COMMENTARY

Online Cancer Genomics Databases Provide Teaching Resources For Pharmacy Education

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Submitted April 6, 2021; accepted August 30, 2021; ePublished September 2021

Connecting scientific concepts with clinical applications is an important objective of pharmacy education. In particular, as the field of precision oncology expands, it is critical that pharmacy students understand how genetic information connects with cancer treatment decisions. However, to effectively teach students about pharmacogenomics and pharmacogenetics, faculty require relevant educational resources, including those that support higher-order learning. In this commentary, we demonstrate the potential utility of publicly accessible cancer genomics databases as teaching resources for pharmacogenomics and pharmacogenetics in oncology pharmacy education. Using clinical data retrieved from a genomics database, we illustrate how case studies can be developed to target core competencies, including understanding tumor genomics profiling, somatic mutations and pharmacotherapy selection, and clinical pharmacogenetics testing. Cancer genomics databases provide readily available, cost-effective, clinical data resources that support active learning related to pharmacogenomics and pharmacogenetics education in oncology pharmacy curricula.

Keywords: cancer genetics, education resources, oncology pharmacy, pharmacogenetics, pharmacogenomics

Teaching students how foundational science concepts apply to clinical practice is an important goal of pharmacy education¹. The Accreditation Council for Pharmacy Education recommends helping “students make connections between scientific understandings and patient care”². In the era of precision medicine, a critical objective for student pharmacists is understanding how to apply genetic information to guide treatment decisions. In their future professional roles, student pharmacists will be in key positions to educate clinical colleagues and patients about evidence-based pharmacotherapy recommendations driven by genetic information. Thus, the American College of Clinical Pharmacy (ACCP) recognizes the urgent need to include pharmacogenomics and pharmacogenetics education in pharmacy school curricula³.

The AACP recently updated the core competencies for pharmacogenomics and pharmacogenetics consistent with those recommended by the National Human Genome Research Institute (NHGRI)⁴. These core competencies align with pharmacist entrustable professional activities (EPAs) and include identifying and interpreting pharmacogenomics data to determine impact on drug pharmacodynamics, response, and adverse reactions⁴. In addition, pharmacogenomics and pharmacogenetics educational outcomes established by the AACP Center for the Advancement of Pharmacy Education (CAPE) include understanding how genetic variants influence response to treatment and recognizing that evidence-based guidelines exist for pharmacogenetics testing and treatment selection^{5,6}. Many pharmacy schools have added pharmacogenomics threads into disease-specific courses, including oncology. However, faculty cite a need for resources that support pharmacogenomics education, including those that can be used to develop higher-order learning activities^{7,8}. In this commentary, we highlight the utility of publicly accessible cancer genomics databases as teaching resources for pharmacogenomics and pharmacogenetics education in oncology pharmacy curricula.

Targeted oncology drugs inhibit specific molecular drivers of cancer progression, including somatic mutations. Clinical trials of targeted drugs that include –omics analyses generally share datasets through publicly accessible cancer genomics databases. Datasets may include tumor genomics, such as differential gene analyses, somatic mutations, polymorphisms, gene amplifications, and chromosomal rearrangements, as well as pharmacotherapy and clinical outcomes data. One example of a cancer genomics database is the cBioPortal database (<https://www.cbioportal.org/>), which contains more than 300 datasets representing over 30 distinct tumor types^{9,10}. The data available in each dataset vary and may include genomics, proteomics, tumor mutation count, gene amplification events, race, sex, age, tumor histopathology, treatment regimens and clinical outcomes. Due to the breadth of genomic and genetic data available from trials of targeted cancer therapies, cBioPortal represents a valuable resource for oncology pharmacogenomics education. Another cancer genomics database, OncoPrint (<https://www.oncoprint.org/>), contains data from more than 4000 gene

microarray experiments ¹¹. Oncomine supports differential gene expression analysis by tumor type, facilitating classroom discussions about pharmacogenomics and cancer precision medicine. Another resource, KM Plotter (<https://kmplot.com>), is designed to identify tumor markers associated with survival outcomes across 21 tumor types ¹². Data retrieved from KM Plotter can be used to support learning activities focused on understanding how genetic variants impact disease course and clinical outcomes.

To illustrate the application of a cancer genomics database in pharmacy education, we provide three examples using datasets from the cBioPortal database. The first two examples target CAPE core competencies to understand how genetic mutations inform pharmacotherapy selection based on an approved pharmacogenetics test. The third example targets a learning objective to understand immunotherapy and tumor genomics profiling. We present a case-based discussion with each example to illustrate how the data support active learning.

Example 1: Discuss how a somatic mutation in *PIK3CA* guides treatment of breast cancer (Figure 1A).

Data retrieval process: In this example, we started by entering a specific tumor type and drug name. Following the steps shown in the flowchart, we mined cBioPortal to obtain data for a single patient case from a clinical trial of alpelisib in breast cancer ¹³. Case details, including tumor subtype, genetic mutation, treatment regimen and response, were downloaded from cBioPortal as shown in the table. Using these data, we created a case-based discussion (shown below) focused on treatment selection guided by molecular and genetic information, pharmacogenetic testing, and drug-drug interactions. In addition to this case, we downloaded data for a larger cohort of patients (shown in the graph) to introduce concepts related to clinical response and resistance.

Case: A postmenopausal female patient presents with advanced breast cancer. The patient's breast tumor biopsy is positive for estrogen receptor (ER) and negative for human epidermal growth factor receptor 2 (HER2). The patient is started on exemestane. Upon progressing on exemestane, pharmacogenetics testing of tumor tissue is performed for the *PIK3CA* gene. The patient is found to have an H1047R *PIK3CA* somatic mutation and is started on alpelisib plus fulvestrant.

Case study questions: (1) What are exemestane and alpelisib? (2) What information guided selection of these treatments? (3) Why does a positive pharmacogenetics test not guarantee response to a targeted treatment? (4) What drug-drug interactions need to be considered with alpelisib?

Case-based discussion guide: The questions should guide discussion about targeted therapies, including those targeting somatic mutations and companion pharmacogenetics testing. Discussion should also note variability in patient responses and could include discussions about intra- and inter-tumoral heterogeneity, patient-specific factors influencing response, and acquired drug resistance. Finally, drug-drug interactions and the effects of cytochrome p450 (CYP) enzymes on drug activity should be discussed.

Example 2: Discuss how a somatic mutation in *BRAF* guides treatment of melanoma (Figure 1B).

Data retrieval process: In this example, we started by entering a specific cancer type and gene name. Similar to the process described above, we mined cBioPortal to obtain a single patient case of *BRAF*-mutant melanoma following the steps in the flowchart ¹⁴. In addition to the single case, we downloaded a graph showing responses in a larger cohort of patients with *BRAF*-mutant melanoma treated with dabrafenib or vemurafenib to discuss other compounds in this class of drugs. We also introduce the concept of pharmacogenetics testing to assess a marker associated with adverse events.

Case: A 44-year old female patient with metastatic melanoma is found to have a somatic *BRAF*^{V600E} mutation. The patient is also found to have wild-type alleles for the glucose-6-phosphate dehydrogenase (*G6PD*) gene. The patient is treated with dabrafenib for 30 weeks with minimal toxicity and exhibits complete response to therapy.

Case study questions: (1) What information guided the selection of dabrafenib as a treatment in this patient? (2) What is the mechanism of action of dabrafenib and vemurafenib? (3) Why is pharmacogenetics testing for the *G6PD* gene important when considering dabrafenib as a potential treatment?

Case-based discussion guide: The questions should guide discussion of *BRAF* mutations, pharmacogenetics testing for somatic mutations, and mechanisms of action of kinase-targeted therapy. The question about *G6PD* testing should guide discussion about patient-specific factors that may influence adverse drug effects.

Example 3: Discuss PD-1-directed immunotherapy and tumor genome alterations (Figure 2).

Data retrieval process: In this example, we started by entering a drug name and mined cBioPortal to display tumor gene analysis from a translational study in patients with melanoma ¹⁵. We downloaded differential gene expression data for pre-treatment tumor biopsies of responders and non-responders and a case profile to discuss concepts related to immunotherapy and tumor genomics.

Case: An 84-year old male patient with metastatic melanoma has progressed on prior therapy with a mitogen-activated protein kinase (MAPK) inhibitor. The patient is treated with pembrolizumab as part of a trial evaluating pembrolizumab or nivolumab in patients with melanoma. Immune cell profiling and pre-treatment tumor genomics profiling are performed as part of this trial.

Case study questions: (1) What is the mechanism of action of pembrolizumab and nivolumab? (2) Why was immune cell profiling performed? (3) What do the data in the tumor genomics table show?

Case-based discussion guide: The questions should guide discussion about cancer immunotherapy, immune cell types and functions, and the role of genomics data in biomarker and drug discovery research.

These examples are provided to illustrate the potential utility of genomics databases for case study development in the area of cancer pharmacogenomics and pharmacogenetics. Although student feedback, perceptions and knowledge gains remain to be assessed, we anticipate a number of advantages to this approach. First, integrating clinical datasets into active learning may assist students in applying foundational concepts to solve practical problems¹⁶, such as the use of genetics data to create informed treatment plans. Second, faculty who lack clinical context may benefit from the ability to retrieve real-life cases from genomics databases, rather than creating hypothetical scenarios. Thus, clinical genomics databases may support pre-course preparation and potentially reduce interdisciplinary workload¹⁷. Third, students can be introduced to emerging pharmacogenomics research, which may enhance their awareness of academic research and related career opportunities^{18,19}. Fourth, the functions we used to retrieve data were freely accessible, making these cost-effective options¹⁹. Pharmacy programs with limited resources can integrate genomics databases into mentored research experiences to foster critical thinking and problem solving^{18,19}. Finally, online databases can be used in synchronous, asynchronous, in-person, blended, and virtual learning environments, making them versatile resources.

Despite the benefits of publicly accessible cancer genomics databases, there are limitations. Due to a wide range of user interfaces, databases vary in complexity and the amount of time and skill required to retrieve and analyze data. Additionally, although there are many publicly accessible databases suitable for oncology pharmacy education, faculty must be made aware of these resources and know where to find datasets appropriate for their specific learning objectives. We found online tutorials, manuals, and published research articles helpful as we learned to use these databases.

Incorporating clinical genomics data into active learning targets a number of pharmacy student core competencies, such as identifying and interpreting pharmacogenomics test results, determining the impact of genetic variants on drug activity and adverse events, and educating others about the applications of genetic information for optimal drug therapy⁴. These competencies map to multiple EPA domains, including patient care provider, population health promoter, and information master. Genomics databases also address a number of CAPE outcomes, including integrating and applying foundational knowledge (domain 1), interpreting data (domain 2), and problem solving (domain 3)²⁰. Ultimately, understanding the application of genetics to inform treatment selection, gaining awareness of evidence-based guidelines for pharmacogenetics testing, and developing a strong knowledge of precision cancer medicine are important objectives targeted by these resources. Thus, publicly accessible cancer genomics databases represent rich sources of clinical pharmacogenomics and pharmacogenetics data that can be adapted for active learning in oncology pharmacy education.

ACKNOWLEDGMENTS

We thank Dr. Milap Nahata, PharmD, for critically reviewing this commentary.

Conflicts of Interest and Disclosures: RN reports personal holdings in GlaxoSmithKline PLC., Pfizer, Bristol Myers Squibb, and Eli Lilly and Company.

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Figure 1. Examples of Pharmacogenetics Case Studies from the cBioPortal Cancer Genomics Database

A. Case of complete response to alpelisib in *PIK3CA*-mutant breast cancer

Patient ID: P-0001396	
Attribute	Value
Treatment Arm	D
Treatment Best Response	Complete Response
Alpelisib Dose (mg)	350
Alpelisib Scheduling	Intermittent (5/2)
Endocrine Therapy	Exemestane
Measurable Disease	Yes
Weeks on Study	150
Best RECIST Response	-100
Breast Cancer Subtype	IIR+/IIR2-
Clinical Benefit	Yes
Number of Samples Per Patient	5
Off Study Reason	POD
Patient Display Name	P042
PIK3CA Pre Treatment Tumor	MUT
PIK3CA Pre Treatment Tumor Mutation	H1047R
Sex	Female

B. Case of complete response to dabrafenib in *BRAF*-mutant melanoma

Patient ID: Pat_21	
Attribute	Value
Diagnosis Age	44
duration of therapy weeks	30
Early Resistance	No
medication	Dabrafenib
Number of Samples Per Patient	1
Sex	Female
Treatment best response	CR
Mutation Count	31
Cancer Type	Melanoma
Cancer Type Detailed	Melanoma
Matched Normal Tissue	Paraffin Embedded Tissue
mean target coverage normal	104
mean target coverage tumor	82
Oncotree Code	MEL
Somatic Status	Matched

Figure 1. Examples of Pharmacogenetics Case Studies from the cBioPortal Cancer Genomics Database. (A) Left, Flowchart showing steps from data retrieval to case development. Top right, an individual patient case from the trial of alpelisib in *PIK3CA*-mutant breast cancer¹³ was selected, and the data were downloaded as shown. Bottom right, graph shows best responses to treatment with alpelisib in *PIK3CA*-mutant breast cancer; $p < 0.001$, chi-squared test. (B) Left, Flowchart showing steps from data retrieval to case development. Top right, an individual patient case from the trial of BRAF^{V600E} kinase inhibitor dabrafenib in melanoma¹⁴ was selected, and the data were downloaded as shown. Bottom right, graph shows best responses to treatment with dabrafenib in BRAF^{V600E}-mutant melanoma; $p < 0.001$, chi-squared test. CR, complete response; PR, partial response; PD, progressive disease; POD, progression of disease; SD, stable disease.

Figure 2. Example of Pharmacotherapy Gene Analysis from the cBioPortal Cancer Genomics Database

Figure 2. Example of Pharmacotherapy Gene Analysis Case Study from the cBioPortal Cancer Genomics Database. (A) *Left*, Flowchart showing steps for retrieving pharmacogenomics table. *Top right*, table of differential gene analysis in pre-treatment tumor tissues from responders and non-responders to pembrolizumab and nivolumab ¹⁵. *Bottom right*, an individual patient case was selected, and the clinical and immune cell profiling data were downloaded as shown.

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Accepted Draft