# A Local Community Outreach Educational Program on Genetic Testing: A Pilot Study

Haruyo ATSUMI[*1], Anar DAMDINSUREN[*1], Satomi ASAI[*1], Hidefumi KAKIZOE[*1], Asuka NAGAKAWA[*1], Hideo IWASHITA[*1, 2], Kazuo UMEZAWA[*3] and Hayato MIYACHI[*1, 4]

[*1]*Department of Laboratory Medicine, Tokai University School of Medicine*
[*2]*Department of Prosthetics, Kanagawa Dental University*
[*3]*Department of Emergency Medicine and Critical Care, Tokai University School of Medicine*
[*4]*Faculty of Clinical Laboratory Sciences, Nitobe Bunka College*

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**Objective: To develop and implement a pilot educational program on genetic testing at the Tokai University School of Medicine with a public engagement approach through a local junior-high school outreach program.**
**Methods: Seven medical students underwent 2 weeks of education and training to act as instructors for a one-day course on genetic testing for local junior-high school students. The one-day course comprised a lecture and an experimental lesson. The variation of UDP-glucuronosyltransferase 1A1 gene (*UGT1A1*) was selected as the teaching topic. A commercially available cultured human leukemia cell line was used as the source of human genomic DNA to circumvent the ethical concerns associated with obtaining samples from participants for genomic analysis. The medical students received instructions on the basics of conducting laboratory work and handling the equipment and reagents during the 2-week training.**
**Results: The seven medical students completed the 2-week training. They then taught PCR and restriction enzyme experiments and the meaning of the results to junior-high school students.**
**Conclusion: A pilot educational program on genetic testing with a local community outreach approach was successfully developed and implemented.**

**Key words: genetic education, early exposure, medical students, junior-high school, *UGT1A1***

## INTRODUCTION

Recent advances in the field of genome sequence analysis and its clinical implementation have led to a dramatic increase in the clinical use of genetic testing [1]. However, the training of care providers, particularly medical students, remains insufficient [2, 3]. The importance of an effective educational program for medical students has been emphasized in previous studies [4]. Several educational approaches have been explored in recent years; however, a universally effective educational approach remains to be established. Collaborative efforts with local community outreach have recently been explored as a promising educational approach for skill development in university students through community involvement [5, 6].

A 2-week educational course on DNA diagnostics, comprising a lecture and an experiment on a particular subject, was formulated for medical students at the Tokai University School of Medicine to provide insight into molecular diagnostic testing. A local community outreach approach was used to improve the effectiveness of educational programs and meet the demand for competent genetic testing methods. To this end, a pilot educational program funded by the Tokai University School of Medicine as part of the project of the Tokai University Community Linking Laboratory, or To-Collabo, was developed and implemented in 2016. This program was developed as an original and unique educational program conducted by the Ministry of Education, Culture, Sports, Science, and Technology of Japan in cooperation with the local community [7]. The program comprised an education and training program wherein medical students played the role of student instructors. The purpose of this paper is to describe an initiative for medical students to teach genetic testing to junior-high school students, thereby increasing their own understanding and knowledge of genetic testing and teaching junior-high school students who live near the university hospital. In this paper, we describe a one-day lecture and experimental course for the basics of genetic testing with one-on-one instructor support conducted for local junior-high school students from Isehara in Kanagawa.

## MATERIALS AND METHODS

### Preparation of the To-Collabo teaching course

Participants

Seven medical students from the Tokai University were enrolled as instructors in this study. Among these seven participants, two were assigned the role of leader instructors, and five were assigned the role of regular instructors. Seven junior-high school students, comprising two male and five female students were

Satomi ASAI, Department of Laboratory Medicine, Tokai University School of Medicine, 143 Shimokasuya, Isehara, Kanagawa 259-1193, Japan
Tel: +81-463-93-1121 Fax: +81-463-93-8607 E-mail: sa@tokai.ac.jp

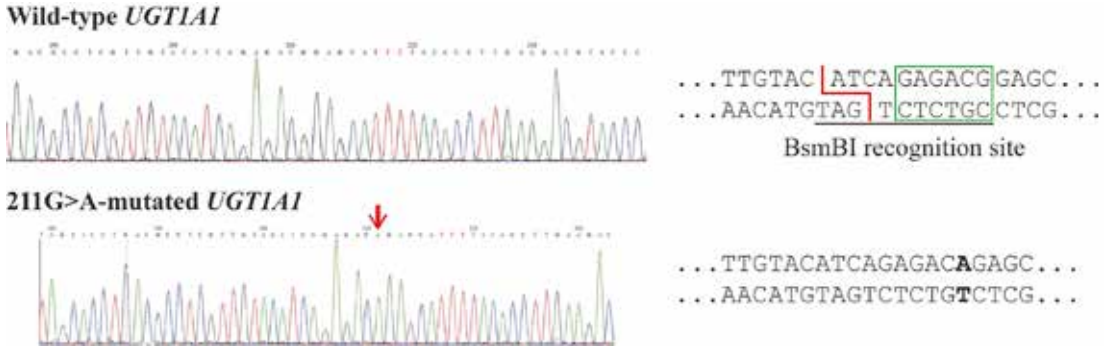


**Fig. 1** The sequence of *UGT1A1* gene.
Sequences of the wild-type (upper panel) and 211G > A-mutated (lower panel) *UGT1A1*. The *BsmBI* restriction enzyme recognizes the 5'-GAGACG-3' sequence in the coding region exon 1 of *UGT1A1*.

recruited from Isehara in Kanagawa, to participate in the program.

Framework of the educational program

The university teaching staff provided the student instructors with instructions regarding the learning strategy, and the learning and behavioral objectives. The educational program comprised a 2-week preparation course for the medical students and a one-day To-Collabo teaching course for the junior-high school students. The two leader instructors participated in the development of experimental protocols and teaching materials under the supervision of the teaching staff during the 2-week preparation course. All seven instructors received instructions on the rules and precautions to be followed while working in the laboratory, including the handling of equipment and reagents, as well as the pilot experimental procedures. The instructors also received instructions on basic teaching methods before the commencement of the teaching course. Medical students also received direct instructions from primary school teachers on basic teaching methods before the commencement of the one-day teaching course for junior-high students.

Design and source of the wild- and mutant-type of *UGT1A1*

The variation of NM_000463.2:c.211G > A in the UDP-glucuronosyltransferase 1A1 gene (*UGT1A1*) was selected as the target owing to its extensive use in pharmacogenomic testing in the field of medicine [8]. A commercially available cultured human leukemia cell line was used as the source of human genomic DNA to circumvent the ethical concerns associated with obtaining samples from the participants for genomic analysis. DNA from HL-60 cells was used as the source of the wild-type *UGT1A1*. A plasmid DNA containing exon 1 of the *UGT1A1* was constructed via PCR mutagenesis as described in a previous study owing to the absence of cell lines with variations in the *UGT1A1* [9]. Guanine at position 211 was replaced with adenine (Fig. 1).

Design of the PCR primers for restriction fragment length polymorphism

A PCR primer set was designed for the analysis of exon 1 of *UGT1A1* so that restriction fragment length polymorphisms could be used to detect the presence of variations in the amplified fragment. The primer pairs used were as follows: forward, 5'AGGAGCAAAGGCGCCATGGC3' and reverse, 5'CTGGGATAGTGGATTTTGGT3'. An online database (http://www.restrictionmapper.org/) that mapped the restriction endonuclease positions in the DNA sequence was used to determine the position of the *BsmBI site*.

**Time schedule and workflow of the To-Collabo course**

Time schedule

The instructors presented the goals of the To-Collabo course at the beginning of the course: a basic introduction to molecular biology and basic techniques used in medicine, and precautions to be followed in the laboratory environment. The experiment was conducted with a flexible time schedule, checking the understanding and competence of the junior-high school students.

Experimental protocol

The human cells were cultured and prepared prior to the commencement of the educational course by the laboratory staff. A total of $2 \times 10^6$ cells were harvested from the cell culture maintained in RPMI 1640 supplemented with 10% fetal bovine serum. These cells were rinsed twice with cold phosphate-buffered saline (PBS) and pelleted via centrifugation at 1,500 rpm for 5 minutes at room temperature. The cell pellet was resuspended in 500 μL of PBS, and 800 μL of cell membrane lysis buffer (CMLB; 10 mM Tris-HCl [pH 7.5], 5 mM $MgCl_2$, and 0.32 M Saccharose, 1.5% Triton X-100) solution was added and mixed thoroughly. The mixture was centrifuged at 5,000 rpm for 1 minute at 4℃. The cell pellet was rinsed twice with 400 μL CMLB solution subsequently and resuspended in 200 μL of nuclear membrane lysis buffer (NMLB; 6 M Guanidine-HCl, 0.1 M NaAcOH [pH 7.5], 0.2% 2-Mercaptoethanol). Lastly, 70% ethanol was added to visualize the DNA strands.

Plasmid DNA constructs containing wild-type or 211G > A-mutated exon 1 fragment of the *UGT1A1* were amplified via PCR to ensure the consistency of the experiment and the quality of genomic DNA.

PCR was performed according to standard methods [8]. The master mixture solution for PCR without the primers and sample DNA was prepared in advance.

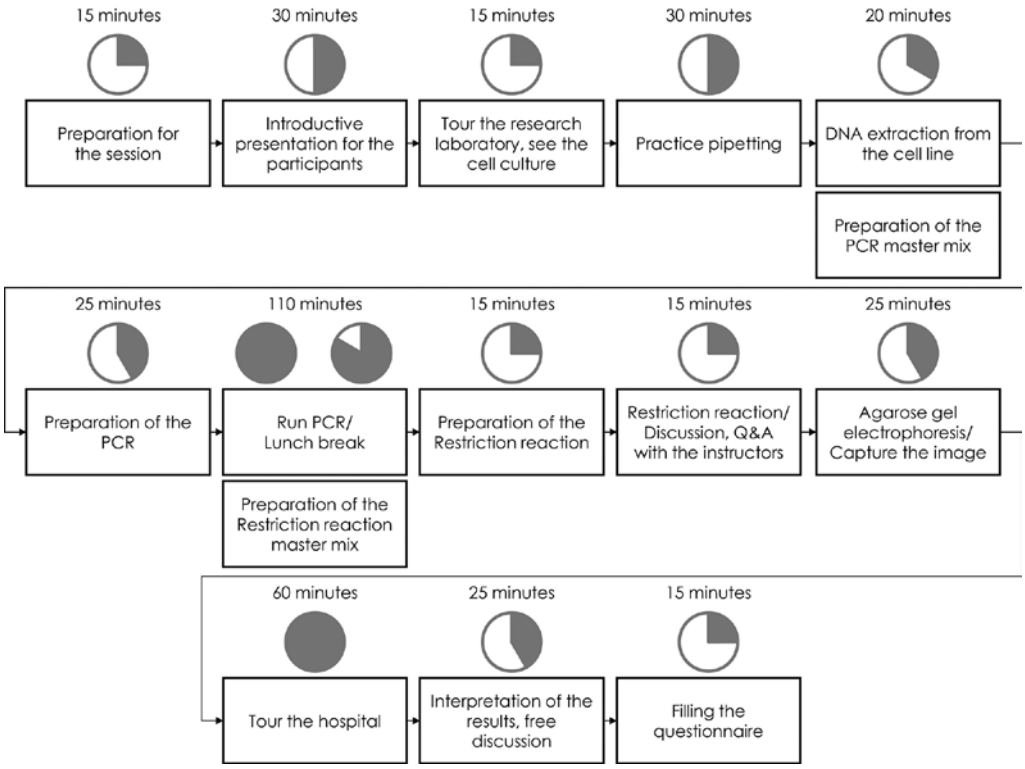


**Fig. 2** Scheme of the To-Collabo teaching course.
The scheme depicts each step of the experimental procedure along with the average time spent. The overlapping boxes represent the preparation made by the instructor for the subsequent experiment.

Distilled water samples were used as blanks. PCR was performed using a thermocycler (Takara Bio) under the following conditions: 98℃ for 5 minutes, followed by 30 cycles at 98℃ for 10 seconds, 60℃ for 30 seconds, 72℃ for 1 minute, and extension at 72℃ for 7 minutes. The temperature was subsequently maintained at 4℃.

Buffer 3.1 (1 μL) and *BsmBI* "time-saver" qualified restriction enzyme (1 μL; New England Biolabs, Ipswich, MA, USA) were added to an 8-μL aliquot of PCR products transferred to new microtubes. Restriction enzyme digestion was performed at 55℃ for 15 minutes.

A 2-μL aliquot of 6 × Purple Loading Dye was added to five 0.2-μL microtubes, followed by 10 μL of each PCR product and the respective *BsmBI*-digested counterparts. The dyed mixtures were applied to the wells of 1.5% agarose gel containing ethidium bromide (1:50,000-fold dilution of the stock solution). A 100-bp DNA ladder was used to estimate the size of the DNA fragments. Electrophoresis was performed at 135V in 1 × TBE buffer. The gels were placed on a UV illuminator and the DNA fragments were visualized after covering the surface with a protective screen. The experimental results were captured using a digital camera.

## RESULTS

### Preparation of the To-Collabo teaching course

First, a two-week preparation course was provided to medical student instructors. During the first week, all seven instructors received instructions on the rules and precautions to be followed while working in the laboratory, including the handling of equipment and reagents, and the pilot experimental procedures. During the two-week preparation course, two of the seven medical student instructors, designated as leader instructors, participated in the development of experimental protocols and teaching materials under the supervision of the teaching staff. The instructors also received direct instruction on basic teaching methods from primary school teachers before the start of the teaching course. During the latter part of the second week, the medical student instructors reviewed easy-to-understand teaching materials and methods of explanation. The students created educational materials to be used in the To-Collabo teaching course for junior-high and high school students at the end of the course. The materials included a presentation for the introductory lecture, a laboratory instruction manual, experimental protocols, and a form for obtaining informed consent for sample collection from the participant. The materials were distributed to the remaining instructors and the junior-high school students.

The lecture was conducted in a modular format using a PowerPoint presentation that provided an introduction to the general concepts of cell biology, the target disease and its molecular pathogenesis, and the clinical approach. The presentation also included an introduction to the research laboratory environment, and equipment including micropipettes.

### Time schedule and workflow of the To-Collabo course

Fig. 2 provides an outline of the steps and duration of the To-Collabo course. The instructors presented the goals of the To-Collabo course at the beginning of the course: a basic introduction to molecular biology and

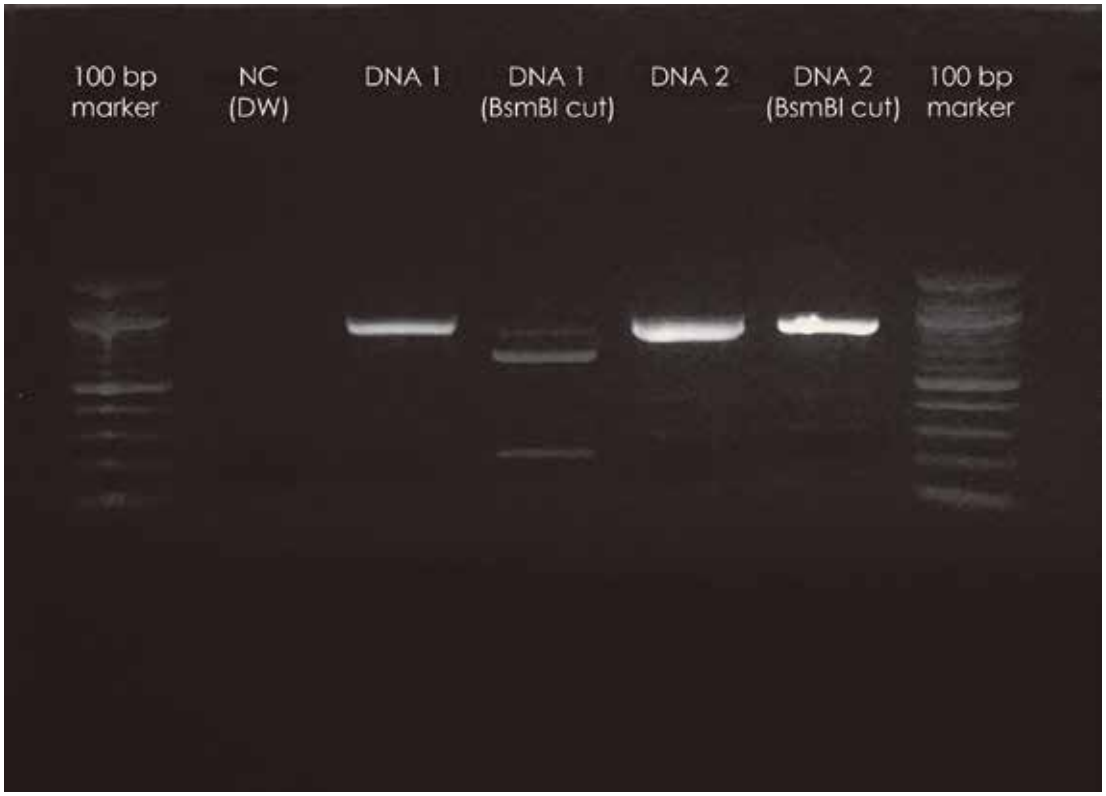


**Fig. 3** A representative gel electrophoresis image.
The exon 1 fragments of the two genotypes (wild-type and 211G > A-mutated) of the *UGT1A1* were amplified using PCR (lanes 3 and 5) and digested with *BsmBI* restriction enzyme (lanes 4 and 6). Lane 2 contains a PCR blank. Electrophoresis was performed on a 1.5% agarose gel at 135V for 25 minutes.

basic techniques used in medicine, and precautions to be followed in the laboratory environment.

The students were familiarized with the research laboratory and paired with an instructor to practice the appropriate handling of micropipettes and manipulation of small volumes of reagents (aliquots from 1 mL to 10 μL). Colored water was used as a replacement for the reagents.

The students were shown the cultured cells under a microscope at the beginning of the practice session to provide a thorough representation. After receiving the cell pellet, the students extracted DNA from the pellets in accordance with the steps of the DNA extraction protocol with the assistance of the instructor. The students prepared the PCR solution in cold tube racks with empty tubes using the PCR master mix, primer sets, and DNA samples (distilled water as a control, non-mutated, and mutated plasmid DNA) in accordance with the manufacturer's protocol and set up the reaction in a thermocycler.

The students were provided another cold tube rack upon completion of the PCR run for the preparation of the restriction enzyme reaction. The students participated in free discussion and question and answer sessions during the restriction enzyme reaction. The students loaded the agarose gel with the PCR products (blank and two samples) and the respective enzyme-digested products subsequently and acquired images of the gel electrophoresis. The results and their interpretation were discussed with the instructors.

**Experiment results and interpretation**

Although a brief introduction regarding wild-type, 211G > A-mutated *UGT1A1*, and the *BsmBI* restriction enzyme was provided to the students, information regarding whether the DNA samples were wild-type or mutated was not provided. The students interpreted the results based on the acquired image of the PCR products and their *BsmBI*-digested products and explained their conclusions to the instructors. Fig. 3 presents a sample experimental image. The students were informed that the 879-bp band was a fragment of the human *UGT1A1* amplified by the primers that specifically targeted the portion of coding exon 1 of this gene. The *BsmBI* restriction enzyme recognized the 5'$(N)_5$GAGACG3' sequence in the wild-type *UGT1A1* and cut the DNA into two bands of 660 bp and 215 bp. The 211G > A mutation resulted in an uncut DNA fragment with a single band of the same length as the PCR product.

All students obtained the correct results in the experiments, indicating that the experimental protocol was suitable for students who had never performed such an experiment before.

## DISCUSSION

This study developed and piloted an educational program with a public engagement approach through a local junior-high outreach program on genetic testing at the Tokai University School of Medicine. Through this program, medical students completed a 2-week training to act as instructors in a one-day teaching course for local junior-high school students,

comprising a lecture and an experimental lesson.

Attempts were made to enhance the educational effectiveness of genetic testing for medical students during the development and implementation of the program by designing the most suitable "hands-on" experiments relevant to education and patient practice. The subjects focused on in this study, such as DNA and proteins, are invisible matters that are difficult to grasp, even with the use of an imaginary concept. Thus, junior-high school students were provided an opportunity to visualize the molecular basis of biological processes individually using the facilities and equipment in our laboratory. The 211G > A variation of the *UGT1A1* was used in this study as it has been widely used in pharmacogenomic testing in the field of medicine. This variation affects the metabolism of therapeutic agents such as metabolites of irinotecan and increases the risk of toxicity. Consequently, a lower dosage of irinotecan should be considered for the initial treatment of patients with Gilbert's syndrome. Defects in exon 1 of the *UGT1A1* diminish the activity and induce unconjugated hyperbilirubinemia [10]. The incidence of 211G > A variation in exon 1 of the *UGT1A1* is relatively high in Asian populations [11]. A commercially available human cell line was used for the development of the experimental protocol and material owing to the ethical concerns associated with obtaining biological samples from healthy non-adult participants in a disease-related genetic study. The educational tool developed using immortalized cell lines established in the present study bypassed the ethical concerns. Moreover, this tool ensured experimental reproducibility. This approach can be used to develop teaching materials for future educational programs in universities, junior-high and high school students.

This program was beneficial for the medical students who acted as instructors. This hands-on approach that addressed the current problems in medicine and the transfer of knowledge to others broadened their understanding of scientific research, particularly molecular diagnostics. The To-Collabo experience provided medical students with an opportunity to evaluate their skills and interact with the public using appropriate words while remaining precise. This experience increased their confidence when speaking in public and increased their organizational skills.

The educational program was also of educational benefit for both the medical students who acted as instructors and the junior-high school students who participated. The most notable outcome for all participants was the increase in the understanding of the basics of molecular biology and its association with the field of medicine. This one-day activity helped students understand that diseases are often the result of genetic abnormalities and spurred their interest in research. The To-Collabo study provided them with a basic understanding of the important roles of proteins and DNA; the structure, function, and replication of DNA; the molecular mechanisms underlying the influence of genes on traits, including transcription and translation; the molecular biology of variations; and genetic engineering. The tangible context in medicine generated interest and motivation and helped medical students to connect basic science with a broader view of medical problems by providing a real example of a disease and its molecular cause.

The general population has gained exposure to terms such as DNA, proteins, and biotechnology through daily news and observes the deeper integration of these technologies in daily life [12]. Hence, educating the younger generation is a necessity. Basic knowledge of molecular biology and its application in research has been incorporated into the educational curriculum. However, science has become sophisticated; thus, it has become difficult for people to grasp the entire picture and use their knowledge in daily life. It is difficult for teachers to keep up with new concepts owing to the rapid progress in molecular biology and its applications in modern medicine. The To-Collabo teaching course comprises a series of experimental and discussion activities that help junior-high school students understand that DNA and proteins are not imaginary concepts. This course helps students understand crucial components of the human body that affected functions and characteristics and how genetic information in DNA results in the formation of different versions of proteins that subsequently influence characteristics. These concepts were conveyed via discussions, as well as web-based and hands-on learning activities, that was conveyed as an introductory unit in molecular biology. This helped students make connections between what they learned and what they observed in daily life.

In conclusion, this study successfully developed and implemented a pilot educational program on genetic testing with a local community outreach approach. It can be inferred that the introduction of this outreach approach based on genetic testing experiments, effectively aided undergraduate medical students in acquiring professional skills that it can facilitate the provision of simple explanations to patients in their future clinical work. However, there are two major barriers to promoting the program. The first is to train an adequate number of instructors. As the students use sophisticated laboratory equipment and apparatus that junior-high school students would not normally use in school practical work, it is necessary to ensure that an adequate number of instructors are available to give advice as appropriate. The second is the characteristics of the students. The junior-high school students who participated in this pilot were interested in science and were able to carry out the experiments with ease. It is necessary to further improve the compact practical system and to provide simple explanations so that children with little interest in science can also enjoy participating in the future.

## ACKNOWLEDGEMENTS

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