduled, and the content of medical procedures, such as administered medication, stated on declaration forms or medical certificates, and this information is handled with basic respect for human rights.

○The results of genetic tests are not collected or used during the aforementioned handling of information. Furthermore, if the results of genetic tests are included in the submitted declaration form or medical certificate, or information equivalent to the results of genetic tests can be identified from the name of the disease, family history, or records of genetic counselling provided by a doctor, these results of genetic tests and equivalent information to the results of genetic tests are not used. The same applies to handling of the results of genome analysis conducted for research.

○If new issues are recognized, such as advances in medical care and the maturation of social debate in response to changes in the environment and circumstances, especially with the future spread of genomic medicine and progression in the accurate understanding of genetic information by consumers, we will respond in a timely and appropriate manner, including reviewing these handling procedures with reference to the guidance of regulatory authorities and the opinions of persons involved in medical care and medicine. However, we will maintain these handling procedures until the time of review.

US Genetic Information Nondiscrimination Act

- Prohibiting health insurance and employment discrimination based on genetic information
- It shall in principle be unlawful to request or require an individual or a family member of the individual to undergo genetic testing
- It shall in principle be unlawful to request, require or purchase genetic information with respect to an individual or a family member of the individual
- The purpose of the legislation is two-fold
  - ① Suppress discrimination based on genetic information and prevent eugenics
  - ② Misuse of genetic information in the fields of medical insurance and employment causes unease in those who intend to use genetic testing to obtain the latest preventive and therapeutic technologies, and in those who intend to participate and cooperate in human genome research. These actions may negatively impact the curbing of medical expenses and progress of human genome research.

United States Antidiscrimination Laws

	Law	Summary of the law	Corresponding law in Japan
Level 5	GINA, 2008	Prohibits discrimination based on genetic information with respect to health insurance and employment	None
Level 4	Americans with Disabilities Act, 1990	Prohibits discrimination against individuals with disabilities in all areas of public life, including employment and public facilities	Disability Discrimination Act (2013)
Level 3	Rehabilitation Act, 1973	Prohibits discrimination based on disability in programs conducted by federal agencies	None
Level 2	Age Discrimination in Employment Act, 1967	Prohibits employment discrimination against persons 40 years of age or older	None
Level 1	Civil Rights Act, 1964	Prohibits discrimination based on race, color, religion, sex or national origin in education, public facilities, government, and employment	None

- GINA is positioned at the cutting edge and top level of the United States antidiscrimination debate and legal system
- From submission (1995) to enactment (2008): Enacted after 13 years of deliberation

Summary

- Patient information and genomic information must be handled as special care-required personal information

- ELSI topics related to cancer genomic medicine: Content explained to the patient, persons informed of the test results, handling of secondary findings, and genetic discrimination

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