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ARTICLE

The survey of public perception and general knowledge of genomic research and medicine in Japan conducted by the Japan Agency for Medical Research and Development

Yutaka Hishiyama[1,2] · Jusaku Minari[3,4] · Narufumi Suganuma[1]

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Abstract

Japan has been proactively promoting genomic medicine initiatives as national policy. With rapid pace developments in genomic medicine, an increasing number of patients and their families will be able to access genomic information. In such circumstances, a consideration of public interests and an assessment of the general knowledge about genomic research and genomic medicine are becoming imperative. This study aims to elucidate public attitude to the handling of genetic information during research and general medicine. The results of the questionnaire survey of 3000 people have revealed the following points: (1) older participants were likely to have better knowledge of genetic information than younger ones; (2) people with better understanding of genetic information tended to care more strongly about technical issues; (3) respondents with higher literacy regarding genetic issues favored stricter rules for handling of genetic information compared to handling of ordinary medical data; and (4) research community and funding agencies should preserve and develop public trust in genomic research and medicine. These results suggest the importance of education for younger people, the need of different types of explanation and transparency aimed at individuals with different levels of knowledge about the genome, and indicate the adequacy of the current governmental guidelines.

Introduction

Human genome research is associated with inherently embedded controversies. Numerous ethical, legal, and social implications have been debated in not only national but also international context for long time. Discussions and coordination activities that take place at the United Nations Educational, Scientific and Cultural Organization are representative examples of such debates [1]. The Government of Japan also addressed ethical, legal, and social implications of human genomic research and published corresponding guidelines [2]. The reason why genomic research has been given considerable attention is that it may have an undesirable social impact on the maintenance of genetic privacy and provide tools for potential discrimination due to mishandling of the information about individual genomes [3]. Human genome research has also been specifically considered in recent legal regulations on personal information, including the 2016 EU General Data Protection Regulation and the 2015 amended Act on the Protection of Personal Information in Japan.

Furthermore, nowadays, personal genome information not only underlies the basis of biomedical science but is increasingly utilized in medical practice. In January 2015, the U.S. President Barack Obama announced the "Precision Medicine Initiative" that aimed to accelerate progress toward a new era of precision medicine [4]. Francis S. Collins and Harold Varmus explained the concrete measures of the Initiative that included utilization of

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✉ Yutaka Hishiyama
KHA03262@nifty.com

[1] Department of Environmental Medicine, Kochi Medical School, Kochi University, Kochi, Japan

[2] Ministry of Education, Culture, Sports, Science and Technology, Tokyo, Japan

[3] Japan Agency for Medical Research and Development, Tokyo, Japan

[4] Uehiro Research Division for iPS Cell Ethics, Center for iPS Cell Research and Application (CiRA), Kyoto University, Kyoto, Japan

large-scale biologic databases to share individual genome sequences [5].

In the UK, the 100,000 Genomes Project was launched in 2012. The Project aimed "to create a new genomic medicine service for the National Health Service (NHS)—transforming the way people are cared for. Patients may be offered a diagnosis where there wasn't one before. In time, there is the potential of new and more effective treatments" [6]. Rare diseases and cancer were selected as the areas that had the most immediate potential for clinical benefit from genome-wide analysis using sequencing and in late 2018, whole-genome sequencing will become part of the NHS England commissioned national genomic medicine service for rare inherited diseases and cancer [7].

In Japan, after the publication of the report produced by the Committee for the Promotion of Genomic Medicine under the Headquarters of Health and Medicine, the Consortium on the Promotion of Cancer Genomic Medicine created by the Ministry of Health, Labor, and Welfare worked out an implementation plan on genomic medicine in cancer in June 2016 [8]. These documents have provided the framework for the use of genetic data of cancer patients in practical medicine from 2018. This means that as more patients than ever are getting involved in genomic research, genetic information will become familiar not only to a limited set of people that directly participate in genomic studies but also to broad public in the near future. Thus, understanding of public perceptions and cooperation with the public to implement genomic medicine approaches can be of key importance when considering broad utilization of genetic information in the society in future.

Public attitudes toward genetic research in Japan have been analyzed previously [9, 10]. However, those surveys have not necessarily covered the regulations and utilization of genetic information in research activities and practical medicine from ethical and policy perspectives. The present study aimed to elucidate public attitudes toward handling of genetic information during research activities as well as during general medical practice routine. Such data should contribute to the promotion of scientific and medical activities that use genetic information. In addition, this study also focused on the knowledge of genetic terms by the participants and analyzed the relationships between genomic research literacy and attitudes to the availability of genetic information and rules of its handling.

Methods

Study background

The Japan Agency for Medical Research and Development (AMED) entrusted to the Mitsubishi Research Institute (MRI) in 2015 "The Survey of Public Attitudes toward Genetic Information in Science and Medicine". A simple superficial analysis of the survey results has been already published on the AMED web-site [11]. We received all survey information from the MRI, and the present study utilized and deeply analyzed all survey data to elucidate various points regarding the attitude to and awareness of various aspects of genomic research.

The institutional review board approval for the survey was obtained at the Kochi University (approval ID: 30-96).

Table 1 Characteristics of survey participants

Age (years)	Male	Female	Subtotal
20–29	300	300	600
30–39	300	300	600
40–49	300	300	600
50–59	300	300	600
60–69	300	300	600
Total	1500	1500	3000
Mean age	45.0	44.8	44.9
Standard deviation	13.8	13.7	13.8

Recruitment of the participants

The participants of the survey were 3000 people recruited from the Ordinary Citizens Panel consisting of people aged 20 to 69 years. Demographic data are shown in Table 1. The Panel belongs to the "Ordinary Citizens Market Forecasting System" managed by the MRI. The participants responded to the questions online. Three hundred people selected by sex and age were recruited, so that there were subgroups for every 10 years in the range between 20 and 69 years of age. Although age, sex, and residential prefecture of the participants had been collected as factors, the personal information by which an individual could be identified was not collected. The survey was performed for a week, from March 16 to March 22 in 2016, through the MRI website.

Questionnaire development

The purposes of the survey were to analyze participants' knowledge and perception of genetic information. Those included examining participants' preferences to receive individual genetic results, attitudes toward handling of genetic information, and concerns regarding the provision of informed consent.

To fulfil those purposes, a questionnaire was developed that took into account the surveys on genome research that had been carried out in Japan previously [9, 12]. During questionnaire preparation, suggestions and advices from researchers associated with genome and biobank projects in

Japan were also incorporated. In addition, some of the questions were focused on the regulatory issues regarding genome information, because the amended Act on the Protection of Personal Information was enacted in 2015 and accordingly, the revision of governmental ethical guidelines for genome research was expected at that time. It was envisaged initially that there has to be less than ten short and clear questions in the survey to avoid excessive over-burdening of the respondents. As a result, six questions were carefully selected in accordance with the purposes of the survey (Table 2).

Statistical analysis

Statistical analysis of the survey data was performed using EZR software [13] with a significance level of $\alpha = 0.01$ or 0.05 ($P < 0.01$ or $P < 0.05$, respectively). For the purpose of statistical analysis of relationship between the number of terms the participants knew and the measures of their interest strength in each questionnaire, the answer choices in Q2 were dichotomized into "interested", which included "moderately" and "very much" on the one hand, and "not interested", which included "not at all", "a little" and "neutral" on the other hand. For the same purpose, the answer choices in Q3 were dichotomized into "I wish to know", which included "moderately" and "very much", and "I do not wish to know", which included "not at all", "a little", and "neutral". Furthermore, for the purpose of statistical analysis, the age groups were dichotomized into "younger participants", which included participants in their twenties and thirties, and "older participants", which included participants in their forties, fifties, and sixties. Regarding the classification into "younger" and "older" participants, this study followed the approach of Henneman et al. [14], because there seems to be no clear standard boundaries between "younger" and "older".

Table 2 Questionnaire of the survey

Q1. Do you know the following ten terms: (1) gene, (2) DNA, (3) genetic information, (4) genome, (5) chromosome, (6) personal genome, (7) genome research, (8) pharmacogenomics, (9) DNA evidence, and (10) genetic test?

Q2. Are you interested in research or medicine with respect to genetic information (genetic constitution)? Please select one choice from the next 5 choices: very much, moderately, not at all, a little, neutral.

Q3. Do you wish to know your genetic information on the following points? Please select one answer from five choices for each point.

3.1 Susceptibility to lifestyle diseases (very much, moderately, not at all, a little, neutral). 3.2 Susceptibility to adult-onset clinically actionable diseases, such as breast cancer, ovarian cancer, or colorectal cancer. 3.3 Degree of response to drugs, such as anticancer therapeutics, and susceptibility to side effects. 3.4 Susceptibility to diseases that are difficult to prevent or cure, such as Alzheimer's disease. 3.5 Susceptibility to adult-onset clinically non-actionable diseases.

Q4. What points are considered important when genetic information is handled during research or medical activities? Please select two points from the following seven points: 4.1 purposes and significance of research or medicine; 4.2 accuracy and reliability of genetic information; 4.3 job category and specialization of the person who explains genetic information to participants or patients; 4.4 actions of researchers or medical staffs at return of participants' own genetic information; 4.5 actions of researcher or medical staff after return of their own genetic information; 4.6 strict management system of genetic information; and 4.7 avoidance of discrimination at the time of employment or insurance.

Q5. Personalized treatment and diagnosis are expected when scientific research or medical activities utilize genetic information. What rules should regulate handling of genetic information when it is utilized during scientific research or medical activities? Please choose one of the following five options: 5.1 under the same regulation as other ordinary research; 5.2 under stricter regulation than other ordinary research; 5.3 should not be handled except in very special cases; 5.4 should not be treated under any rules; 5.5 I do not know.

Q6. When research activities or medical treatments that utilize genetic information are performed, informed consent on handling of human samples and information is necessary to obtain. What cases should be clearly explained in the following nine cases when informed consent is obtained? 6.1 Case of providing samples and information to other research institutes and hospitals for research purposes; 6.2 case of providing samples and information to private companies for research purposes; 6.3 case of providing samples and information to overseas institutions for research purposes; 6.4 ase of providing samples and information to other research institutes and hospitals for medical treatment purposes; 6.5 case of providing samples and information to private companies for medical treatment purposes; 6.6 case of providing samples and information to overseas institutions for medical treatment purposes; 6.7 case of providing samples and information to other research institutes and hospitals for commercial purposes; 6.8 case of providing samples and information to private companies for commercial purposes; 6.9 case of providing samples and information to overseas institutions for commercial purposes.

Results

Participants' knowledge of genetics

The participants were asked to choose terms that they knew from the list of ten terms mentioned in Q1 of the questionnaire (Table 2). More than two-thirds of the participants responded that they knew the terms "gene", "DNA", "DNA evidence", and "chromosome", whereas only few participants responded that they were aware of the terms "personal genome" and "pharmacogenomics". Chi-squared tests that explored the effect of age and sex on the knowledge of these terms showed that older participants were more likely to know eight terms ("gene", "DNA", "DNA evidence", "chromosome", "genetic test", "genome", "genetic information", and "genomic research") than younger ones (Table 3). However, younger participants

Table 3 Comparison of the numbers of the individuals who responded that they knew the terms below between younger and older sets as well as between male and female sets

	Gene	DNA	DNA evidence	Chromo-some	Genetic test	Genome	Genetic information	Genomic research	Personal genome	Pharmaco-genomics
Younger participants ($N = 1200$)	1068 (89.0)	1049 (87.4)	927 (77.2)	832 (69.3)	655 (54.6)	535 (41.8)	455 (37.9)	234 (19.5)	108 (9.0)	29 (2.4)
Older participants ($N = 1800$)	1715 (95.3)	1684 (93.6)	1532 (85.1)	1464 (81.3)	1266 (70.3)	939 (52.2)	889 (49.4)	459 (25.4)	117 (6.5)	31 (1.7)
P value	1.27×10^{-10}**	1.07×10^{-8}**	5.39×10^{-8}**	4.22×10^{-14}**	2.20×10^{-16}**	5.51×10^{-5}**	7.62×10^{-10}**	2.20×10^{-4}**	0.01328*	0.231
Odds ratio	0.401	0.479	0.594	0.519	0.507	0.738	0.626	0.713	1.42	1.41
95% Confidence intervals	0.298–0.537	0.369–0.622	0.490–0.720	0.436–0.618	0.434–0.592	0.635–0.857	0.538–0.728	0.594–0.855	1.07–1.89	0.817–2.44
Male participants ($N = 1500$)	1382 (92.1)	1362 (90.8)	1188 (79.2)	1120 (74.7)	908 (60.5)	848 (56.5)	760 (50.7)	415 (27.7)	153 (10.2)	2.7% (41)
Female participants ($N = 1500$)	1402 (93.4)	1371 (91.4)	1271 (84.7)	1175 (78.3)	1014 (67.6)	626 (41.7)	584 (38.9)	268 (17.9)	72 (4.8)	1.3% (19)
P value	0.205	0.608	9.86×10^{-5}**	0.02*	6.46×10^{-5}**	6.97×10^{-16}**	1.32×10^{-10}**	2.06×10^{-10}**	2.93×10^{-8}**	6.17×10^{-3}**
Odds ratio	0.828	0.929	0.6861374	0.815	0.735	1.82	1.61	1.76	2.25	2.19
95% Confidence intervals	0.620–1.10	0.716–1.20	0.566–0.831	0.686–0.969	0.631–0.856	1.57–2.10	1.39–1.87	1.47–2.10	1.67–3.05	1.24–4.01

Figures in parentheses indicate percentage. *$P < 0.05$, **$P < 0.01$

were significantly more likely to know the term "personal genome" than older ones. It was also observed that female participants were more likely to know the term "DNA evidence", "genetic test", and "chromosome" than male participants, whereas male participants were more likely to know the terms "genome", "genetic information", "genomic research", "personal genome", and "pharmacogenomics" than female participants.

Sex had a significant effect on the average number of known genetic terms as male participants knew 5.45 terms (standard deviation, SD = 2.48), whereas females knew 5.22 terms (SD = 2.18; $P = 7.84 \times 10^{-3}$, Student's *t*-test). Furthermore, younger males knew 4.95 terms (SD = 2.60) on average, whereas for older males, the average number of known terms was 5.79 (SD = 2.34; $P = 1.07 \times 10^{-10}$, Student's *t*-test). Similarly, younger females knew fewer terms on average (4.83 terms, SD = 2.29) than did older females (5.49 terms, SD = 2.06; $P = 8.34 \times 10^{-9}$, Student's *t*-test). Thus, the results of the survey demonstrated that older participants of both sexes knew more terms than younger participants.

General interest of the participants in genomic research and medicine and in their own genetic susceptibility to diseases

The participants were asked to select one answer to 5-point Likert scale questions regarding the degree of their interest in genomic research and medicine (Q2 of the questionnaire, Table 2). The Mann–Whitney *U* test was used to analyze the ranked responses (1. Not at all, 2. A little, 3. Neutral, 4. Moderately, 5. Very much) of the participants. It revealed that age affected the degree of interest in genomic research and medicine (Table 4).

The participants were also asked to answer on the 5-point Likert scale whether they wished to receive information about their own susceptibility to four types of diseases and sensitivity to drugs (Q3 of the questionnaire, Table 2). More than half of the participants chose "very much" or "moderately" in each disease case (Table 4). The Mann–Whitney *U*-test was also used to analyze the ranked responses (1. Not at all, 2. A little, 3. Neutral, 4. Moderately, 5. Very much) of the participants. It revealed that age significantly affected responses to questions 3.3 (mean rank of the younger participants was 3.45 and that of the older participants was 3.61, $P = 6.63 \times 10^{-5}$) and 3.4 (mean rank of the younger participants was 3.55 and that of the older participants was 3.71, $P = 2.30 \times 10^{-5}$). In addition, we found that females were more likely to be "interested" than males when responding to 3.2 (mean rank of the male participants was 3.49 and that of the female participants was 3.73. $P = 3.28 \times 10^{-8}$), 3.3 (mean rank of the male participants was 3.43 and that of

Table 4 General interest of the participants in genomic research and medicine and in their own genetic susceptibility to diseases

	1 Not at all	2 A little	3 Neutral	4 Moderate	5 Very much	Mean	SD	*P* value[a]
Q2								
Younger participants ($N = 1200$)	265 (22.1)	267 (22.3)	156 (13.0)	387 (32.3)	125 (10.4)	2.87	1.35	0.0123*
Older participants ($N = 1800$)	239 (13.3)	558 (31.0)	146 (8.1)	711 (39.5)	146 (8.1)	2.98	1.25	
Q3-1								
Younger participants ($N = 1200$)	122 (10.2)	123 (10.3)	224 (18.7)	479 (39.9)	252 (21.0)	3.51	1.22	0.267
Older participants ($N = 1800$)	185 (10.3)	210 (11.7)	250 (13.9)	752 (41.8)	403 (22.4)	3.54	1.24	
Q3-2								
Younger participants ($N = 1200$)	117 (19.1)	116 (9.7)	216 (18.0)	449 (37.4)	302 (25.2)	3.59	1.24	0.187
Older participants ($N = 1800$)	182 (10.1)	200 (11.1)	224 (12.4)	706 (39.2)	488 (27.1)	3.62	1.27	
Q3-3								
Younger participants ($N = 1200$)	119 (9.92)	157 (13.1)	234 (19.5)	441 (36.8)	249 (20.8)	3.45	1.23	6.63×10^{-5}**
Older participants ($N = 1800$)	166 (9.22)	215 (11.9)	228 (12.7)	736 (40.9	455 (25.3)	3.61	1.24	
Q3-4								
Younger participants ($N = 1200$)	120 (10.0)	132 (11.0)	210 (17.5)	449 (37.4)	289 (24.1)	3.55	1.23	2.30×10^{-5}**
Older participants ($N = 1800$)	163 (9.06)	204 (11.3)	199 (11.1)	669 (37.2)	565 (31.4)	3.71	1.27	
Q3-5								
Younger participants ($N = 1200$)	139 (11.6)	154 (12.8)	228 (19.0)	417 (34.8)	262 (21.8)	3.42	1.28	0.815
Older participants ($N = 1800$)	221 (12.3)	288 (16.0)	243 (13.5)	623 (34.5)	425 (23.6)	3.41	1.33	
Q2								
Male participants ($N = 1500$)	265 (17.7)	417 (27.8)	163 (10.7)	525 (35.0)	130 (8.67)	2.89	1.29	0.0598
Female participants ($N = 1500$)	239 (15.9)	408 (27.2)	139 (9.27)	573 (38.2)	141 (9.40)	2.98	1.29	
Q3-1								
Male participants ($N = 1500$)	175 (11.7)	162 (10.8)	243 (16.2)	598 (39.9)	322 (21.5)	3.49	1.26	0.0893
Female participants ($N = 1500$)	132 (8.8)	171 (11.4)	231 (15.4)	633 (42.2)	333 (22.2)	3.58	1.20	
Q3-2								
Male participants ($N = 1500$)	182 (12.1)	158 (10.5)	244 (16.3)	581 (38.7)	335 (22.3)	3.49	1.28	3.28×10^{-8}**
Female participants ($N = 1500$)	117 (7.8)	158 (10.5)	196 (13.1)	574 (38.3)	455 (30.3)	3.73	1.22	
Q3-3								
Male participants ($N = 1500$)	163 (10.9)	193 (12.9)	245 (16.3)	575 (38.3)	324 (21.6)	3.43	1.26	5.57×10^{-4}**
Female participants ($N = 1500$)	122 (8.13)	179 (5.97)	217 (14.5)	602 (40.1)	380 (25.3)	3.63	1.21	
Q3-4								
Male participants ($N = 1500$)	169 (11.3)	172 (11.5)	222 (14.8)	556 (37.1)	381 (25.4)	3.54	1.29	6.00×10^{-6}**
Female participants ($N = 1500$)	114 (7.60)	164 (10.9)	187 (12.5)	562 (37.5)	473 (31.5)	3.74	1.22	
Q3-5								
Male participants ($N = 1500$)	198 (13.2)	215 (14.3)	253 (16.9)	502 (33.5)	332 (22.1)	3.37	1.32	0.0505
Female participants ($N = 1500$)	162 (10.8)	227 (15.1)	218 (14.5)	538 (35.9)	355 (23.7)	3.46	1.29	

Figures in parentheses indicate percentage. *$P < 0.05$, **$P < 0.01$

SD standard deviation

[a]Mann–Whitney *U*-test

the female participants was 3.63, $P = 5.57 \times 10^{-4}$), and 3.4 (mean rank of the male participants was 3.54 and that of the female participants was 3.74, $P = 6.00 \times 10^{-6}$).

The relationship between the number of terms that the participants responded they knew and the strength of their interest in receiving information about their own genetic characteristics was analyzed by using the chi-squared test (Table 5). Furthermore, the Mann–Whitney *U* test was performed to analyze the same relationship (*P* values of Q2, Q3.1, Q3.2, Q3.3, Q3,4, and Q3.5 were 1.83×10^{-53}, 1.81×10^{-15}, 1.23×10^{-15}, 1.74×10^{-24}, 1.03×10^{-21}, and 4.74×10^{-12}, respectively, Supplementary Table 1). We found that the participants who knew many (>6) terms were more "interested" in receiving genetic results about various diseases significantly than the participants who knew few (<5) terms.

Table 5 Relationship between the number of terms the participants knew and the measures of their interest strength in each questionnaire

Questions	Many terms (more than 6 terms)	Few terms (less than 5 terms)	Odds ratio	95% confidence intervals	*P* value[a]
2	888 (64.9)	481 (35.1)	3.23	2.77–3.77	$<2.20\times10^{-16}$**
3.1	1037 (55.0)	849 (45.0)	1.84	1.58–2.15	1.33×10^{-15}**
3.2	1070 (55.0)	875 (45.0)	1.92	1.64–2.24	$<2.20\times10^{-16}$**
3.3	1068 (56.8)	813 (43.2)	2.25	1.92–2.62	$<2.20\times10^{-16}$**
3.4	1094 (55.5)	878 (44.5)	2.06	1.76–2.41	$<2.20\times10^{-16}$**
3.5	947 (54.8)	780 (45.2)	1.68	1.45–1.95	3.52×10^{-12}**
4.1	460 (52.7)	413 (47.3)	1.21	1.03–1.42	0.0198*
4.2	797 (55.9)	628 (44.1)	1.65	1.42–1.92	7.81×10^{-12}**
4.3	125 (51.2)	119 (48.8)	1.08	0.827–1.42	0.549
4.4	111 (50.9)	107 (49.1)	1.07	0.804–1.42	0.673
4.5	135 (55.8)	107 (44.2)	1.32	1.01–1.741	0.0379*
4.6	678 (61.0)	434 (49.0)	2.11	1.81–2.46	$<2.2\times10^{-16}$**
4.7	311 (47.0)	350 (53.0)	0.888	0.744–1.06	0.186
5.1	277 (49.9)	278 (50.1)	1.02	0.843–1.23	0.852
5.2	798 (60.4)	523 (39.6)	2.22	1.92–2.58	$<2.20\times10^{-16}$**
5.3	191 (54.7)	158 (45.3)	1.275	1.015–1.61	0.0351*
5.4	27 (27.0)	73 (73.0)	0.368	0.226–0.583	5.47×10^{-6} **
5.5	188 (27.9)	487 (72.1)	0.308	0.254–0.372	$<2.20\times10^{-16}$**
6.1	1000 (56.6)	799 (44.4)	1.87	1.61–2.18	$<2.20\times10^{-16}$**
6.2	842 (62.0)	517 (38.0)	2.55	2.20–2.97	$<2.20\times10^{-16}$**
6.3	728 (64.9)	393 (35.1)	2.77	2.37–3.24	$<2.20\times10^{-16}$**
6.4	747 (59.1)	518 (40.9)	1.97	1.69–2.28	$<2.20\times10^{-16}$**
6.5	678 (64.2)	378 (35.8)	2.55	2.18–2.98	$<2.20\times10^{-16}$**
6.6	612 (65.7)	319 (34.3)	2.65	2.25–3.12	$<2.20\times10^{-16}$**
6.7	794 (67.6)	380 (32.4)	3.46	2.96–4.06	$<2.20\times10^{-16}$**
6.8	765 (67.6)	366 (32.4)	3.36	2.87–3.95	$<2.20\times10^{-16}$**
6.9	756 (58.7)	531 (41.3)	1.94	1.67–2.25	$<2.20\times10^{-16}$**

Figures in parentheses indicate percentage. *$P < 0.05$, **$P < 0.01$

[a]Chi square test

Participants' perception of important points during handling of genetic information

The participants were asked to choose two of seven points that they considered to be important when genetic information is handled during research and medical activities (Supplementary Table 2). More than 30% of the participants chose points 4.1 "purposes and significance of research or medicine" (956 participants, 31.9%), 4.2 "accuracy and reliability of genetic information" (1425 participants, 47.5%), and 4.6 "strict management system of genetic information" (1112 participants, 37.1%). Point 4.7 "avoidance of discrimination at the time of employment or insurance" was chosen by 22% (661 participants) of all participants, whereas less than 10% of all participants chose points 4.3 "job category and specialization of the person who explains genetic information" (8.13%, 244 participants), 4.4 (7.27%, 218 participants), and 4.5 (8.07%, 242 participants) "actions of researchers or medical staff at (4.4) or after (4.5) the return of participants' own genetic information". Furthermore, when the relationship between the number of terms that the participants responded they knew and the preferences for important points regarding handling of genetic information was analyzed, points 4.2, 4.5, and 4.6 were significantly more frequently chosen by the participants who knew more than six terms (Table 5).

Participants' attitudes to the rules regulating the availability of genetic information

The participants were asked to choose one of the five possible options to regulate the availability of genetic information during research and medical activities (Q5). Forty-four percent of the participants (1321) chose 5.2 "stricter regulation than for other ordinary research", whereas the second most frequently chosen answer was 5.5 "I do not

Table 6 Numbers of participants who would request clear explanations regarding the provision of samples and genetic information for specific purposes 6.1–6.9

	Numbers of people	*P* value[a]	Odds ratio	95% Confidence interval
6.1	1799 (60.0)			
6.4	1263 (42.1)	$<2.2\times10^{-16}$**	2.06	1.86–2.29
6.7	1174 (39.1)	$<2.2\times10^{-16}$**	2.33	2.10–2.59
6.2	1359 (45.3)			
6.5	1056 (35.2)	1.86×10^{-15}**	1.52	1.37–1.69
6.8	1131 (37.7)	2.72×10^{-9}**	1.37	1.23–1.52
6.3	1121 (37.4)			
6.6	931 (31.0)	2.70×10^{-7}**	1.33	1.19–1.48
6.9	1287 (42.9)	1.39×10^{-5}**	0.794	0.715–0.882

Figures in parentheses indicate percentage. $^{**}P<0.01$

[a]Chi square test

know" (22.5%, 675 participants). The answer 5.1 "Under the same regulation as other ordinary research" was chosen by 555 participants (18.5%). Few participants chose 5.3 "Should not be handled except in very special cases" (11.6%, 349) and 5.4 "Should not be treated under any rules" (3.33%, 100). Older participants were more likely to choose 5.2 and 5.3 than younger ones, whereas younger participants chose 5.5 more frequently than older ones (Supplementary Table 3). Options 5.2 and 5.3 were also significantly more frequently chosen by the participants who knew more than six terms. On the contrary, options 5.4 and 5.5 were chosen significantly more frequently by the participants who knew less than five terms (Table 5).

Participants' concerns about the need of additional explanations during the request of informed consent

The participants were asked to consider nine cases when research activities or medical treatment utilize human samples and genetic information and choose those for which they felt clear explanations were needed before informed consent is obtained (Q6). To compare replies about research purposes and medical treatment purposes as well as replies about research purposes and commercial purposes, i.e., the circumstances that may require utilization of human samples and genome information, chi-squared tests between 6.1 and 6.4, 6.1 and 6.7, 6.2 and 6.5, 6.2 and 6.8, 6.3 and 6.6, and 6.3 and 6.9 were implemented (Table 6). As shown in Table 6, cases of provision of samples and information for research purposes to other research institutes, private companies, or overseas institutions (cases 6.1, 6.2, and 6.3) were chosen by the participants more frequently than the ones that involved similar provision for medical treatment (cases 6.4, 6.5, and 6.6) or commercial purposes (cases 6.7 and 6.8). In addition, older participants were more likely to choose all choices except 6.9 than younger participants (Supplementary Table 4; *P*-values for choices 6.1–6.9 were 1.02×10^{-4}, 0.0242, 0.0113, 1.71×10^{-8}, 1.42×10^{-3}, 0.0128, 5.02×10^{-5}, 5.77×10^{-3}, and 0.268, respectively). The relationship between the number of terms that the participants knew and the preference of cases to be explained at obtaining informed consent was analyzed. We found that all choices (from 6.1 to 6.9) were chosen significantly more frequently by the participants who knew more than six terms (Table 5).

Discussion

Public knowledge of genomic research and medicine

This study represents the analysis of responses to a questionnaire that examined the knowledge of and attitude to genome research and medicine in a large sample of Japanese population (3000) covering individuals of 20–69 years of age. According to this survey, many participants considered that they knew the terms "gene", "DNA", "DNA evidence", and "chromosome", although it was not verified how accurate their knowledge was. A study conducted 10 years ago also showed the same tendency that the terms "gene", "DNA", and "chromosome" were known by many participants, whereas the term "genome" was not so known [9]. The fact that fewer participants knew the terms "genome", "genetic information", "genome research", "personal genome", and "pharmacogenomics" indicates that these terms can be unfamiliar and highly technical to lay people. In promoting genomic research and medicine, at least two terms, "genetic information" and "genome", which represent key basic components of those activities, should be explained more proactively to the public. This survey result has another important implication that each organization and institute must carefully consider potential differences in the level of patients' and research participants' knowledge

about those terms when they prepare informed consent documents on genomic research and medicine.

In addition, the number of terms the younger participants knew was smaller than that known to older respondents, both in males and females. These data likely indicate that genetic information literacy of younger people is lower than that of older ones. This result is also consistent with the result of a previous survey [15], where Japanese younger respondents (20–30 years of age) tended to be less interested in the issues of science and technology than American and British respondents. Notably, a study in the U.S. showed that the levels of genetic knowledge were lower among the individuals in older age groups (aged 26–35, 36–49, and >50 years) compared to those in the youngest age group (18–25) [16]. In this survey, an opposite tendency can be seen in the younger participants (20–30 years of age). The reason for this discrepancy could be that it is social environment rather than school education that provides lay people with the familiarity of those terms in Japan, and thus, further school education that explains the significance of genome research and medicine should be encouraged.

Indeed, academic societies specializing in this field have recently raised awareness of this public education issue. In 2015, the Japan Society of Human Genetics and two other relevant societies sent out their message to the Central Council for Education in the Ministry of Education, Culture, Sports, Science, and Technology [17]. It expressed a deep concern about the poor situation regarding the teaching of genetic issues during secondary education in Japan and concluded that young Japanese students did not obtain enough knowledge of human genetics, although understanding of human genetics is essential for the well-being and social life of ordinary people.

A study in the U.K. pointed out that the level of awareness of personal genome testing was low, with only 1 in 8 people (13%) having heard of this service. However, younger people were significantly more likely to be aware of personal genome testing than older people [18]. Another study in the U.S. also pointed out that younger individuals (aged 18–34 years) were more likely to be interested in pharmacogenetic testing to predict serious side effects (vs. individuals aged 55 years) [19]. These results seem to be in sharp contrast to the result of our study, in which the older participants were more likely to know about DNA testing than the younger ones. These differences may result from each country's situation, and therefore, this means that each nation must address the educational issues based on their own unique cultural and social contexts.

Public interest in genomic research and medicine

This survey has shown that about 40% of the older (in Q2, 711 participants chose "Moderate" and 146 chose "Very much") and younger participants (387 participants chose "Moderate" and 125 participants chose "Very much") were interested in genomic research and medicine. According to statistical analysis of this survey, older participants were much more interested in genomic research and medicine than younger participants, and sex had little effect on interest in it. Okita et al. pointed out that people of ~40 years of age show the most positive attitude toward the participation in whole-genome sequencing studies, although this attitude becomes increasingly negative with age after this point, and sex has little effect on the attitude [20]. In addition, Ishiyama et al. pointed out that the promotion of genomic studies was approved by a slightly higher proportion of males (73.8%) than of females (65.6%) [9]. These differences could be partially influenced by distinct research methods and subjects, the order and expression of questions in the surveys, or survey timing.

In addition, we found that the participants who knew many terms had stronger interest in genomic research and medicine. This result is consistent with the outcome of a recent study that showed that people with a high level of genomic literacy tended to approve the promotion of genomic studies [9]. Furthermore, higher genomic literacy levels have been recently associated with a positive attitude towards medical research [21]. Although it is pointed out that a high level of information does not guarantee a positive attitude [22], these results support a view that the number of people who are interested in genomic research and medicine should necessarily increase, because biological samples and genetic information will be used much more frequently in future and thus, genome research and medicine will require considerably more support from the public.

Interest of the participants in the disease-related genetic information

In this survey, the five questions about the wish of the respondents to learn more about their genetic predisposition to diseases and drug sensitivity were expected to reveal varying responses for different diseases (Q3). However, about 60% of the participants answered that they wished to know the results of genetic analysis to all five questions. It means that contrary to our expectation, the participants preferred to receive the results of their genetic testing regardless of the medical actionability. Older participants wished to learn about their sensitivity to drugs and genetic susceptibility to diseases that are difficult to cure (questions 3.3 and 3.4) more frequently than did younger participants. Furthermore, more females than males wished to know their genetic information about the above issues (3.3 and 3.4) and other disease (question 3.2, Table 4). These differential responses could result from the higher personal and social

concerns associated with age, which is a factor in diseases such as cancer and Alzheimer's, among the older participants, and concerns about breast cancer among females, respectively. These results suggest that medical staff with expertise in genetic medicine, such as genetic counselors, should provide more explanations to patients suffering from genetic diseases.

According to a genomic research study conducted in the Tohoku Medical Megabank Project (TMM) in Japan, there were sharp differences in the extent of respondent interest in those diseases [10]. For example, whereas over 80% of the participants wanted to receive genetic information regarding lifestyle diseases, only 41% of the participants enrolled in TMM wanted to learn about their genetic predisposition to diseases that were not clinically actionable. The proportion of the participants of the present survey who wished to know their genetic information relating to clinically non-actionable diseases was much higher than that in the TMM study. The difference between the results of the two surveys could be explained by the fact that TMM respondents participated in a specific research project.

The participants who knew more than six genome-related terms wished to know their susceptibility to diseases regardless of the medical actionability (Table 5). These data indicate that the participants with better understanding of the genetic information might have a stronger interest in learning about their genetic features, so the characteristics of the diseases were less relevant.

Views of participants regarding the important points during handling of genetic information and appropriate regulatory rules

Many participants of this survey were more strongly interested in the reasons for genetic information collection, as well as in accuracy and management thereof (points 4.1, 4.2, and 4.6), rather than in the skills and expertise of the person who interprets genetic information or in the actions of the said person at and after the return of genetic data (points 4.3, 4.4, and 4.5). This indicates that although the participants may strongly trust medical professionals and supporting staff, they tend to be significantly concerned about mishandling of genetic information. In addition, it should be noted that the participants who knew more than six terms, i.e. those with a high level of genomic literacy, tended to focus on technical issues, such as "accuracy and reliability of the genetic information" (4.2) and "strict management system of genetic information" (4.6; Table 5). Therefore, it can be safely concluded that different types of explanation and transparency would be required for people with different levels of genomic knowledge.

In the United States, the Genetic Information Nondiscrimination Act was enacted in 2008, which prohibits discrimination by health insurers and employers on the basis of genetic information [23]. However, a recent meta-analysis indicated that legislation prohibiting genetic discrimination did not seem to completely alleviate the fears of genetic discrimination and that the concern of becoming a victim of genetic discrimination was greater in the health insurance context than in the context of employment [24]. Another study pointed out there is little evidence that genetic discrimination happens or has ever happened on a scale that would justify the current magnitude of academic attention, public concern, or policy-making activity [25]. In this survey, younger participants were more likely (320 participants, 26.7%) to choose "avoidance of discrimination at the time of employment or insurance (4.7)" than the older ones (18.9%, 341 participants) ($P = 7.26 \times 10^{-7}$, chi-squared test, Supplementary Table 2). In Japan, because everyone has a right to receive health insurance, the chances of discrimination in health insurance are considered to be low. However, employment discrimination is a matter of understandable concern to young people.

With regards to the rules of genetic information handling, the majority of the respondents who chose 5.1 and 5.2 (1876 participants, 62.5%) agreed with the utilization of genetic information in research and medicine if genetic information is appropriately managed. In particular, they were mostly of the opinion that genetic information should be under stricter regulation than other ordinary research (point 5.2; 1321 participants, 44.0%). Indeed, this standpoint is in good accord with the rules of genome information handling in the current governmental ethical guidelines in Japan.

The most common answer, "Genetic information should be treated under stricter regulation than other ordinary research (point 5.2)", was chosen by a high proportion of the participants who knew more than six genetic terms (Table 5). It indicates that people with more knowledge tend to choose stricter rules than less aware individuals. Furthermore, the fact that the answer "I don't know (point 5.5)" was chosen by a high proportion of the participants who knew less than five terms indicates that people with less knowledge had a difficulty to respond confidently to this kind of questionnaire. Younger participants chose this answer (348 participants, 29.0%) more frequently than older participants (327 participants, 18.2%, Supplementary Table 3). Overall, these results suggest that laypeople could judge better about their attitude towards the rules regulating availability of genetic information if they learn about basic genetic terms and improve their knowledge of genomic research and medicine. This is consistent with the result of a previous survey on a community-based genome cohort study where it was concluded that individuals who were aware of the study and perceived their comprehension of the terminology

well were more aware of the benefits than those who had lower awareness [26].

Public trust in research

According to the results of the present survey, the participants seem to concern more about the utilization of human samples and genome information for research purposes rather than for medical treatment or commercial purposes (Table 6). It means that the respondents can be unfamiliar and/or concerned about the research. This result could also imply a need to establish more trust with the public by promoting genomic research in Japan. Public trust to genomic research community can play a key role in public involvement in genomic research [27], because genomic research broadly uses potentially sensitive genetic information. In relevance to this point, it has been shown also that when the researchers are trusted, many participants do not mind contributing identifiable personal data to various research projects [28]. A study in Japan has pointed out that enabling more communication with the research participants could help building and maintaining public trust [29]. These studies suggested that in order to promote trust between researchers and participants, the institutional review boards should consider how the consent process could foster respectful engagement rather than merely mitigate risk [30]. These considerations imply that the research community and funding agencies should take every effort to preserve and develop public trust when they plan and manage human genomic research and its clinical application.

Limitation and conclusions of the study

As the participants of this survey were recruited through an online system, many more people who were interested in genomic research and medicine might have participated in the survey than in the case of random sampling. However, the analysis in this study suggests the importance of educating younger people about human genetics and the need of different types of explanation and transparency aimed at individuals with different levels knowledge about the genome. It also indicates that public trust should be fostered in order to achieve the promotion of genomic research and its translation into clinical setting.

In this survey, the participants were asked a simple question about whether they knew the terms listed in Table 2. We recognize that further questions are necessary to assess more precisely the literacy of the public in genomic matters. However, such questions were beyond the scope of this study because it only aimed to elucidate public attitude to the handling of genetic information during research and general medical activities. Thus, public awareness of genomic information will be a theme of future surveys.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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