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Abstract

Objective: *To evaluate a pilot of a laboratory model for relating pharmacogenetics to clinical decision making.* ***Case Study:*** *This pilot was undertaken and evaluated to help determine if a pharmacogenetics laboratory should be included in the core Doctor of Pharmacy curriculum. The placement of the laboratory exercise in the curriculum was determined by identifying the point in the curriculum where the students had been introduced to the chemistry of deoxyribonucleic acid (DNA) as well as instructed on the chemistry of genetic variation. The laboratory included cytochrome P450 2C19 genotyping relative to the *2 variant. Twenty-four students served as the pilot group. Students provided buccal swabs as the source of DNA. Students stabilized the samples and were then provided instructions related to sample preparation, polymerase chain reaction, and gel electrophoresis. The results were reported as images of gels. Students used a reference gel image to compare their results to. Students then applied a dosing algorithm to make a "clinical decision" relative to clopidogrel use. Students were offered a post laboratory survey regarding attitudes toward the laboratory. Twenty-four students completed the laboratory with genotyping results being provided for 22 students (91.7%). Sixteen students were wild-type (*1/*1), while six students were heterozygous (*1/*2). Twenty-three students (96%) completed the post laboratory survey. All 23 agreed (6, 26.1%) or strongly agreed (17, 73.9%) that the laboratory "had relevance and value in the pharmacy curriculum".* ***Conclusion:*** *The post pilot study survey exploring a laboratory model for pharmacogenetics related to clinical decision making indicated that such a laboratory would be viewed positively by students. This model may be adopted by colleges to expand pharmacogenetics education.*

Introduction

The importance of teaching pharmacogenetics (PGt) to pharmacy students is becoming increasingly evident. Pharmacogenetics, relating variation in drug response to a specific gene, is gaining acceptance as support data in therapeutic decision making.[1-4] In fact, the Clinical Pharmacogenetics Implementation Consortium (CPIC) has published dosing guidelines related to specific gene-drug pairs.[5,6] These guidelines are intended to help clinicians apply PGt data in therapeutics to maximize drug efficacy and minimize or avoid adverse drug reactions.[5] Currently more than 110 drugs have PGt information in their package labeling and 17 of these fall within the top 200 most commonly prescribed drugs.[7,8] The list of drugs with PGt information in their package labeling will continue to grow as the use of PGt data increases in drug development.[9] As pharmacists have been drug-drug interaction experts, the advent of pharmacogenetic data will result in pharmacists being gene-drug interaction experts. In order to be proficient at utilizing genetic testing and interpreting and applying pharmacogenetics, the pharmacist must have an extensive knowledge of the subject. This laboratory exercise is intended to provide students with experience in using pharmacogenetic data for clinical decision making.

Increasingly, pharmacy students will be required to apply the science of PGt to clinical practice.[1-4] To address this, colleges of pharmacy continue to develop their curricula in PGt, with approximately 90% of schools including the subject matter in their Doctor of Pharmacy curricula as of 2009; an increase from 39% as reported in 2005.[10,11] However, only 2.9% of colleges of pharmacy required a PGt laboratory exercise.[10] Yet, recent evidence suggests that laboratory exercises in PGt are invaluable in teaching students how science "connects" to clinical application.[12,13]

Knoell et al. described a genotyping exercise targeting the angiotensin converting enzyme gene as part of an elective PGt course, with ten student volunteers providing DNA samples via buccal swabbing.[12] The genotyping results were integrated into five didactic lectures throughout the course to enhance the students understanding of PGt. The expected objective of developing the genotyping exercise was to "improve pharmacy students' comprehension of pharmacogenomic principles that apply to patient care."[12] In response to a post exercise/post elective course survey, 71.9% of responding students agreed or strongly agreed that "observing the actual results of a PCR-based genotype analysis first-hand in class was very useful for future practice."

Also, Krynetskiy et al. incorporated genotyping the n-acetyltransferase 2 (*NAT2*) gene into a pharmaceutics course offered to students in the second year of their professional program.[13] A total of 150 students participated in two three-hour laboratory periods and one one-hour discussion period. A stated goal of the exercise was to "demonstrate to the students the universal character of genetic variability in genes coding for drug-metabolizing enzymes and the importance of genetic analysis for practical pharmacotherapy." A survey of student attitudes showed that 88.9% of the students agreed or strongly agreed that the laboratory exercise helped them understand "why pharmacogenetics is so important."[13]

These PGt laboratory exercises were highly advantageous but as yet, no model has been established that can be easily integrated into existing curricula. Additionally, to date, no model focuses on a gene that directly influences dosing of a commonly prescribed medication and requires minimal resources in terms of both cost and instructor time. To complement the didactic components of PGt education in our curriculum, we sought to develop a laboratory exercise that directly related the science of PGt to its clinical application. We intended to develop an exercise that linked basic science to clinical science, where the biochemical information of DNA is translated into clinical information which has a clear purpose when considering genetic-based dosing guidelines used for clinical decision making. Here we present a model that meets the above criteria and may be applied to various pharmacy curricula.

The Rationale and Objectives of Exploring a PGt Laboratory Exercise

The growing emphasis on the clinical applications of PGt provided the rationale for exploring an exercise linking the science of genetics to its application in our curricular sequence. The objective of our PGt education is to have our students understand the scientific basis of genetic variation and to be able to interpret and apply that information in patient care through personalized medicine. The specific objective of the PGt laboratory exercise is to link genetic variability to clinical decision making.

The cytochrome P450 2C19 (*CYP2C19*) gene was selected as the target for this exercise due to its clinical relevance and established PGt-based dosing guidelines.[14,15] An excess of one million coronary artery stents are placed annually in the United States to prevent complications, including death, in patients with coronary artery disease.[16,17] Dual antiplatelet therapy is a standard of practice and clopidogrel is a common drug used in this setting.[17] Clopidogrel, a prodrug, requires bioactivation to form an active compound, which inhibits platelet aggregation by inhibiting adenosine diphosphate (ADP) binding to $P2Y_{12}$ receptors on platelets. This effectively decreases platelet aggregation, helping to prevent thrombosis. Clopidogrel has been one of the most commonly prescribed drugs, with more than 28 million prescriptions dispensed in 2011, alone.[8] While commonly used, the pharmacologic response to the drug shows wide interpatient variability. This variability has been attributed, in part, to genetic variability in the enzyme responsible for the bioactivation of clopidogrel, CYP2C19.[14,15]

Numerous single nucleotide polymorphisms (SNPs) have been identified for the *CYP2C19* gene, resulting in the observed interpatient variability associated with response to clopidogrel therapy. The most common or wild-type *CYP2C19* gene sequence (designated CYP2C19*1) produces a full-functioning CYP2C19 enzyme. Variant alleles that result in a loss-of-function CYP2C19 enzyme have been identified and are designated as *2, *3, *4, *5, *6, *7, and *8. Other variant alleles of lesser frequency exist.[14,15] Indeed, approximately 30% of Caucasian stent placement patients who take clopidogrel may not be optimally benefiting from the drug. There is a three-fold increased risk of stent thrombosis following placement of the stent(s) in patients carrying at least one loss-of-function allele.[18,19] Of the patients not fully benefiting from clopidogrel therapy, approximately 95% carry the *2 loss-of-function allele as heterozygotes *1/*2 or homozygotes *2/*2.[14,15] Additionally, the percentage of individuals carrying a loss-of-function or reduced function allele is greater in other populations (African ~40%; East Asian populations ~55%).[14-19] Genetic-based dosing guidelines for the use of clopidogrel in the stent patient population have been introduced and are gaining acceptance as a standard of care.[14,15,20]

Details of the Pilot Pharmacogenetics Laboratory Exercise

The placement of the model PGt laboratory exercise at a specific point in our curriculum was based on the examination of our overall PGt content. We chose to include the laboratory towards the end of the semester of the first of a two-course biochemistry sequence, after the students had sufficient instruction on the chemistry of DNA.

Twenty-four students enrolled in the first of two sequential biochemistry courses volunteered to participate in the pilot testing of the PGt exercise. Each student was provided a random four-digit number.[21] The number was placed on the tube containing a swab (Isohelix SK-1; Cell Projects Ltd.; Harrietsham, Kent, UK) used for buccal cell sampling. During the 11th week of fall semester, three sampling days were scheduled, with each limited to eight student volunteers. On each sampling day, students reported to the College's common laboratory and received instruction on the process

of buccal swabbing as described by the manufacturer. After one minute of swabbing, each student placed his or her swab into the tube corresponding to the random number he or she received. A DNA isolation kit (Isohelix DDK-50; Cell Projects Ltd.; Harrietsham, Kent, UK) containing lysis buffer, proteinase K, a capture buffer and rehydration buffer was used to isolate and stabilize DNA from each buccal sample. Each student used single-channel pipettes to add the lysis buffer and proteinase K to his or her sample. The stable samples were then stored at room temperature until preparation for polymerase chain reaction (PCR).

Upon stabilization of their DNA samples, students were presented with the process of how their samples would be analyzed. A detailed description of sample preparation including the use of buffers, specific primers, deoxynucleotides, and DNA polymerase was provided. The details of the PCR protocol were presented as was the process involved with gel electrophoresis.

Alleles for *CYP2C19*1* (wild-type) and *CYP2C19*2* (loss-of-function) were genotyped by tetra-primer PCR essentially as described by Hersberger et al.[22] Briefly, approximately 50 ng of genomic DNA in 2.0 µL TE buffer (10 mM) Tris, pH 8.0, 1 mM EDTA was amplified by PCR (cycling conditions: 10 min at 94˚C; 44 cycles of 30s at 94˚C, 30s at 50˚C, and 60s at 72˚C; 7 min at 72˚C) using four primers (Ex5U: CAGAGCTTGGCATATTGTATC, Ex5L: GTAAACACACAACTAGTCAATG, 2mutU: ATCATTGATTATTTCCCA, 2wtL: AATTGTTATGGGTTCCC). Products were resolved by 2% gel electrophoresis and identified as 321-bp (control), 229-bp (*CYP2C19*2* allele) and 127-bp (*CYP2C19*1* or wild-type allele). This method was employed as it is reproducible as published by Hersberger et al.[22] While more advanced technologies are available it is likely the approach utilized here would be more feasible for most institutions as standard PCR and electrophoresis are commonplace. This method can be used as a "start-up" with relatively low expense.

A faculty member and student research assistants (none of which were volunteers for the PGt exercise) prepared the samples for PCR and performed the PCR and gel electrophoresis procedures to obtain genotyping results. Figure 1 presents a flow chart of the laboratory model.

Student Interpretation of Pharmacogenetic Testing

Following the processing of the samples, an image of the electrophoresis gel with results for each student was provided for analysis. The students, in groups of four to six, reported to the common lab or faculty office and were asked to identify their individual results by analyzing images of the DNA bands in the lane corresponding to the four-digit identification number. The students compared their DNA band image to those presented by Hersberger et al. in order to determine their genotype (Figures 2a and 2b).[22] Results were confirmed using positive control samples derived from individuals who were wild-type (*1/*1) or heterozygous (*1/*2) for *CYP2C19*, as determined by commercial sequencing (23andMe; Mountain View, CA, USA; Illumina BeadChip; Laboratory Corporation of America; Burlington, NC, USA). The results of each student's interpretation, i.e. genotype, were recorded next to the four digit number on a laboratory form. In the context of the CPIC *CYP2C19*-clopidogrel dosing guidelines, each student determined the approach they would take regarding the use of clopidogrel or an alternative antiplatelet drug for an individual of their specific genotype. Here, the students were concerned with drug choice only.

Seeking Student Opinions Regarding the Laboratory Exercise

After this exercise was completed, students were offered, by email, a six-question survey to gather their opinions on the laboratory experience relative to biochemistry, PGt, and the pharmacy curriculum (Figure 1). The survey questions were formulated by the faculty piloting the laboratory exercise.

PGt and the Institutional Review Board

The Ohio Northern University Institutional Review Board (IRB) exempted the laboratory exercise pilot study from review as the PGt sampling procedure was done with safeguards ensuring volunteer anonymity and as the results were not associated with an identifiable volunteer.

Yield of PGt Testing Results

Twenty-four students originally volunteered for the genotyping exercise. One student withdrew prior to the exercise and was replaced by another student. The students would be considered a population of North American Caucasians. Of the 24 students who participated, 19 had genotype results available to them. Results for five students were not provided as technical difficulties prevented analysis of the results. Samples from the five students that could not be analyzed originally were processed a second time. This yielded results for three more students. Of the 22 students that were able to interpret their genotype, 16 (72.7%) were wild-type (wt/wt;*1/*1) and 6 (27.3%) were heterozygous (wt/*2; *1/*2). Our genotyping data provided confirmation of the reproducibility of the method of Hersberger et al. (Figure 2b) and indicated the buccal swab sampling method can be employed in the classroom as it would be in the clinical setting.[22] However, it is likely that, while instructed on proper collection, some buccal samples did not contain enough DNA for amplification. This has been noted previously and it

should be expected that some samples will not contain enough DNA due to poor sampling technique.[23] With discussion of the CPIC guidelines (Figure 3), the six students with the heterozygous (*1/*2) genotype concluded that antiplatelet therapy with a drug other than clopidogrel would be appropriate for a stent placement patient with their genotype, whereas students with the wild-type (*1/*1) genotype concluded clopidogrel was a valid therapeutic option for antiplatelet therapy in stent placement patients with this genotype.

Student Opinions of the PGt Laboratory Exercise

Twenty-three of the 24 students (95.8%) completed the post exercise survey. Overall, the exercise was viewed positively as indicated by the responses (Table 1). Across all questions, relative to the scale of 1=strongly disagree, 2=disagree, 3=neither agree nor disagree, 4=agree, and 5=strongly agree, the mean value was 4.56 $\pm$ 0.5. Seventeen of the 23 students (73.9%) strongly agreed that "the genotyping exercise has relevance and value in the pharmacy curriculum." There was not one negative (strongly disagree or disagree) response to any question. Two neutral (neither agree nor disagree) responses were noted regarding the exercise and understanding the concept of a prodrug. One student expressed that they neither agreed nor disagreed that the exercise provided a rationale for performing genotyping (Table 1).

Placement of the PGt Laboratory Exercise in the Curriculum

We examined our curriculum to identify a specific point where we thought the laboratory exercise would best fit. As a "zero-six" program, PGt education at the Raabe College of Pharmacy at Ohio Northern University spans six years. In the fall of their first year, students are introduced to PGt in the introductory biology course, where they search genomic data using the Ensembl genome browser to explore cytochrome P450 2C9 (*CYP2C9*) and warfarin dosing.[24] In the subsequent spring, students learn more about PGt in the broader context of personalized medicine during the "Profession of Pharmacy" course. Here, a video of a Plavix® (clopidogrel) television commercial in which a statement about genetic testing is made is shown to the students and discussed. In the second year, students learn about the human genome project and DNA sequencing in the "Applied Science of Pharmacy" course. The students are introduced to polymerase chain reaction and gel electrophoresis. In the third year, students learn the "chemistry of DNA" in a two-course biochemistry sequence. The "Biomedical Science (BMS)" module teaches PGt related to pharmacokinetics and pharmacodynamics in the early spring of the fourth year. Starting that semester, following the BMS module and throughout the fifth year, students learn about specific drug-gene interactions as they progress through a sequence of five "therapeutics" modules. The topics of PGt and personalized medicine are updated in late spring semester of the fifth year, in a "capstone" course, prior to the students starting their advanced pharmacy practice experiences (APPEs). Some students take the opportunity to participate in an elective APPE focusing on PGt in the sixth year. In total the students receive over 30 hours of required PGt and related instruction.

We had considered the cardiovascular therapeutic module as a potential "home" for the exercise, however, the module is presented considerably later in the curriculum relative to the basic science "chemistry of DNA" subject matter. Therefore, we chose to include the exercise in the first biochemistry course. In this course, the mechanism of DNA replication is covered in detail. Deoxyribonucleic acid replication fidelity and processivity are explained, and carefully differentiated. The topics of fidelity and processivity introduce a more detailed discussion of DNA errors and repair mechanisms. The types of DNA errors that exist are introduced as well as their relative rate of occurrence. DNA repair mechanisms are then covered including nucleotide and base excision repair, direct repair, mismatch repair and transpositional recombination. During class discussion, students are encouraged to consider the meaning of loss of function of proteins based on DNA variation and to think of examples, after which the instructor guides them to consider PGt examples. Following the presentation of content related to replication of both DNA and ribonucleic acid (RNA), a didactic series on transcription and translation begins. A list of the general functions of various transcription factors is provided. Following the presentation of the transcription factors a summary is presented of methods for gene expression regulation. This includes regulation at the chromatin level, transcription initiation, and finally transcription beyond the basal level. In addition to these general genetic processing topics, specific examples are provided. For example, the importance of variation in DNA resulting in an altered amino acid sequence is discussed in reference to warfarin dosing. This example is provided to emphasize the effects that a SNP can have on an amino acid sequence and subsequently on protein function. It is at this point we chose to include the PGt laboratory exercise.

Similar to colleges/schools of pharmacy that offer a "2-4" program, the majority of the basic science courses are offered in the first two years of our "0-6" program and integration of the pharmacogenetics laboratory into the curriculum was considered in light of the students having a sufficient basic science foundation. Other colleges may choose a different point in their curriculum to introduce a PGt laboratory exercise. The current laboratory model can be

utilized in any number of places in a given curriculum, once the students have a basic science knowledge base.

The Gene-Drug Pair

A clear benefit of this model is the use of published genotype-based dosing guidelines related to one of the most commonly prescribed drugs.[14,15] In fact, in 2011 clopidogrel was the seventh most commonly prescribed drug.[8] When considering this exercise, we chose to have the students engage in the collection of a DNA sample, as may typically be done in the clinical setting, and to perform the process of stabilizing the DNA. We chose a gene-drug pair that has clear clinical relevance, here being *CYP2C19* genotyping relative to clopidogrel. The indication-specific use of *CYP2C19* genotyping in stent placement patients has recently been discussed and has been made clear to our students.[20] As approximately 30% of individuals carry a loss-of-function *CYP2C19* variant, and as 95% of those with a variant have the *2 form, the choice of specifically testing for *CYP2C19*2* was made. In this exercise, 27.3% (6 of 22) individuals were heterozygous *1/*2 individuals, similar to the frequency observed in a similar Caucasian population.[15] As students were in groups of four to six when reviewing the gel images, there was some discussion between them about how to interpret the bands (not specific to an individual as the data were randomly coded with a four-digit number), which likely influenced some genotype determinations. Similarly, once some of the students discussed the use of the algorithm to determine the appropriate antiplatelet drug, others seemed to make their decision more rapidly, likely because they had been provided with "instructions" from their student colleagues' discussions in the group setting. The "call" of the genotype was not a specific "test" question noted as "correct" or "incorrect".

Importantly, regardless of the number of students participating, anonymity must be maintained. IRB approval was based on the design including anonymity. Certainly, a student could opt out of providing their DNA. Here, a student making this decision could be provided with anonymous data to use. However, the exercise may have more "appeal" to some students based on the use of their own DNA.

In the current exercise, the students utilized their own DNA results to make a "clinical decision" based on their genotype. The students were informed that the data provided through this exercise came from a non-Clinical Laboratory Improvement Amendment (CLIA) certified laboratory and was not to be utilized in a true clinical setting. In fact, although not required by the IRB and to address some concerns of educational DNA testing, we had the students sign a statement that they understood this point.[25] Additionally, we discussed that the data they evaluated was not presented in the format they would see in the clinical setting. i.e., they would refer to a laboratory report for data and not be interpreting images of gels.

Connecting the science of DNA with clinical application of PGt is a way to raise the expectations of pharmacy students regarding personalized medicine and this model provides a method to accomplish this.[26] A clear benefit of this model is the use of published genotype-based dosing guidelines related to one of the most commonly prescribed drugs.[14,15] In fact and as stated earlier, in 2011 clopidogrel was the seventh most commonly prescribed drug.[8]

As eventual pharmacotherapy experts, it is important to have the students see the origin of genotyping data and understand that they, as pharmacists, will be expected to know when to recommend PGt testing and importantly interpret and apply PGt testing results. This laboratory exercise provided the students with an example of generation of DNA data. The exercise provided the students with experience in interpreting data and applying the data through use of genetic-based dosing guidelines as applied in pharmacy practice.[4, 6, 14]

PGt Laboratory Time Commitments

The student volunteers involved in this exercise spent a total of 50 minutes involved in sample collection, stabilization, and instruction on sample handling, processing and reporting. Thirty-five minutes were used with the initial meeting for the swabbing, DNA stabilization, and presentation of the PCR and gel electrophoresis procedures and 15 minutes were used later to view the data and interpret the results. The time commitment for the faculty member was 8.4 hours, including the time with the students, performing sample preparation, PCR and gel electrophoresis. The student lab assistants spent approximately five hours working with the faculty member processing the samples. The time increased to approximately 7.5 hours for the student lab assistants as they ran the repeat analysis of samples that were not able to be evaluated after the first attempt. The turn-around time on the samples, from collection to reporting of results was six days. At our institution, with typical class sizes of 165 students, expanding this exercise to the entire class would potentially increase faculty time commitment to 13 to 14 hours per semester. The laboratory assistant's time would increase also, however, genotyping, for other reasons is part of the typical daily workload and the additional work would not significantly increase their time commitment. The turn-around of samples will necessarily take longer due to the larger volume of samples. With larger class sizes, it may be efficient to have the students perform the buccal swabbing only and forgo the

DNA stabilization step using the pipettes. In this case, the sample processing, PCR conditions and gel electrophoresis technique could be presented after the students complete the buccal sampling. This would significantly decrease faculty time commitment as the material would be presented once to the entire class as opposed to multiple times to small groups.

PGt Laboratory Costs

The cost associated with this pilot exercise includes supplies and reagents for sample collection, preparation, PCR reagents and supplies, as well as supplies for gel electrophoresis. The total cost per sample (per student) was approximately $6. This cost was not considered to be prohibitive. With class sizes of approximately 165 students, an annual budget for the lab of $990 would be expected. Regardless, the instrumentation and equipment for the genotyping exercise is relatively minimal, including a vortex mixer, heat block, micro-centrifuge, thermocycler, and gel electrophoresis equipment, with a total cost of $8,000 to $10,000. Many institutions will have the laboratory equipment/instrumentation available as PCR and gel electrophoresis are common techniques.

Next Steps

Student response to the genotyping exercise pilot indicated the importance of the exercise. The results will help us to move forward with implementing the exercise for the entire biochemistry class in the subsequent academic year. At that time, with the entire class interpreting their individual results, we will use a "real time" capture technology to record the frequency of individuals who are wild-type (*1/*1), heterozygotic or homozygotic for the *2 allele. Here, students will compare the class aggregate data with published genotype frequencies in a similar population. The students understanding of the use of genetic data in the context of clinical decision making will be tested on two occasions, including a multiple choice exam and a comprehensive final exam with various question formats.

Additionally, the laboratory exercise will be considered relative to pharmacogenomics (PGx; encompassing PGt) competencies for pharmacists, which are currently being developed.[27] Pharmacy student education relative to PGx must be considered in the context of the practice of pharmacy where pharmacists will be viewed as the gene-drug interaction experts. Colleges of pharmacy must work to make this an expectation of the pharmacy student.

Conclusions

This approach can be adopted by other colleges of pharmacy with the expectation of students: 1) relating biochemistry and pharmacogenetics to clinical application, 2) understanding the basic process of genetic sampling and genotyping, 3) realizing the rationale for performing genotyping, and 4) recognizing the relevance and value of the laboratory exercise in their pharmacy education. Key to this approach is tying in the science with the use of clinical dosing guidelines. As students progress through a curriculum, the use of pharmacogenetic information, whether it is based on population allele frequencies or individual genotype, can be pointed to as a clear example of the clinical application of basic science. When a gene-drug pair is presented in the context of genetic testing, the student will relate the laboratory exercise to clinical application. This shows the student the direct connection of the science with clinical decision making. This model is unique in that the students learn skills that are translational to practice and can be applied clinically; obtaining genomic DNA through a buccal swab and interpreting PGt results relative to specific dosing guidelines.

The laboratory model proved to be successful and has resulted in adoption of the model for subsequent biochemistry courses as a required exercise. The model was easily implemented and both time and dollar investments were considered to be reasonable.

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Table 1. Post pilot genotyping exercise survey results. (N=23)

Question	Strongly Disagree (1)	Disagree (2)	Neither Agree/Disagree (3)	Agree (4)	Strongly Agree (5)	Mean ± SD
The genotyping exercise related biochemistry and pharmacogenetics to clinical application.	0	0	0	7 (30.4%)	16 (69.6%)	4.70 ± 0.47
The genotyping exercise helped me understand the concepts of genetic variation and polymorphisms.	0	0	0	15 (65.2%)	8 (34.8%)	4.35 ± 0.49
The genotyping exercise helped me understand the concept of a prodrug and metabolism to an active drug.	0	0	2 (8.7%)	10 (43.5%)	11 (47.8%)	4.39 ± 0.66
The exercise helped me understand the basic process of how genetic sampling and genotyping is performed.	0	0	0	7 (30.4%)	16 (69.6%)	4.70 ± 0.47
The exercise provided me with a rationale for performing genotyping.	0	0	1 (4.3%)	14 (60.9%)	8 (34.8%)	4.30 ± 0.56
The genotyping exercise has relevance and value in the pharmacy curriculum.	0	0	0	6 (26.1%)	17 (73.9%)	4.74 ± 0.44

Figure 1. Flow chart describing the pharmacogenetic laboratory pilot.

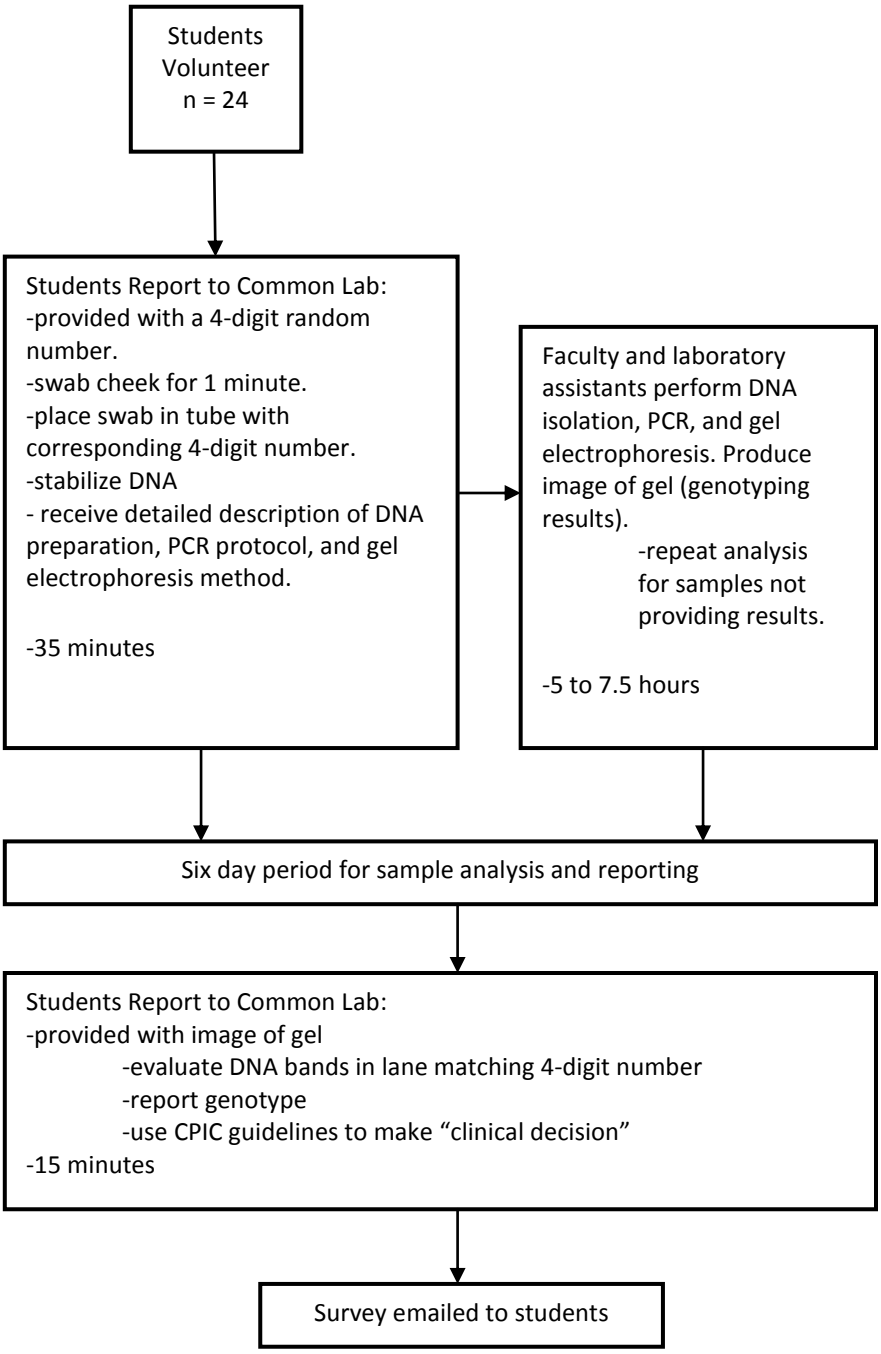

Figure 2a. Example image of gel electrophoresis results.

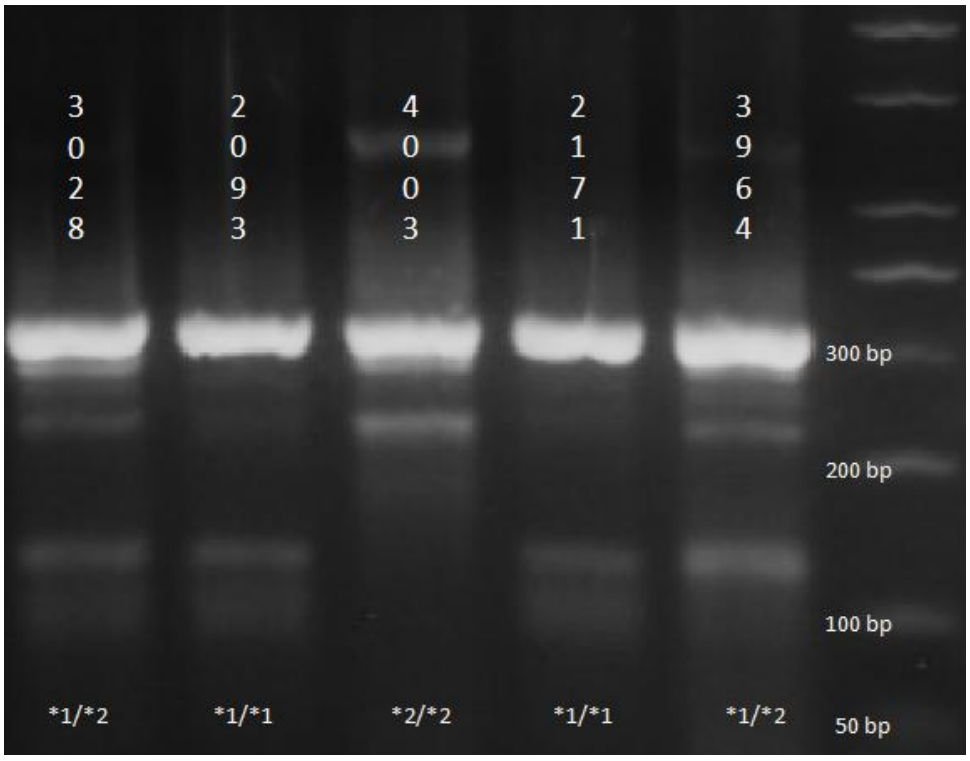

Figure 2a. Representative image of gel electrophoresis with an example four-digit random number as assigned to each volunteer. The genotype of each volunteer is noted at the bottom of each lane. *1/*1 = extensive metabolizer, *1/*2 = intermediate metabolizer, *2/*2 = poor metabolizer. The results here, presented as examples, were not related to students in the described pilot exercise.

Figure 2b. Reference image of gel electrophoresis results as presented by Hersberger et al.[22]

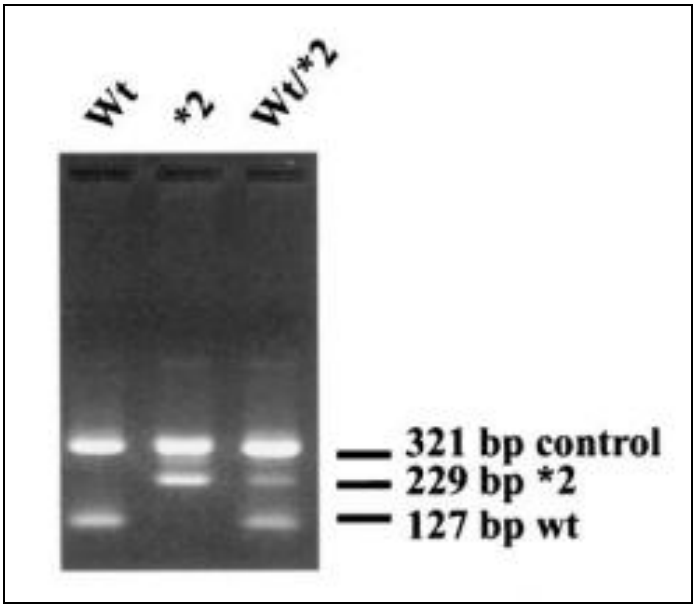

Figure 2b. Reference image of gel electrophoresis results for CYP2C19 genotyping.
Wt = normal function allele (*1), *2 = loss-of-function allele, Wt/*2 = heterozygous (*1/*2).
Reprinted by permission from the American Association for Clinical Chemistry: [Clinical Chemistry] Hersberger M, Marti-Jaun J, Rentsch K, Hänseler E. Two single-tube tetra-primer assays to detect the CYP2C19*2 and *3 alleles of S-mephenytoin hydroxylase. *Clin Chem*. 47:772-774, copyright 2001.

Figure 3. CPIC CYP2C19-clopidogrel dosing algorithm.

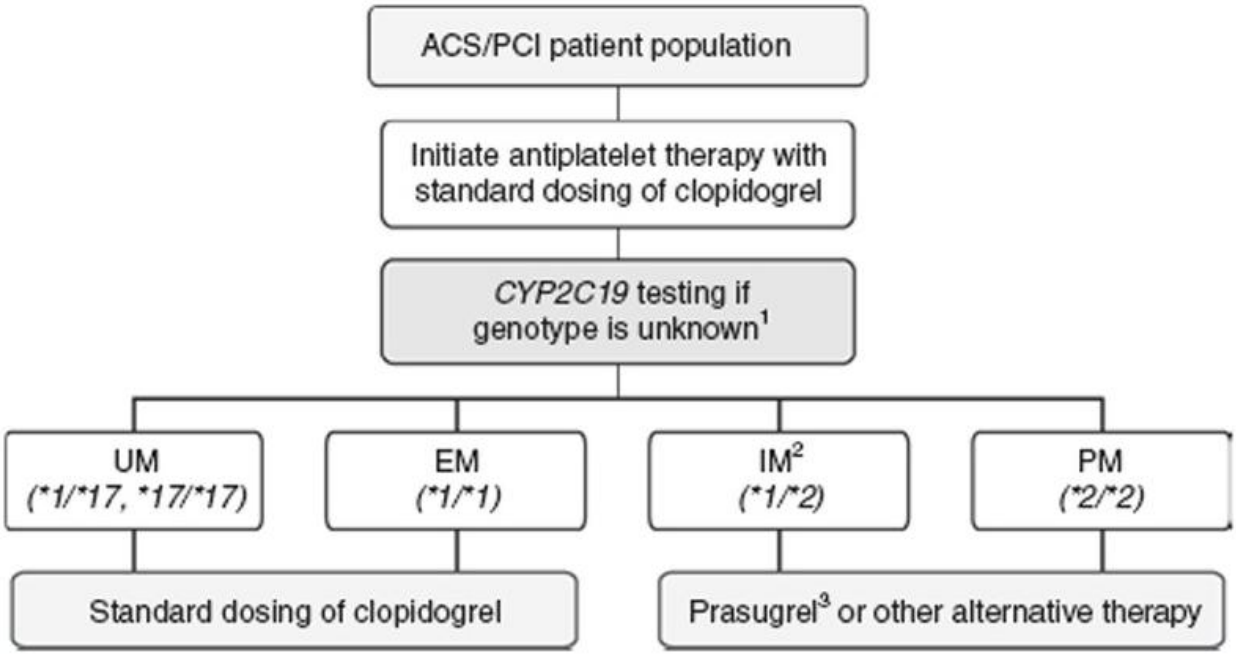

Figure 3. Algorithm for suggested clinical actions based on *CYP2C19* genotype in patients with acute coronary syndromes initiating antiplatelet therapy. ACS, acute coronary syndrome; EM, extensive metabolizer; IM, intermediate metabolizer; PCI, percutaneous coronary intervention; PM, poor metabolizer; UM, ultrarapid metabolizer. Other rare *CYP2C19* genotypes exist apart from those illustrated. Higher-dose clopidogrel has not been adequately studied at the time of this writing but may improve platelet function in a subset of IMs and PMs. Note that prasugrel is recommended only when its use is not clinically contraindicated. Reprinted by permission from Macmillan Publishers Ltd: [Clinical Pharmacology and Therapeutics] Scott SA, Sangkuhl K, Gardner EE, et al. Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450-2C19 (CYP2C19) genotype and clopidogrel therapy. *Clin Pharmacol Ther*. 90(2):328-332, copyright 2011.