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Author	荒川, 和晴(Arakawa, Kazuharu)		
	冨田, 勝(Tomita, Masaru)		
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[研究論文]

Genome Analysis Workshop: a Personal Genomics Class at Keio SFC

SFCにおけるパーソナルゲノム時代のリテラシー教育

Kazuharu Arakawa

Project Associate Professor, Graduate School of Media and Governance, Keio University

荒川 和晴 慶應義塾大学大学院政策・メディア研究科特任准教授

Masaru Tomita

Director, Institute for Advanced Biosciences, Keio University / Professor, Graduate School of Media and Governance, Keio University / Professor, Faculty of Environment and Information Studies, Keio University

冨田 勝

慶應義塾大学先端生命科学研究所所長 / 慶應義塾大学大学院政策・メディア研究科教授 / 慶應義塾大学環境情報学部教授

Abstract: Because of the development of sequencing technologies, the era of personal genomics is rapidly approaching, and several Direct-to-Consumer genetic testing services are already available. However, sociopolitical guidelines for personal genomics have lagged behind technological advances. Here, we report our innovative literacy education class on personal genomics in Keio University Shonan Fujisawa Campus, using an actual personal genome as the course material.

DNA 配列決定における技術革新などにより、近い将来に個別化医療などの パーソナルゲノム時代が到来することは確実であろう。一方で、残念ながら パーソナルゲノム時代を受け入れるために必要な法律やガイドラインなどの 社会システムや、一般市民のリテラシーに関しては、技術に対して大きく遅れ をとっているのが現状である。そこで、本論文ではこのような問題に対応で きる人材育成のために我々が SFC にて取り組んでいるパーソナルゲノム時 代のリテラシー教育における先進的試みについて報告する。

Keywords: personal genomics, literacy education, molecular biology, bioinformatics, DNA sequencing

1 Introduction

Within a decade after the completion of the landmark \$3 billion international Human Genome Project in 2003 (International Human Genome Sequencing Consortium, 2004), more than 1,000 human genome sequences are publicly available (1000 Genomes Project Consortium, 2012). A project to sequence 100,000 human genomes over the next five years is ongoing (Rossolatos and Aitchison, 2014), and another project to sequence a million genomes began in 2011 (Normile, 2012). This dramatic progress in genome projects was facilitated by the advent of the next-generation DNA sequencing technologies, which have decreased the time and cost of sequencing by approximately 10,000-fold over the last decade, surpassing the prediction of Moore's law of semiconductors (Mardis, 2011; Shendure, et al., 2004). Affordability is a prerequisite for personal genome sequencing to be clinically feasible, and the highly anticipated milestone of "\$1,000 genomes" has recently been reached. The Archon Genomics XPRIZE, a \$10-million competition to rapidly and accurately sequence the whole genomes of 100 humans at a cost of \$10,000 or less per genome was cancelled before it began in August 2013 because it was "outpaced by innovation" (Diamandis, 2013). In January 2014, Illumina, Inc. launched the HiSeq X Ten Sequencer, which generated a \$1,000 genome at 30x coverage, including the cost of sample preparation, reagents, and instrument depreciation (Sheridan, 2014). Although the current cost does not include informatics analysis and necessary personnel expenses, the projected milestones are likely to be achieved rapidly considering the current pace of innovation. Therefore, we are entering the era of personal genomics.

The generation of a reference genome by the Human Genome Project has significantly contributed to genetics, molecular biology, biochemistry, and medicine, enabling the identification of disease-related genes and their functions, as well as the physiological and pathological implications of the systematic interactions of these genes. However, knowledge of the genomes and genetic variations of individuals can further such studies and transform current approaches in medicine and healthcare (Khoury, et al., 2009). A highly significant contribution of personal genomics is in preventive healthcare. While current medical practice predominantly comprises curative care and treatment of disease, understanding of the genetic variations based on personal genomes provides information on innate susceptibility and risks for various diseases, enabling proactive control of individual lifestyles to prevent health consequences. For example, if an individual has a genetic variation leading to a higher risk of obesity or type-II diabetes, practicing appropriate calorie control and limiting a high-fat diet can improve the individual's chances of remaining in good health. Disease prevention directly leads to a better quality of life, and preventive healthcare also has profound sociopolitical implications, especially in nations undergoing population aging, such as Japan. Considering the decreasing birth rate and overall population aging, the old-age dependency ratio (number of elderly individuals (65 years and older) as a percentage of the working-age population (20 to 64 years)) is expected to reach 47% by 2060 in Japan; this is the highest among major industrialized nations, imposing a fiscal challenge due to increased healthcare costs (Mühleisen and Farugee, 2001). Therefore, preventive care would reduce healthcare costs, and personal genomics provides indispensable information for this purpose. Personal genomics also contributes to the *identification* and *prediction* of the cause and physiology of rare orphan diseases for which resources or treatments are either unavailable or insufficient. Human nucleotide diversity is estimated to be approximately 0.1%; therefore, there are approximately 3 million nucleotide differences between any two individuals (Jorde and Wooding, 2004). Only a very small number of variations actually account for a specific disease; however, the availability of a large collection of singlenucleotide polymorphisms from healthy individuals and a sufficient amount of genetic information from patients with a specific disease would facilitate the elimination of common polymorphisms and the identification of variations that

are only present in patients. Therefore, with active community participation, the use of personal genomics has the potential to identify cures for orphan diseases. Personal genetic variations also lead to differing drug responses or varying symptoms, and treatment effectiveness requires *personalized* and tailored medicine. For example, specific populations are either sensitive or resistant to the anticoagulant warfarin, a drug used to prevent thrombosis, necessitating careful control of the optimal dose (Daly and Aithal, 2003). Warfarin response can be partly explained by specific single-nucleotide variations. Knowledge on drug responses and their relationships with various genotypes is rapidly accumulating, including for anti-cancer drugs such as Gefitinib (Cusatis, et al., 2006; Mayo, et al., 2012) and Crizotinib (Cusatis, et al., 2006; Mano, 2008; Ou, et al., 2012), where knowledge of the genotype is extremely useful for avoiding serious side effects and for tailoring the most effective drug suited to the specific individual. Therefore, personal genomics can benefit medicine and healthcare; new healthcare concepts in the era of personal genomics have been described previously, for instance, the "P4 medicine" discipline, which encompasses the predictive, preventive, personalized, and participatory aspects described above (Hood and Friend, 2011).

Among the 3 billion base pairs in the human genome, only 1% or 30 million bases comprise the protein-coding exome (Ng, et al., 2009). Furthermore, exome mutations may not necessarily cause amino acid changes because of codon degeneracy, and the phenotypic implications of genetic variations are subtle or not well understood in the majority of genomic positions. Therefore, it is not always necessary to sequence the entire human genome to understand an individual's genotype: the study of exomes or common sites of single-nucleotide polymorphisms (SNPs) is a sufficient and cost-effective alternative. Although whole-genome sequencing costs thousands of dollars, targeted exome sequencing or array-based capture of common SNPs can be commercialized at lower costs, approximately hundreds of dollars. Therefore, commercial direct-to-consumer (DTC) personalized genetic testing services are increasingly available to the general public through companies such as 23andMe, Navigenics, deCODEme, Pathway Genomics, and GeneQuest. For example, genetic testing at 23andMe costs only \$99 to analyze approximately 1 million SNPs and includes a report comprising the genotyping results for 260 genes including those related to health conditions and inherited traits as well as the carrier status of recessive alleles and genealogy. As of December 2013, 23andMe had more than 500,000 genotyping customers (Wojcicki, 2013). Therefore, personal genomics is already highly accessible to the general public using these DTC services; however, the quality of genotyping, the scientific validity of risk assessments, and the availability of adequate explanations or counseling to support careful interpretations of the results are not always sufficient in these services, leading to criticisms and concerns (Hudson, et al., 2007; Khoury, et al., 2009; Prainsack, et al., 2008). Thus, in November 2013, the US Food and Drug Administration (FDA) ordered 23andMe to stop the sale of healthrelated genotyping due to the insufficiency of scientific evidence to satisfy the FDA requirements for medical diagnosis (Wojcicki, 2013).

The interpretation of genotyping results is inherently complex and difficult. Phenotypes or diseases can be highly multi-factorial, and causes are most often non-genetic, such as lifestyle and other environmental factors. For example, the allelic profile of 54 genomic loci considered related to human height only explains 4-6% of actual measurements (Aulchenko, et al., 2009), and risk behavior such as smoking and high-calorie diet often results in a higher contribution to lifestyle-related diseases. Furthermore, there may be yet undiscovered genotypes with higher predictive power or unknown linkages between genotypes and phenotypes; overall, there is insufficient quantitative data to accurately calculate risk percentages. Therefore, the use and interpretation of genotyping requires care and caution to avoid misinterpretation; nevertheless, the rate of technological advances clearly exceeds the rate of policy making, and personal genomic information will soon be ubiquitous, most likely before all the necessary policies and guidelines for social and ethical issues (summarized in Table 1) are discussed (Fisher and Harrington McCarthy, 2013). It is therefore crucial for as many citizens as possible to have sufficient literacy about personal genomics, and this type of literacy education should not be limited to scientists and physicians. Shonan-Fujisawa Campus (SFC) of Keio University is a unique and ideal location for such literacy education because of the diverse interdisciplinary nature of the departments encompassing all major disciplines, including advanced biosciences as well as business management, policy making, and others. In the following sections, we describe the design of a one-semester course on personal genomics titled the "Genome Analysis Workshop", which began in 2012 in SFC using actual personal genome sequence data as a course material.

2 Requirement Analysis

2.1 Related Studies

When the course was developed in 2011, there was limited publicly available information on educational effort in the field of personal genomics worldwide because this field and DTC services were in their infancy. One of the pioneers in this regard was the Personal Genome Project (PGP) initiated in 2005, which is dedicated to creating public genome, health, and trait data by sequencing the genome of thousands of volunteers to identify novel associations between genotypes and phenotypes and to observe the social implications of personal genomics (Church, 2005; Jones, 2012). Because PGP predominantly relies on the participation of volunteers willing to donate their personal information as a public resource, genetics education and thorough informed consent were essential prerequisites of the project. Considering the emergence of DTC services and to target a broader body of citizens, the Personal Genetics Education Project (pgEd) based at Harvard Medical School provides a wide range of lesson plans and interactive exercises designed to provide education on the benefits and ethical implications of personal genetics mainly

Issues	Description
validity of the results	Genotyping may not be entirely accurate. Even with 99.999%
	accuracy, analysis of 3 billion nucleotides of genome results in
	unnegligble percentage of error. At the current level of precision,
	alternative testing is required for validation for actual diagnosis.
limite current knowledge	Negative results, such as no known genotype to a certain
	disease, may not be accurate, since a novel genetic risk
	association may be discovered in the future. Likewise, new
	discoveries may elucidate unexplected or undesirable risks even
	for positive results.
shortage of genetic	Interpretation of genetic test results require expert knowledge
counsellors	in genetics, medicine, and healthcare, and therefore genetic
	counsellors that can appropriately deliver and consult the results
	are currently lacking.
genome stays unchanged	Every person's genome is unique, and remains unchanged
for life	throughout one's life. A genotype once identified remains
	unaltered by aging or other environmental factors. Therefore,
	once a genome sequence is made available to others by any
	means, it is impossible to revamp the personal information. This
	is different from other personal data such as name or address
	that can be altered.
data protection	Genetic information is the ultimate private information,
	containing multitude of information related to the physical traits
	and disease risks. Since this information remains unchanged
	unought one's me, nandling and protection of the data require
	sale means to prevent information reakage. However, as
	such as dropped bair skin contact by touching, or saliva on
	tableware With decreased cost in the near future, it is possible
	for strangers to gather such traces and sequence the genome
	unnoticed
presymptomatic diagnosis	Genetic tests predict risks to diseases before any sign of
presymptomatic diagnosis	symptoms Risk is given as a percentator relative to a certain
	nonulation group, but such statistics requires sufficient
	knowledge for appropriate interpretation. Even with relatively
	high risk to a certain disease, it is only a matter of likelihood
	for he/she to actually develop the illness. Moreover, current
	healthcare system in Japan is not generally applicable to
	preventive care for healthy individuals.
lack of working treatment	Predicted high-risk factor may not have a working treatment.
	For example, several SNPs are identified to significantly elevate
	the risk of Alzheimer's disease, but there are no definitive
	treatment for this disease at the time being.
presymptomatic diagnosis lack of working treatment	and disease risks. Since this information remains unchanged throught one's life, handling and protection of the data require safe means to prevent information leakage. However, as living organisms, it is impossible to leave biological traces such as dropped hair, skin contact by touching, or saliva on tableware. With decreased cost in the near future, it is possible for strangers to gather such traces and sequence the genome unnoticed. Genetic tests predict risks to diseases before any sign of symptoms. Risk is given as a percentatge relative to a certain population group, but such statistics requires sufficient knowledge for appropriate interpretation. Even with relatively high risk to a certain disease, it is only a matter of likelihood for he/she to actually develop the illness. Moreover, current healthcare system in Japan is not generally applicable to preventive care for healthy individuals. Predicted high-risk factor may not have a working treatment. For example, several SNPs are identified to significantly elevate the risk of Alzheimer's disease, but there are no definitive treatment for this disease at the time being.

Table 1 Technical, social, political, and ethical issues surrounding personal genetic testing

right to "not know"	Since the knowledge of high genetic risk to certain disease may become mental burden, especially when there is currently no working cure, such knowledge could possibly lower the quality of life. Therefore, the right to "not know" one's own genotype should be respected. On the other hand, in order for the society to reduce the medical costs, it is most effective to have a mass- screening of genotypes, possibly at the time of birth, and the means for the delivery of such results must be debated respecting the right to "not know".
test for children	Genetic tests require thorough informed consent due to the many issues, and the right to "not know" certain genotype should be respected. Such consideration requires one to be an adult, and genetic test of children should be handled with caution. On the other hand, preventive actions are most effective when the genotypes are tested at the time of birth.
family relationships	Since mitochondrial sequence is strictly inherited from the mother and the Y-chromosome is from the father, genetic testing identifies the family relathionships and ancestry. In case of adaptions, genetic testing identifies non-paternity, which could be undesirable in some cases.
genetic discrimination	When personal genomic information becomes common in the society, employer or insurance companies may choose to treat people differently based on the genetic risks. Preventive actions must be taken to prohibit such discrimination based on inherited conditions. In the United States, the Genetic Information Nondiscrimination Act has been effective since 2008 to prohibit the use of genetic information in health insurance and employment, but analogous law is still not available in Japan.
carrier status	For recessive Mendelian diseases, a person can be a carrier of the gene without displaying the symptom of the disease due to diploid nature of the human genome. Therefore, knowledge of the carrier status will likely affect the choice of mating partners.
prenatal screening	Non-invasive prenatal screening by sequencing of fetal DNA in mother's blood is already available for Down's syndrome, and could be extended to other genetic features. However, prenatal screening often leads to the decision of abortion, and thus is an area of intense debate.
designer's baby	While genetic modification of human embryo is banned in most countries, preimplantation genetic screening of embryos, or screening of gametes prior to in vitro fertilization is possible to certain extent, leaving possibilities in selecting or even "designing" the genotype of a newborn.

to high school students (Kung and Gelbart, 2012). Personal genomics education should ideally be coupled with personal genetic testing, but performing such testing on a minor is ethically challenging (i.e., high school students); therefore, personal genetics classes were first attempted at the undergraduate level in 2010. One such attempt, "Bring Your Genes to Cal" program at the University of California, Berkeley, initially announced plans to offer voluntary genetic testing to all 5500 incoming undergraduate students to test three genes related to alcohol metabolism from saliva samples. However, this plan met with immediate criticism even from the state of California, leading to abandonment of the plan to deliver individual results (Hendershot, 2011). The ethical issues of genetic testing in classrooms have proved controversial (Callier, 2012; Rogers and Taylor, 2011; Taylor and Rogers, 2011). Considering the difficulty seen in Berkeley, subsequent efforts have incorporated thorough instructions on the risks before obtaining informed consent and using DTC services for genotyping. A medical graduate course in Stanford School of Medicine entitled "Genomics and Personalized Medicine" partnered with the DTC companies 23andMe and Navigenics for genotyping and reported that students who voluntarily participated in personal genetic testing learned better compared with students who declined to participate (Salari, et al., 2013). Several undergraduate and graduate courses are now available, mostly as honors seminars partnered with 23andMe, for instance, in the University of Iowa, University of Illinois, University of Texas, and Duke University (Foley, 2013).

2.2 Requirements

Through careful reviewing of related courses and discussions with colleagues studying personal genomics, we defined the following requirements for a new personal genetics course at SFC.

• (R1) Targeting a wide variety of interdisciplinary students. Previous related courses were predominantly held at biological or medical colleges,

presumably due to the nature of existing departments as well as limitations in human resources; however, the social implications of personal genomics goes well beyond biology and medicine, requiring active participation from business, politics, and many other areas of society. Keio SFC provides a unique and ideal environment for this purpose.

- (R2) Use of personal genomic information. As shown by the Stanford group (Salari, et al., 2013), the use of personal genomic information enhances the motivation and learning of the students.
- (R3) Avoiding the ethical issues of individual genetic testing. As majority of the students enrolled in the first two years of undergraduate course are under-aged, their personal genetic testing may raise significant ethical concerns even if we carefully obtain informed consent under the Japanese law.
- (R4) Affordability and accessibility. Comprehensive DTC genetic testing
 was not available in Japan at the time of course development, and genetic
 testing should be affordable, with price points ideally around those of
 expensive textbooks (<\$100).
- (R5) Interactive course work. Personal genomics is still in its infancy, and issues surrounding this new discipline are mostly exploratory. Therefore, traditional one-directional lectures are not sufficient, and a more interactive means of learning is essential.
- (R6) Helping students to understand the complicated nature of the genotypephenotype linkage. Phenotypes such as physical traits and disease risks are the result of a highly complex interaction of multi-factorial genotypes and environmental factors. Furthermore, current knowledge in genotypephenotype associations is very limited, and new discoveries of unexpected associations are highly likely. Therefore, a key lesson of personal genomics education is that these links are difficult to identify.
- (R7) Reusability. The course will become one of the first attempts for personal genomics education in Japan and should serve as a model that can be copied elsewhere to promote such education nation-wide.

3 Design of the Genome Analysis Workshop

3.1 Course Design

The course "Genome Analysis Workshop" has been available since 2012 as a 15-week course in the spring semester aimed at freshman undergraduate students in Keio SFC. Because the overall curriculum of SFC becomes specialized over the four-year college period, freshman students presumably represent the most interdisciplinary population (R1). To achieve high interactivity and participation within the course, group work was set as the central activity of the workshop (R5). The course outline is shown in Figure 1. The 15-week course is divided into two parts: the first 6 weeks comprise mostly hands-on lectures on the various concepts of personal genomics and its analysis, and the latter 6 weeks comprise predominantly group work in which the lecturer and student assistants provide support *ad hoc* to each group depending on the progress. Concurrent with the hands-on lectures, the students are placed in groups of 5-8 in the 3rd week, and each group discusses and decides an analysis theme for the second part until the mid-term presentation, where they present the analysis plans. Due to the space limitation of the computer lab required for the hands-on lectures, the number of students was expected to be around 50, resulting in about eight groups. Student assistants were required to have the knowledge of computational tools used during the hands-on lectures.

In the Genome Analysis Workshop, the whole-genome sequence of Professor Masaru Tomita is provided and used as the course material. Professor Tomita was the dean of the Department of Environment and Information Studies, and he frequently appears in news coverage and on television. Therefore, first-year students have most likely seen him in person several times during orientations, and we assume that students are fairly familiar with him; by analyzing his genome throughout the semester and by presenting the analysis results at the end of semester with his presence in the last two classes, we hope to provide a sufficient sense of handling personal



• What theme to analyze

- Background information about the theme
- Which genes to analyze



Figure 1 Outline of the Genome Analysis Workshop course in SFC.

genomics information (R2), while avoiding the issues related to genetic testing of students (R3, R4). We have deposited Professor Tomita's genome data in a public database, which is now freely accessible online (accession:DRA000583), and we also provide other course materials such as the slides used in the hands-on lectures upon request; therefore, with the wide media recognition of Professor Tomita, we believe that it will be relatively easy to host a similar course elsewhere (R7).

DTC genetic testing commonly yields genotyping reports based on the allele types of SNPs. This bottom-up report of phenotype-genotype links can be misleading because it often overlooks or underestimates the multiple genes related to individual phenotypes. For example, while there are tens of genes involved in pathways related to type-II diabetes, only a few SNPs with known associations to the disease are considered in the report. Therefore, we have reversed the analysis approach to begin with the phenotype of interest and then examine the related genotypes (R6). For example, if a group works on assessing the risk of Professor Tomita for lifestyle-related diseases, the group must first identify the types of lifestyle-related diseases, such as type-II diabetes and hypercholesterolemia. Next, the group must identify the biological processes responsible for such diseases, such as the sensing of blood glucose levels in the pancreas, secretion of insulin, and differentiation of adipose tissues in the case of diabetes. Subsequently, tens of genes involved in these biological processes can be elucidated, and finally the SNPs within these genes are considered in the calculation of risk. Although it is currently possible to identify SNPs directly from a phenotype of interest, through the series of experiences in the group work, we attempt to reveal the complexity of genetic networks that influence individual phenotypes.

3.2 Preparation of Personal Genome Data

Genomic DNA was extracted from the saliva of Professor Masaru Tomita using Oragene (DNA Genotek) and was purified using the DNeasy Blood and Tissue Kit (Qiagen) according to manufacturers' instructions. Library preparation and sequencing were performed at the Beijing Genomics Institute following the manufacturer's instructions (Illumina). Briefly, $8 \mu g$ of genomic DNA was fragmented into approximately 500-bp fragments by Covaris (Covaris, E210). T4 DNA polymerase and the Klenow enzyme were then used to convert the overhangs into blunt ends. An 'A' base was added to the 3' end of the blunt phosphorylated DNA fragments, which was ligated with adapters (Illumina) on both ends. The correctly ligated products were purified by 2% agarose gel electrophoresis followed by the QIAquick gel extraction kit (Qiagen). DNA fragments with adapter molecules on both ends were selected and amplified. Polymerase Chain Reactions (PCR) was performed with two primers that anneal to the ends of the adapters. The number of PCR cycles was minimized to avoid skewing the representation of the library. The PCR products were verified and purified by agarose gel electrophoresis. The fragment size and molar concentration of the library were determined using a Bioanalyzer (Agilent, 2100) and Real-Time PCR System (ABI, StepOnePlus), respectively. The qualified library was sequenced on an Illumina HiSeq 2000 platform following the manufacturer's instructions, as paired-end reads of 90 bp. The sequence reads with adaptor sequence or a high rate of low quality bases were removed, yielding a total of 1.299,459,974 reads, representing a coverage of approximately 40x. The resulting sequence data were deposited in the DDBJ Sequence Read Archive (DRA) under accession number DRA000583, along with health record information in CCD/CCR formats. The study was approved by the Faculty's Ethics Committee (No. 48, 2012).

Sequence reads were mapped to NCBI Build 37, Feb. 2009 Assembly (hg19) using Burrows Wheeler Aligner (BWA) (Li and Durbin, 2009), and SNPs were called using the SOAPsnp software (Li, et al., 2009) and annotated using ANNOVAR (Wang, et al., 2010). A total of 4,036,647 SNPs were identified. Two alleles were separately re-inserted into the reference sequence using a custom Perl script, generating two pseudo-diploid chromosome sequences with the called SNPs. These sequences were used as the database for the online BLAST server (Altschul, et al., 1997). For computational efficiency and visualization purposes, the online BLAST parameters were modified as follows: Expect=1e-25 and Alignment view=master-slave with identities.

4 Conclusions and Outlook

In 2012, 39 (40 enrolled) students completed all the group work, including three required presentations and a five-page final report, and the number of participants increased to 58 (67 enrolled) in 2013. Group-work themes covered highly unique topics, including the following:

- Assessment of Professor Tomita's driving aptitude based on genetics
- Which Olympic sport is genetically optimal for Professor Tomita?
- Discovering the ancestry roots of Professor Tomita
- Genetic carrier aptitude test for Professor Tomita
- Professor Tomita's risk for lifestyle-related diseases
- How sensitive is Professor Tomita to various types of allergies?
- What type of games is Professor Tomita genetically suited for?

Overall, the students were remarkably motivated to participate in the group work, and the use of Professor Tomita's actual personal genome as a course material and his presence at the final presentation seemed to enhance the learning of personal genomics. Figure 2 shows the course survey result at the end of semester in 2012 and 2013, and the reactions were generally favorable, mostly scoring over four, with the rating of five being the majority. It is notable that the questionnaire B, asking if the course was challenging, scored highest in both of the semesters, indicating a certain level of success in communicating the complexity of the subject of personal genomics. However, we also experienced difficulty in teaching the concept of multi-factorial risks



 Figure 2
 Results of course survey in 2012 and 2013.

 All questionnaires A ~ D were scored with 1 ~ 5 rating, 5 being the best.

because the students lacked sufficient statistical knowledge. Knowledge of the genotype is often perceived in a similar manner to the popular personality analysis myth based on blood type, which happens to be an example of genotype-phenotype association. The tendency to perceive genetic information in a manner similar to fortune-telling may possibly be unique to Japan due to the popularity of blood-type tests, and special care may be required when explaining such aspects. Based on such impression of the course in 2012, we have revised the lectures to allocate more time in teaching the ethical topics as well as statistical aspects of genetics. This change may have resulted in the overall decrease of score in the survey, as well as the increase of score in questionnaire B. In order to improve the learning experience while maintaining the necessary content, we will try to use more real-world examples to describe the ethical and statistical topics in the future courses.

In 2013, we have surveyed whether the students want to know their genotypes, at the beginning and end of the semester (Figure 3A). Approximately



Figure 3 Result of a survey asking whether s/he wants to know his/her genotypes in 2013. A: Survey result before and after the course. B: Composition of answers in the end of semester by the beginning of semesters.

70% of students answered "Yes" and this percentage stayed roughly the same; however, as many as 37% of the students actually changed their opinion during the semester (Figure 3B). Although there was a slight tendency to become favorable to know his/her own genotype (i.e. change from No to Yes), basically the changes were bidirectional. As an undergraduate class, the purpose of this course is obviously not in persuading the students about the usefulness of personal genomics, but in provoking their critical thinking on this controversial subject. This survey result presumably suggests that the students were stimulated by the new knowledge, engaged in thinking and discussions, and finally helped in taking their own positions regarding the subject of personal genomics.

Because of the rapid technological advances in DNA sequencing and genotyping, DTC testing is likely to become extremely affordable in the near future, introducing the possibility of using individual personal genetic data for educational purposes instead of Professor Tomita's genome. However, the use of common data also has considerable merits because the availability of such material allows group-based work and can be used without the risk of disclosing private information. By adopting careful measures for the ethical issues listed in (R3), we believe that personal genetic testing can be used to supplement the current course work based on Professor Tomita's genome.

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