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An Interdisciplinary Experience focused on Pharmacogenetics: Engaging pharmacy and physician assistant students in conversations about antiplatelet therapy with respect to *CYP2C19* genotype

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Keywords: interdisciplinary, interprofessional, laboratory, pharmacogenetics, pharmacogenomics

Abstract

***Objective**: The goals of the interdisciplinary laboratory were to educate and engage pharmacy and physician assistant (PA) students in a discussion focused on the collection, interpretation, and application of pharmacogenetic data. **Design**: Interdisciplinary teams participated in a one-hour, case-based discussion and provided a therapeutic recommendation using the Clinical Pharmacogenetics Implementation Consortium guidelines. **Assessment**: All students were surveyed before and after the laboratory on knowledge and application of pharmacogenetics and working in interdisciplinary teams. The interdisciplinary laboratory successfully enhanced the student's knowledge about sample collection and interpretation of pharmacogenetic information. Additionally, the laboratory improved student confidence in working in interdisciplinary teams to apply pharmacogenetic information to clinical decision making. Furthermore, the majority of students indicated that the interdisciplinary laboratory is valuable and useful in healthcare curriculums. **Conclusion**: The laboratory highlighted the differences between pharmacy and PA education regarding PGt, and brought to light several important uncertainties: (1) What is the depth of PGt knowledge that healthcare practitioners need? (2) What are best practices for conveying PGt information?*

Description of Case

Pharmacogenetics (PGt), the study of an individual's drug response as it relates to a single gene, is changing therapeutic decision making.[1] The acceptance of PGt into clinical practice necessitates the education of all healthcare providers in genetics and particularly PGt (or pharmacogenomics (PGx), the study of drug response as it relates to multiple genes). In fact, the Accreditation Council for Pharmacy Education (ACPE) Standards 2016 will require all colleges of pharmacy to include PGx/PGt subject matter in the doctorate of pharmacy (Pharm.D.) curriculum.[2] Just as pharmacists have historically been the drug-drug interaction experts among an interprofessional healthcare team, pharmacists will become the drug-gene interaction experts. Therefore, an interdisciplinary education (IPE) experience that is focused in PGt provides pharmacy students a meaningful opportunity for professional training.

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In choosing another discipline for the laboratory, the logical choice was a healthcare provider that can prescribe medicine. We partnered with a neighboring school that offers a physician assistants (PA) program to recruit PA students for the IPE laboratory. The standards governing PA education dictate that basic pharmacology and genetic mechanisms must be included in the curriculum, but do not include specific requirements on PGt/PGx.[3] For several of the PA students, the IPE laboratory was the first introduction to PGt. In purposefully partnering pharmacy and PA students, the responsibilities of each discipline could be emphasized.[4, 5] For instance, pharmacy students should interpret PGt findings, utilize the Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines to recommend therapeutic choices, and explain the rationale for any recommendations to the PA students. Similarly, the PA students should engage the pharmacy students in a discussion about the CPIC guidelines and gather enough concise information to share with their patients. As a whole, the field of PGt will rely on interdisciplinary teams for implementation in patient care settings and this laboratory was focused on providing students that experience.

The goals of the IPE laboratory were to educate, as well as, engage pharmacy and PA students in a discussion focused in the collection, interpretation, and application of PGt data.

To measure student perceptions about PGt/PGx, the pharmacy and PA students were surveyed before and after the IPE laboratory experience. The themes, design and implications of this innovative IPE laboratory are discussed. At the time of this publication and to the best of the authors' knowledge, this is the first laboratory of its kind in healthcare education.

Rationale and Design

The IPE laboratory was housed within the Manchester University College of Pharmacy, Natural and Health Sciences Pharmacy Program. Several key elements were considered when placing the laboratory within the pharmacy curriculum. Most importantly the pharmacy students needed to have progressed to a point of full understanding of a drug (i.e. – therapeutic uses, mechanism of action, and metabolism) that has PGt considerations. Additionally, the laboratory should be part of the requisite curriculum, given that PGt is a required component of the pharmacy curriculum per the ACPE Standards 2016.[2] Therefore the IPE laboratory was housed in the required pharmacy practice laboratory that coincides with a didactic integrated cardiovascular module. In the didactic course the antiplatelet drugs are taught, including clopidogrel (Plavix®), an ideal choice for considering a drug-gene interaction.

The IPE laboratory was also a mandatory component of the PA curriculum. The Master of Science in Physician Assistant Studies is a 27-month program, and this laboratory fell within the 18th month of the program. At the time of the laboratory, the PA students had studied antiplatelet therapy, but had not been introduced to PGt. The pre-laboratory knowledge base of each of the student cohorts, pharmacy and PA, may accurately reflect the current status of healthcare teams in clinical practice, which is ideal for the experience.

The laboratory was an hour-long session and consisted of a presentation on the use of buccal swabs to obtain DNA, PCR amplification of target genes, and interpretation of PGt testing results. Following the presentation, teams comprised of 3-4 pharmacy students and 1-2 PA students were provided unique patient cases. The patient cases, developed in collaboration with a pharmacy practice faculty member, provided a scenario in which antiplatelet therapy would be recommended. Each of the patient cases also provided the *CYP2C19* genotype of the patient. Appendix A provides an example patient case. Following discussion of the case, the interprofessional teams provided a recommendation for antiplatelet therapy based the CPIC guidelines for the clopidogrel-*CYP2C19* drug-gene interaction.[6]

Students from both disciplines were surveyed prior to and following the laboratory. The number of pharmacy students and PA students that participated in the survey were 71 and 25, respectively. The survey used a 0-5 point Likert scale, where 0 equates to "not confident", 3 is "somewhat confident", and 5 is "very confident."[7] The survey consisted of 12 questions focused on student confidence in understanding PGt and perceptions about utilizing PGt data in an interdisciplinary team to make therapeutic decisions. The survey questions were created using the ACPE Standards 2016 as a guide and with consideration of the goals for the IPE laboratory. The IPE laboratory is an evolution of previous PGt laboratories that were conducted at other institutions. For comparison's sake, several of the survey questions from the previous laboratories were also included.[8] Unique to the IPE laboratory survey were questions regarding interprofessional communication. The median responses to the pre- and post-laboratory survey from each student group were analyzed using a Wilcoxon signed test in SPSS 22.0, with statistical significance designated as $p < 0.01$. This study was approved by the Manchester University Institutional Review Board.

Student Response

For every question on the survey, and in both the pharmacy and PA student cohorts, the median response significantly increased post-laboratory (Table 1). The questions with the largest increase in median Likert response were shared across student cohorts, namely "I feel confident in my ability to explain pharmacogenetic data to other members of an interprofessional team," "I feel confident in my ability to interpret pharmacogenetic data, and "I feel confident in my ability to recommend prescriptions or dosages for certain drugs based on pharmacogenetic data." In general, the difference between the pre- and post-laboratory responses was greater for the PA students than the pharmacy students. Overall, the increase in the median Likert responses indicates that students' confidence in understanding and ability to explain PGt improved during the hour-long IPE laboratory.

In addition to survey data, several observations were made by the IPE laboratory designers. One is that the pharmacy and PA students worked well in the interprofessional teams. Most of the teams quickly established a team approach, in that groups were eager to converse about the patient cases and representation and input was equally divided among the professions. Given that the PA students had less PGt background knowledge, this was especially positive to observe. In addition, the laboratory designers noted that while both pharmacy and PA students consulted and utilized the CPIC guidelines, each profession brought a unique perspective to the discussion of the patient case. For example, the pharmacy students noted the cost of the alternative therapies that are indicated by the CPIC guidelines, and began a debate about cost versus best practices. The PA

students remarked on the protocol for changing therapies in patients, and the interprofessional teams worked together to find correct protocols for changing antiplatelet therapies. Overall, the students engaged in authentic interprofessional interactions, participated in peer-peer teaching, and shared conflicting viewpoints collegially.

Development of Case Themes

There are two themes in this work. First, the interpretation and clinical application of PGt data was a focus of the education and evaluation. Second, this work stressed the importance of utilizing team members' strengths to educate each other and treat patients in the best manner possible. Both themes are crucial in pharmacy education, and are mandated to be included in pharmacy curricula by the ACPE Standards 2016. This report describes the first documented intersection of PGt and IPE in pharmacy education.

There is little guidance from educational governing bodies with respect to the depth and breadth of PGt education necessary. There are several potential pedagogies to teach PGt, although recent evidence suggests that laboratory exercises centered in PGt provide invaluable opportunities for connecting the science of PGt to clinical application.[8-10] Previous literature reports have described PGt centered laboratories in which pharmacy students provide samples and participate, in various degrees, in the genotyping procedure.[8, 11, 12] Each of these reports confirm that student understanding of genetic sample procurement and genotyping and comprehension of PGt principles increased following the laboratory. In this PGt centered laboratory, genotyping of the laboratory participants did not occur; instead the process of genotyping was described with a short presentation. Both pharmacy and PA students, reported an enhanced understanding of genetic sample procurement and genotyping following the laboratory. Herein lies a difficult uncertainty. All of the student groups reported an improved understanding of PGt principles, yet it is impossible to speculate and compare the extent of each student group's PGt knowledge. Furthermore, what extent of PGt education is necessary in pharmacy education? Recall that most pharmacists will not conduct actual genotyping procedures, but will play a critical role in interpreting potential drug-gene interactions and explanation of drug-gene interactions to patients and other healthcare providers.[4] While the novelty of genotyping laboratory participants is exciting and may generate heightened student engagement, it may be an unnecessary expense given that similar outcomes were achieved without genotyping participants. Of course, inclusion of genotyping depends on the goals of the educational experience. Perhaps future PGt centered laboratories should focus on training pharmacists in data interpretation and explanation of clinical results to standardized patients or other healthcare providers, in order to more accurately reflect real world scenarios.

Introducing PGt as an IPE experience is novel. Previous IPE laboratories within pharmacy education have focused on a myriad of topics (e.g. – pediatric prescribing, patient safety, diabetes care, and social and health-related issues to caring for the elderly, etc.).[13-16] These laboratories have successfully demonstrated that perceptions of interprofessional collaboration are improved and comfort level with other healthcare providers increased.[17] The survey data collected from the IPE PGt laboratory supports other IPE laboratory findings. In particular, the survey questions regarding confidence in the ability to explain best practices for collecting samples to other healthcare professionals and the ability to explain pharmacogenetic data to other members of an interprofessional team had large increases on the Likert scale post-laboratory. Similar to other topics that have been covered in IPE laboratories, PGt is a defined niche. A niche that lends itself nicely to IPE experiences because it can be introduced and explored by students quickly, it engages several healthcare professions, and PGt will play a role in the practitioners' careers. Engaging the pharmacy and PA students in the IPE experience will prepare students to be practice- and team-ready. The IPE laboratory also demonstrated to both pharmacy and PA students the members on an interprofessional team that could provide assistance or guidance in analyzing and utilizing PGt in the clinical setting.

Based on the survey and observational data from the IPE PGt experience, students became engaged in the subject matter, became more comfortable with PGt knowledge and sharing of that knowledge, and worked well in their interprofessional teams. The Manchester University Student Personalized Medicine Coalition noted that experiences like this laboratory could reduce any barriers that healthcare professionals may have with regards to PGt knowledge and application.[18, 19]

Exploration of Case Impact

This one-hour interdisciplinary laboratory is a simple, cost-effective, and nonthreatening way to introduce healthcare students to PGx. This IPE experience demonstrates that within the confines of a one-hour laboratory, students can become more confident in their abilities to understand, utilize, and discuss PGt data. To the authors' knowledge, this is the first use of IPE to explore PGt in pharmacy education, and given the success of the laboratory, implementation of similar laboratories in pharmacy curricula is recommended.

The laboratory can be easily adapted into various circumstances. Given that the laboratory consisted of a

PowerPoint presentation and case discussions, it could easily be adapted to an online format. In this way programs that are not co-located could easily participate and proximity no longer becomes a requirement for the experience. Additionally, the clopidogrel-*CYP2C19* drug-gene interaction was featured in this laboratory because it is a simple PGt interaction and CPIC guidelines exist for the interaction, although several other drug-gene interaction examples exist and could be utilized as well.[20]

One challenge the designers faced was partnering with other professional programs to create the IPE experience. Given that Manchester University has only one professional degree program, the organization and logistics for partnering with other local professional programs required prospective planning. Although, given one successful completion of the laboratory, several other professional programs are now interested in participating. The designers suggest utilizing this publication to demonstrate the ease, accessibility, and attained objectives of the IPE PGt experience.

As discussed earlier, several PGt laboratories in pharmacy education feature a genotyping exercise in which students are genotyped. While the IPE PGt laboratory successfully achieved the designer's objectives for the laboratory, genotyping may further ensure student engagement in pharmacogenetic exercises. The added cost for genotyping ~100 students would be approximately three hundred US dollars. Recent advances in our own research laboratories will allow us to genotype the pharmacy and PA students within sixty minutes of DNA extraction, so that the students will be provided the genotypes during the laboratory period. In the next iteration of the IPE PGt laboratory, students will be genotyped for *CYP2C19*2,* the most common loss-of-function single nucleotide polymorphism (SNP) for *CYP2C19*. To date, there have been no publications on including multiple disciplines in this experience, and it will be interesting to compare the student 2016 survey results with that of the 2015 laboratory where genotyping was not included. Providing students' genotypes may enhance student interest and participation in the laboratory and in the subject matter, although if no differences are observed between the 2015 and 2016 laboratories, then inclusion of the genotyping component may be an unnecessary expense, as previously noted.

Several minor adjustments will also be made in the future laboratory. For instance, pre-laboratory work will be assigned to all of the students. The pre-laboratory work will consist of a video focusing on sample acquisition, processing and data interpretation followed by an assessment to determine student learning from the video. The purpose of the pre-laboratory work is to create a similar knowledge base for all of the students and to generate extra time in class for case-based discussion and presentation. In addition, the sample acquisition portion of the pre-laboratory video will include a description of several methods to obtain DNA samples. Several students noted that only one method for sample collection was demonstrated and that discussion on other methods may increase their confidence with regards to sample collection for pharmacogenetic analysis. Also, additional patient cases will be added to the interdisciplinary laboratory, so that both pharmacy and PA students can explore the guidelines in greater detail and generate further discussion about PGt.

The one-hour IPE laboratory successfully engaged pharmacy and PA students in discussions about PGt and increased the students' confidence in understanding and utilizing PGt in clinical decision-making. Given their experiences from this laboratory, students may be more confident in utilizing PGt data for clinical decision making in practice settings. In addition, the exercise may have reduced the possible intimidation by PGt data and application, when it inevitability is incorporated as a standard of care. Given that the vast majority of the students found the exercise to be relevant to their curriculum, the laboratory will continue to be a part of both professional programs with the minor modifications noted above. An IPE PGt laboratory experience can aid in successfully preparing practitioners for the future of precision medicine.

References

1. Evans WE,Relling MV. Pharmacogenomics: translating functional genomics into rational therapeutics. *Science.* 1999;286(5439):487-491.
2. Accreditation Standards and Key Elements for the Professional Program in Pharmacy Leading to the Doctor of Pharmacy Degree "Standards 2016". Accreditation Council for Pharmacy Education. Available at: https://www.acpe-accredit.org/deans/StandardsRevision.asp. Accessed May 20, 2015.
3. Accreditation Standards for Physician Assistant Education. Accreditation Review Commission on Education for the Physician Assistant. Available at: http://www.arc-pa.org/documents/Standards4theditionwithclarifyingchanges9.2014%20FNL.pdf. Accessed June 16, 2015.
4. History of the Pharmacist Competencies in Pharmacogenomics. Available at: http://g-2-c-2.org/files/Pharmacist-Comp.pdf. Accessed June 16, 2015.

5. Rackover M, Goldgar C, Healy K, Feiger J,Jenkins J. Establishing essential physician assistant clinical competencies guidelines for genetics and genomics. *J Physician Assist Educ.* 2007;18(2):47-48.
6. Scott SA, Sangkuhl K, Stein CM, Hulot JS, Mega JL, Roden DM, Klein TE, Sabatine MS, Johnson JA,Shuldiner AR. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. *Clin Pharmacol Ther.* 2013;94(3):317-323.
7. Likert R. A technique for the measurement of attitudes. *Arch Psychol.* 1932;140:1-55.
8. Kisor DF, Talbot JN, Stockert AL,Smith A. Exploring a laboratory model of pharmacogenetics as applied to clinical decision making. *Innov Pharm.* 2013;4(112):1-12.
9. Lee KC, Hudmon KS, Ma JD,Kuo GM. Evaluation of a shared pharmacogenomics curriculum for pharmacy students. *Pharmacogenomics.* 2015;16(4):315-322.
10. Murphy JE, Green JS, Adams LA, Squire RB, Kuo GM,McKay A. Pharmacogenomics in the curricula of colleges and schools of pharmacy in the United States. *Am J Pharm Educ.* 2010;74(1):7.
11. Knoell DL, Johnston JS, Bao S,Kelley KA. A genotyping exercise for pharmacogenetics in pharmacy practice. *Am J Pharm Educ.* 2009;73(3):43.
12. Krynetskiy E,Lee Calligaro I. Introducing pharmacy students to pharmacogenomic analysis. *Am J Pharm Educ.* 2009;73(4):71.
13. Shrader S, Hummel H, Byrd L,Wiley K. An intraprofessional geriatric medication activity within a senior mentor program. *Am J Pharm Educ.* 2013;77(1):15.
14. Taylor D, Yuen S, Hunt L,Emond A. An interprofessional pediatric prescribing workshop. *Am J Pharm Educ.* 2012;76(6):111.
15. Vyas D, McCulloh R, Dyer C, Gregory G,Higbee D. An interprofessional course using human patient simulation to teach patient safety and teamwork skills. *Am J Pharm Educ.* 2012;76(4):71.
16. Pittenger AL, Westberg S, Rowan M,Schweiss S. An interprofessional diabetes experience to improve pharmacy and nursing students' competency in collaborative practice. *Am J Pharm Educ.* 2013;77(9):197.
17. Remington TL, Foulk MA,Williams BC. Evaluation of evidence for interprofessional education. *Am J Pharm Educ.* 2006;70(3):66.
18. Lam YW. Scientific challenges and implementation barriers to translation of pharmacogenomics in clinical practice. *ISRN Pharmacol.* 2013;2013:641089.
19. McKinnon RA, Ward MB,Sorich MJ. A critical analysis of barriers to the clinical implementation of pharmacogenomics. *Ther Clin Risk Manag.* 2007;3(5):751-759.
20. Relling MV,Klein TE. CPIC: Clinical Pharmacogenetics Implementation Consortium of the Pharmacogenomics Research Network. *Clin Pharmacol Ther.* 2011;89(3):464-467.

Table 1: Pre- and post-interprofessional laboratory survey results

	Pharmacy Students (N = 71)		Physician Assistants Students (N = 25)	
	Pre Lab	*Post Lab*	*Pre Lab*	*Post Lab*
Indicate your agreement with the following statements[a]:	Median (IQR[b])	Median (IQR[b])	Median (IQR[b])	Median (IQR[b])
I feel confident in my ability to describe the concept of a prodrug and metabolism to an active drug.	3 (3-4)	4 (4-5)*	2 (1-3.5)	4 (3-4)*
I feel confident in my ability to explain and understand the concepts of genetic variation and polymorphisms.	3 (2-3)	4 (3-4)*	3 (0.5-3)	4 (3-4)*
I feel confident in my ability to describe pharmacogenetics and pharmacogenomics.	3 (1-3)	3 (3-4)*	1 (0-2.5)	3 (2.5-4)*
I feel confident in my ability to employ best practices for collecting samples for pharmacogenetic analysis.	2 (1-3)	3 (3-4)*	1 (0-1)	3 (1.25-4)*
I feel confident in my ability to describe the basic process of genetic sampling and how genotyping is performed.	2 (1-3)	3 (3-4)*	1 (1-2)	3 (2.5-4)*
I feel confident in my ability to interpret pharmacogenetic data.	2 (1-2)	3 (3-4)*	1 (0-1)	3 (2-4)*
I feel confident in my ability to recommend prescriptions or dosages for certain drugs based on pharmacogenetics data.	2 (1-3)	4 (3-4)*	1 (0-2)	4 (3-4)*
I feel confident in my ability to utilize CPIC guidelines.	0 (0-2)	4 (3-4)*	0 (0-0)	3 (1.5-4)*
I feel confident in my ability to explain best practices for collecting samples for pharmacogenetic analysis to other healthcare professionals.	1 (0-2)	3 (3-4)*	1 (0-1)	3 (1.5-4)*
I feel confident in my ability to explain pharmacogenetic data to other members of an interprofessional team.	1 (0-2)	3 (3-4)*	0 (0-3)	4 (2.5-4)*
I feel confident in my ability to provide rationale for performing genotyping.	2 (0-3)	4 (3-4)*	1 (0-3)	4 (3-4)*
This exercise is relevant in the healthcare curriculum.	4 (3-5)	5 (4-5)*	2 (0-4)	4 (3-5)*

[a]0: not confident, 3: somewhat confident, 5: very confident, [b]IQR: interquartile range,*comparison between pre-and post-laboratory aggregate survey data for each discipline, statistical significance with $p < 0.01$.

Appendix A – Example of a Patient Case used in the IPE PGt laboratory

SR is a 54 year old male with a history of NSTEMI 6 months ago with placement of a drug eluting stent. He presents to the hospital with recurrent angina and EKG findings and laboratory data are consistent with a new NSTEMI. He is currently receiving both clopidogrel and aspirin to prevent stent thrombosis. The physician is concerned about the potential that SR isn't responding well to clopidogrel and is obtaining genetic data to help guide future therapy. Genotyping results reveal that SR's CYP2C19 genotype is *2/*2. Recommend therapy for SR