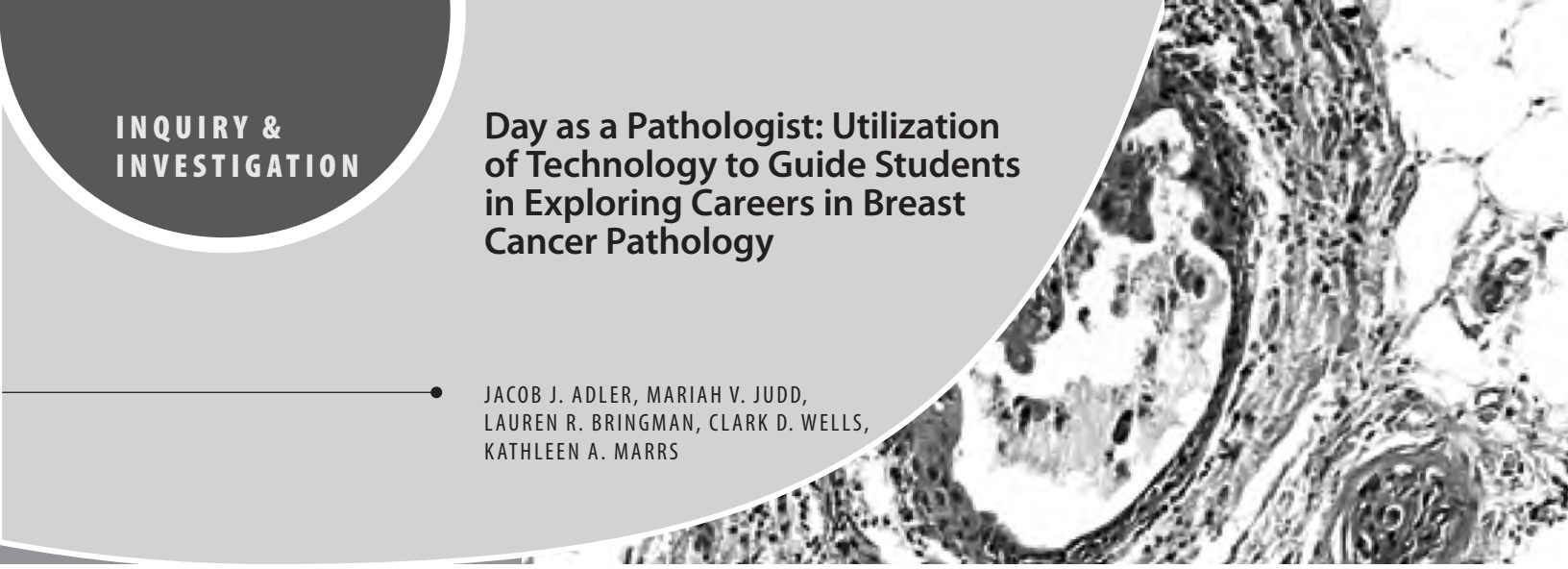
INQUIRY & INVESTIGATION

Day as a Pathologist: Utilization of Technology to Guide Students in Exploring Careers in Breast Cancer Pathology



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Abstract

We developed an interactive laboratory that allows students to identify and grade tissue samples from human breast biopsies, using techniques similar to those used by actual pathologists. This unique lab develops a practical and intellectual understanding of basic tissue structures that make up living systems, utilizing technology to bring together pathology, cancer biology, genetics, and bioethics in a relevant and engaging way that leaves a lasting impression on students. The activities described are appropriate for students at all levels of high school and college, especially those with an interest in health care careers.

Key Words: *Breast cancer; pathology; tissue biopsy; health care; classroom technology.*

For many students, interest in learning science is directly linked to the relevance of the topic to the student's life and their confidence in their abilities to do science (Bybee, 2002). Developing laboratories that capture the interest of students, are relevant to their lives, and allow students to actively participate as a scientist is one of the goals of the National Science Foundation's GK–12 program, which pairs a high school science teacher with a university graduate student, or GK–12 Fellow, bringing research and scientific activities into a classroom for an entire year (Ufnar et al., 2012).

Breast cancer is the second leading cause of cancer deaths in women.

Breast cancer is the second leading cause of cancer deaths in women, claiming over 40,000 lives a year, and most high school students will likely know someone who has had breast cancer (Eheman et al., 2012). With this in mind, we developed a laboratory experience based on breast cancer research done in the university lab of three of the coauthors (J.J.A., L.R.B., and C.D.W.). This activity not only encourages students to learn about – and thereby become interested in entering – the medical community, but also enables them to better understand issues that personally affect them.

The study of human pathology has almost exclusively been taught at medical schools and rarely is included in undergraduate curricula, much less in the high school biology classroom. This is unfortunate, because the lack of information available to high school students hinders their ability to make choices regarding career paths into the variety of fields in this discipline. Medical science careers are in high demand, and many students are interested in the variety that such fields have to offer. Further, pathology is often excluded in advanced cancer biology courses that tend to focus on the genetic, chemical, and molecular characteristics of cancer. By contrast, the lab we developed covers the basic pathology of the structural characteristics of cancerous tissues. This approach is designed for a broad audience in that it requires a minimal level of background knowledge to participate. Specifically, this lab uses the physiological appearance of breast cancer tissues to introduce the basic methods for grading the malignant (cancerous) potential of one of the most commonly discussed cancers, ductal breast cancer. Our primary goals were for students to be able to

1. Describe key events that occur in the breast tissue during a woman's life cycle.
2. Explain the phenotypic difference at the cellular and tissue levels between precancerous ductal carcioma in situ and invasive ductal carcinoma.
3. Apply cell form and function characteristics of the breast tissue.
4. Propose and defend their analysis of case studies of breast tissue biopsies.
5. Present their predictions and conclusions on pathological questions in written form.
6. Judge their understanding of tissue tumor grade through case studies and examination.

Although the training time for pathologists typically requires many years, this course involving three 50-minute class periods was sufficient for 86% of students to gain the skills needed to correctly identify biopsy tissue and, surprisingly, for 70% of students to correctly score the malignant grades of ductal carcinoma histological samples.

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○ Setting the Foundation: Breast Cancer Pathology

The breast, while maintaining a basic overall structure, undergoes key remodeling events during puberty, pregnancy/lactation, and menopause that require cells to move, change size, and divide or die (Kumar et al., 2005). The composition of the breast is mainly deposits of fat (adipose) cells, along with the glands, blood vessels, and muscle that are embedded in connective tissue called the *stroma* (Figure 1). The glands, in turn, are composed of hollow tubes (ducts) that are formed by epithelial cells and are held in place by a layer of myoepithelial cells. Such ductal tissue forms a tree-like branching system that arises from the lobules. During lactation, milk is produced in the lobules and travels through the lumens (hollow openings) of the ducts to reach the nipple. The ductal tissue develops and grows during puberty and, when mature, is a crucial element in the function of the breast. Conversely, morphological changes in ductal epithelial cells may disrupt the localized epithelium and, potentially, the entire breast. These changes can be normal (physiological) or abnormal (pathological). Key remodeling events such as pregnancy and lactation promote healthy physiological changes. Distinguishing between these normal physiological changes and abnormal ones is the first big objective of this lab.

Abnormal changes can occur anywhere in the breast, which could lead to cancer at that location. Breast cancers are categorized into particular types based on the origin of the tissue from which they arise. For instance, ductal tumors arise out of ducts, whereas lobular tumors arise from the lobules. The focus of this lab is the most frequently diagnosed type, ductal carcinoma. Typically, pathological events in the ducts occur when the epithelial cells, as a result of environmental or genetic cues, begin to divide and grow inappropriately (hyperplasia) and fail to form normal ductal structures (Figure 2). This typically is observed as cells growing into the lumen of the duct, in a process termed *intra-ductal hyperplasia*, also known as *benign proliferative breast disease* (Hussein & Hassan, 2006). As benign hyperplastic cells undergo deregulated cell growth, they have an increased probability of acquiring cancer-initiating mutations that further drive higher rates of cell growth and loss of ductal morphology. When these cells remain within the confines of the duct, this is termed *ductal carcinoma in situ* (DCIS), which is not diagnosed as invasive breast cancer. However, when these cells break through the ductal layer and invade the surrounding tissue (stroma), they are then recognized as cancer and are called *invasive ductal carcinoma* (IDC).

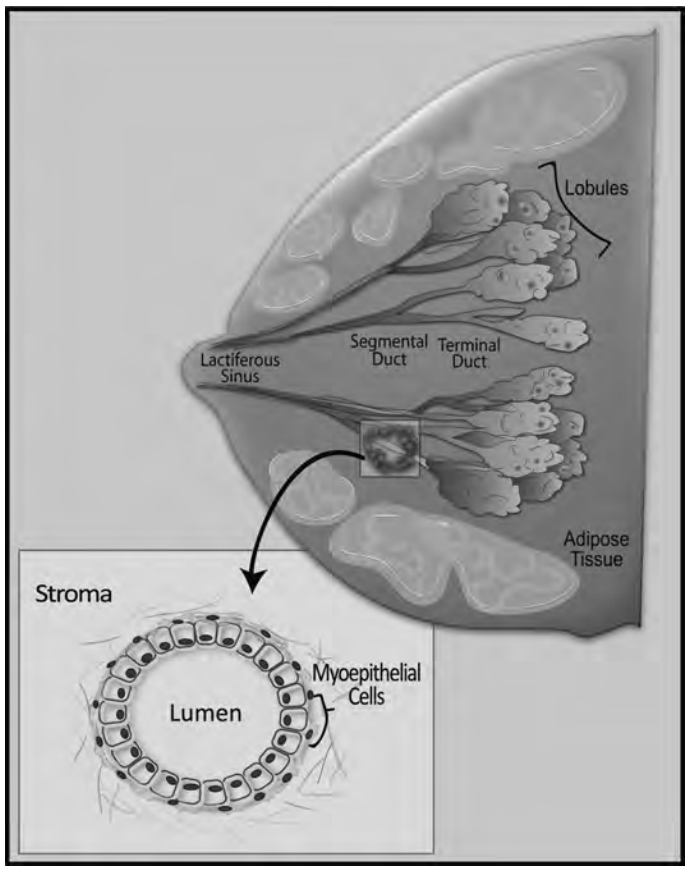

Figure 1. The breast with a cross-sectional magnified single terminal duct subunit, highlighting the stroma, myoepithelial cells, luminal epithelial cells, and internal lumen.

Although the molecular events that drive DCIS to transition to IDC are not well understood (Polyak & Kalluri, 2010), the histological appearance of these tissues along this continuum are well defined and classified as different grades of increasing cancer malignancy. The different grades of the tumor are diagnosed by pathologists following several diagnostic tests. Most commonly, a mammogram is used to determine whether abnormal growth is present. Once the growth is found, and if it is contained in the breast, a biopsy (small core tissue samples) may be done prior to surgical excision. Biopsies are examined by pathologists for the physical appearance of the tissue and for expression of diagnostic protein markers, which are both used to determine the tumor grade, candidacy for surgery, and likelihood of tumor recurrence. Tumor physical appearance is judged histologically: tissues are sectioned and placed on slides that are stained with hemotoxylin and eosin. These two stains give color to the different cellular structures so that the overall cell shape and nuclear condition can be assessed (Figure 3). Identification of breast cancer grade is based on the appearance and characteristics of cells contained within the tissue sections (cytology). These stained tissue sections are examined by pathologists for key physical characteristics that help determine the differences between cancer and normal tissue (Figure 3 and Table 1; National Cancer Institute, 2012). The final diagnosis of the patient biopsy by the pathologists helps determine future treatment options and helps lead to quicker recovery.

○ Becoming a Pathologist

The Training

For a budding pathologist, proper training must occur before practicing the profession in the field. Therefore, preceding the activity itself, the students were led through an interactive lecture, which laid the foundation required for them to be successful in the Becoming a Pathologist activity. This lecture, "Becoming a Pathologist: Training" (see Links below), walks the students through the information presented in the background section of this article. At the end of the lecture, students were able to identify particular points in a woman's life cycle and their corresponding physiological changes. They also became familiar with basic breast physiology and how the breast's cellular architecture contributes to its important functions.

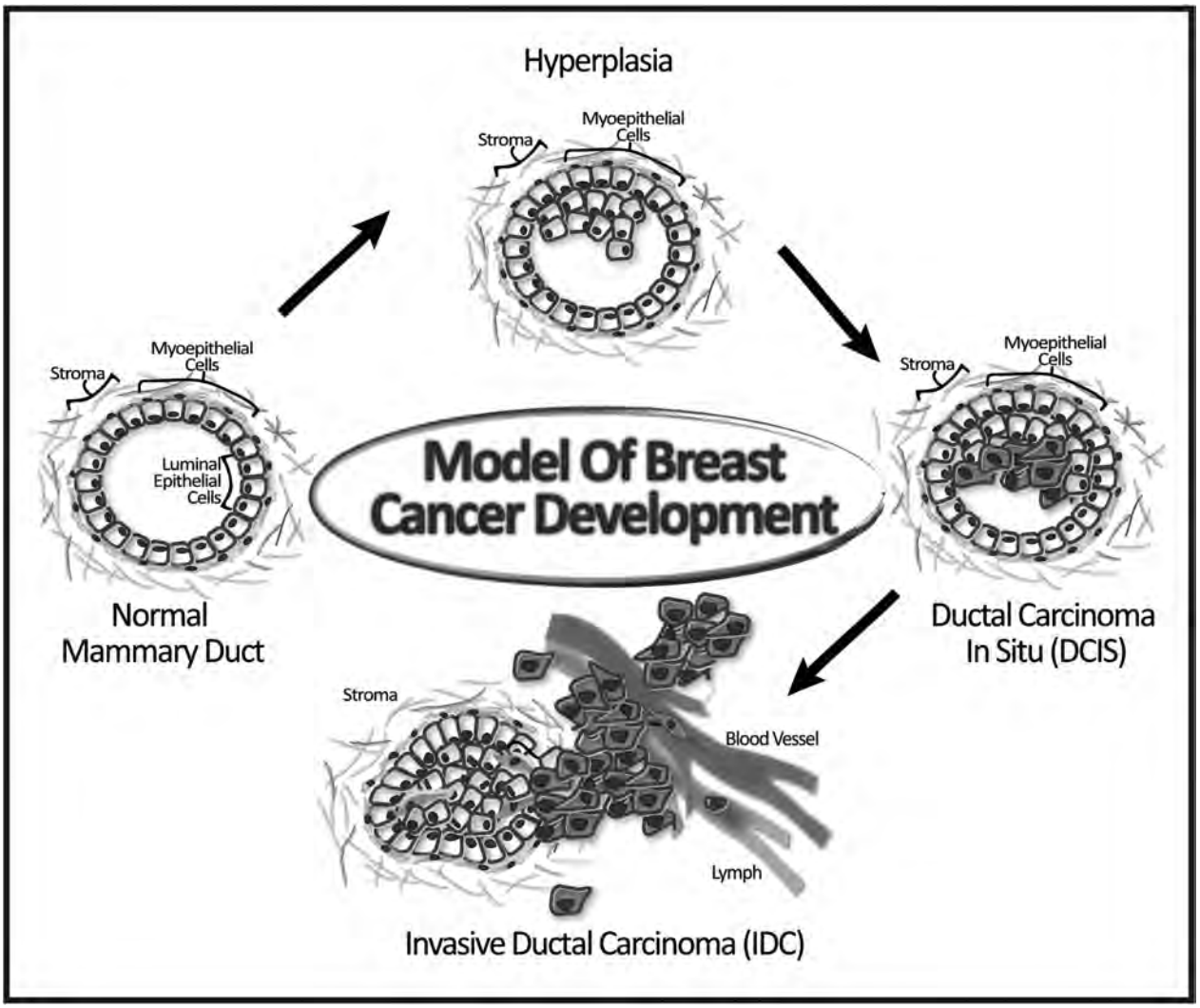

Figure 2. The progression of breast cancer, focusing on the cross section of a single duct. This progression likely occurs at multiple locations within the breast tissue. Here the duct undergoes hyperplasia (rapid growth), followed by ductal carcinoma in situ (contained abnormal growth) and, finally, full invasive ductal carcinoma (invading cancer).

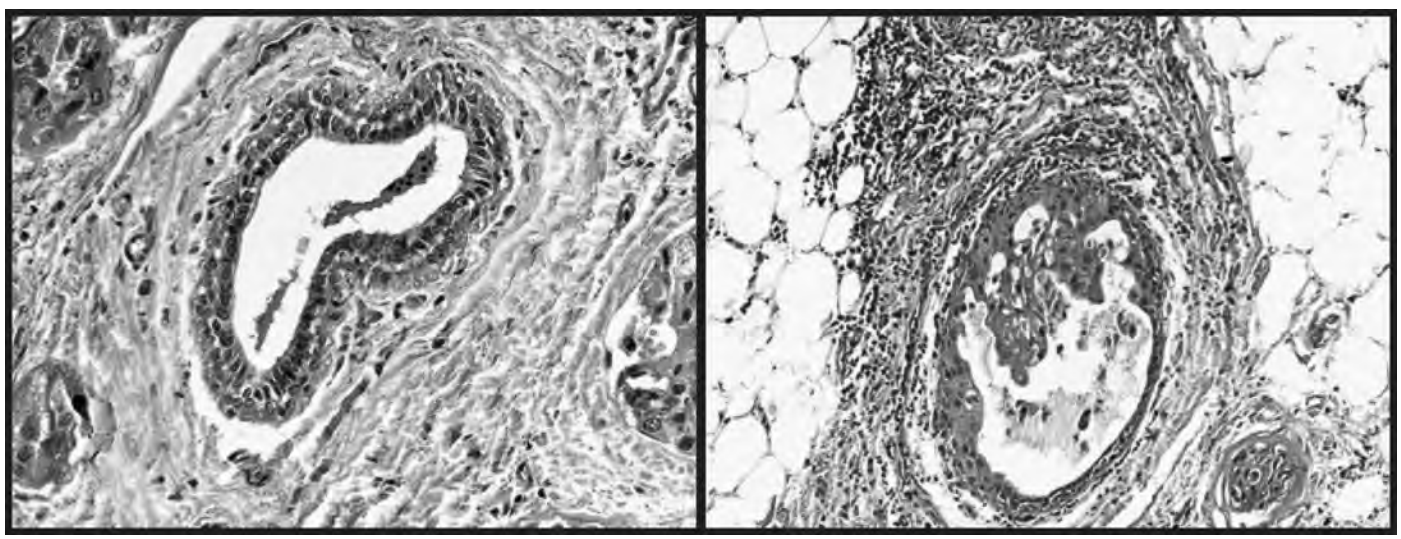

Figure 3. Tissue biopsy sample of normal tissue (left) and near invasive ductal carcinoma (IDC, right). The normal tissue contains a duct with a hollow lumen (white) and defined epithelial cellular arrangements. The near IDC has the lumen invaded and contains many white blood cells (small black dots, seen on the upper part of the duct), a sign of inflammation. These two samples were used for student analysis.

Making the Initial Diagnosis

After being introduced to the structure and function of the breast organ, the students were introduced to breast tissue biopsies, cytology, and tissue tumor grading with an interactive online presentation, "Becoming a Pathologist: Diagnosing Breast Cancer" (see Links below). This online presentation walks them through how a pathologist might analyze a breast tissue biopsy. Throughout, the students were asked to answer questions related to the topic using information already presented to them and external references such as Internet research (see Figure 4: Handout no. 1). The "Becoming a Pathologist: Diagnosing Breast Cancer" online presentation addresses the key characteristics of cancerous tissue as outlined by the National Cancer Institute (Table 1), used by pathologists to identify and grade cancerous tissue. After the foundation was set, the students were asked to moonlight as a real-world pathologist by analyzing two actual patient samples and making a diagnosis. In order for the students to correctly diagnose these samples, they had to go beyond the material presented and back up their findings with sound evidence and reasoning from what they learned. The activity was designed to go beyond their ability to "get the right answer" and pushed them to develop their skills in independent research, deductive reasoning, and critical thinking.

Table 1. Key biopsy characteristics.

Growth Characteristics	Cellular Characteristics	Tissue Characteristics
Normal growth	Size of cells	Arrangement of cells
Hyperplasia (increased growth)	Shape of cells	Tumor boundary condition
Dysplasia (disorganized growth)	Size of nuclei	
Ductal carcinoma in situ	Shape of nuclei	
Invasive ductal carcinoma	Cytoplasmic:nuclear ratio Cellular features	

Confirming the Diagnosis

Using their newly acquired training, the students were placed into "Diagnostic Teams" and given two unknown patient samples (Figure 3). They were then asked to perform a full analysis of the samples, which included noting key growth, cellular, and tissue characteristics (Table 1) to help make their diagnosis. The students followed the outline provided (see Figure 5: Handout no. 2) and answered questions to keep them on the right track. Students did remarkably well on their analysis and interpretation, as outlined in Table 2, which contains summarized student responses, whether they gave a solid (full credit) explanation, and whether the answer they gave was correct. An example of a student response for the patient samples is included in Table 3. Student comprehension

Congratulations! You have been given the opportunity to be a pathologist for the next couple of days. You will be able to examine in detail, identify, and label actual patient samples. The online presentation will give you an array of patient samples to help identify characteristics of breast tissue. Then you will be given some information about two unknown patients. You must use your knowledge from class, the online presentation, and your own independent Internet research to determine the diagnosis for these patients.

Step 1: Read through the online tutorial, taking notes as you go.

Step 2: Guided Learning Questions: Answer these questions by researching online (taking notes) and using help from your class notes and the online presentation.

1. Determine how hemotoxylin and eosin staining works, why it is used, and what it identifies.
2. What is the function of the stroma that surrounds the ducts of the breast?
3. Why is it important to have functioning ducts?
4. What is the myoepithelium and what is its function?
5. Explain these key events in a woman's life cycle and changes that occur at these stages in the breast: puberty, pregnancy/lactation, menopause.
6. Explain in a short paragraph the key differences on the tissue and cellular level between *ductal carcinoma in situ* and *invasive ductal carcinoma*.

Figure 4. Handout no. 1: Becoming a Pathologist.

Using knowledge from your Internet research and class notes, determine the diagnosis of the two unknown patient samples at the end of the online presentation. Make sure to review the samples for key growth, cellular, and tissue characteristics to help make your diagnosis. Use the Observation Records Table to record your observations. Then, answer the following questions in your final response.

1. What is the diagnosis?
2. What evidence (cytology) led you to believe that your diagnosis is accurate?
3. Consider why your diagnosis may be incorrect. How could your diagnosis be improved?

We do not expect you to give us tumor grade (if applicable), but if you do so and correctly identify the grade, extra points will be given. Make sure to answer all the questions and give supporting evidence for why you gave that diagnosis. Even if you give the incorrect grade, partial credit will be given if your rationale is appropriate.

Observation Records Table

Patient Sample	Growth Characteristics	Cellular Characteristics	Tumor Characteristics
Unknown patient sample no. 1			
Unknown patient sample no. 2			

Figure 5. Handout no. 2: Patient Diagnosis.

Table 2. Summary of student diagnoses of unknown patient slides.

Slide 1	Group	Student Response	Explanation Given?	Full Credit Received?	Correct Diagnosis Given?
Near invasive ductal carcinoma	Group 1	Near invasive ductal carcinoma	YES	YES	YES
	Group 2	Signs of invasive ductal carcinoma	YES	YES	YES
	Group 3	Signs of invasive ductal carcinoma	YES	YES	YES
	Group 4	Low-grade ductal carcinoma in situ	NO	NO	NO
	Group 5	Near invasive ductal carcinoma	YES	YES	YES
	Group 6	Low-grade ductal carcinoma in situ	YES	YES	NO
	Group 7	Invasive breast cancer	YES	YES	NO
Slide 2	**Group**	**Student Response**	**Explanation Given?**	**Full Credit Received?**	**Correct Diagnosis Given?**
Normal breast tissue	Group 1	Carcinoma in situ	YES	YES	NO
	Group 2	Healthy breast ducts	YES	YES	YES
	Group 3	Normal breast tissue	YES	YES	YES
	Group 4	Normal	NO	NO	YES
	Group 5	Normal tissue	YES	YES	YES
	Group 6	Normal breast tissue	YES	YES	YES
	Group 7	Normal breast tissue	YES	YES	YES

Table 3. Example of a student response.

Patient 1 has near invasive ductal carcinoma. The duct of the breast should be clear – and it is apparent that tissue cells have invaded into the duct. However, it is still in the earlier stages because there is only a small number of invading cells. The cells are arranged in no specified order.
Patient 2 shows signs of normal breast tissue. The cells are lined along the region, with no uncertain patterns. Cell express normal cell features and size. Also, there is an even balance between the cytoplasmic to nuclear ratio.

Table 4. Results of student identification.

Patient 1 Slide Identification	Yes	No
Correct diagnosis	4	3
Full credit	6	1
Explanation	6	1
Patient 2 Slide Identification	**Yes**	**No**
Correct diagnosis	6	1
Full credit	6	1
Explanation	6	1

and ability were high for this activity, as evidenced by the analyzed responses to the handout. Table 4 details selected responses to the pathology assignment. Not only were the students, as a whole, able to correctly diagnose the patient, which went beyond expectations, their rationale and depth of knowledge far exceeded their level of education on the subject of breast cancer pathology.

The Path to Becoming a Pathologist

Following this activity, some students may show interest in actually becoming pathologists. It is important to inform them about the training required. Significantly, this career involves a lot of post-secondary education. Typically, the individual will take 4 years in a chemistry- or biology-centered major for the bachelor's degree, followed by another 4 years for a medical doctor (M.D.) degree and advanced medical training through a 4-year residency program in pathology. Finally, in order to practice, the individual will need to complete state certification and be nationally certified by the American Board of Pathology. Correctly diagnosing patient samples takes many years of preparation. Other careers that use similar skills and training include anatomical, clinical, veterinary, forensic, and mortuary pathology.

○ Logistics & Reflection

Accurately diagnosing tissue on the basis of physical appearance alone is not an easy task. However, through this activity, students were largely successful in connecting physical concepts related to tissue appearance and making an accurate diagnosis. In the students' responses, 86% correctly gave sound scientific reasons for their diagnosis and, impressively, 70% gave the exact correct diagnosis. Students were fully successful in the main purpose of the activity, gaining knowledge of the differences between cancer and normal cells: each of them (100%) gave three accurate examples contrasting cancer versus normal cells in an open-ended post-session examination. Students still struggled with assessment questions that were more research driven and not explicitly given in the online presentation or lecture. Student groups worked well for this activity, with each group having access to a computer to take full advantage of the research time. As part of the activity, the students were asked to explain and rationalize their diagnosis. This prevented groups from merely guessing at the pathologically correct diagnosis. This activity requires students to utilize technology and information given to provide an answer that is backed by scientific evidence. The entire activity was completed in 3 days (50-minute classes), as outlined in Table 5. To extend this activity, you could apply its approach to any number of pathological diseases. Additional topics that the students could examine for deeper learning include predicting the stage of the life cycle of the patient, cancer subtypes, and hormonal impact on cancer growth. We have provided a presentation of additional patient slides, "Becoming a Pathologist: Additional Unknown Samples" (see Links below), that can be used to extend this activity. The activity could also be generalized for younger groups (middle school or introductory high school biology) by lightening the preparation presentation and focusing less on the "how" and more on the physical differences between the cellular structures of a cancer versus a normal cell.

Students were engaged in the material because it centered on them as pseudo-professionals (i.e., pathologists for a day). The presentation of new material challenged the students to go beyond the normal walls of their school and tackle a difficult task that is relevant in today's society, which gave them confidence and inspired some to go further. Overall, this simple activity allowed students to see what skills pathologists need to accurately diagnose patients, forced them to use and cultivate their critical-thinking skills, and challenged them to think beyond the course and put themselves in a real-world profession. Thus, it was beyond successful.

○ Student Profile

This investigation was conducted in the senior-level Biomedical Interventions high school class, a Project Lead the Way course designed to prepare students for careers in health care and biological science. Students did not have experience or training with pathology or breast cancer prior to the activity.

Table 5. Outline of interactive laboratory.

Day	Activity
Day 1	Becoming a Pathologist: Training & Becoming a Pathologist: Diagnosing Breast Cancer Introduction
Day 2	Becoming a Pathologist: Diagnosing Breast Cancer and Handout no. 1
Day 3	Becoming a Pathologist: Diagnosing Breast Cancer and Handout no. 2

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Links

Becoming A Pathologist Presentations: Training, Diagnosing Breast Cancer, and Additional Unknown Samples

http://www.gk12-iupui.org/lessons/lessonplans.html#dialog

American Board of Pathology

http://www.abpath.org

Project Lead the Way

http://www.pltw.org

References

Bybee, R.W., Ed. (2002). *Learning Science and the Science of Learning.* Arlington, VA: NSTA Press.

Eheman, C., Henley, S.J., Ballard-Barbash, R., Jacobs, E.J., Schymura, M.J., Noone, A.M. & others. (2012). Annual report to the nation on the status of cancer, 1975–2008, featuring cancers associated with excess weight and lack of sufficient physical activity. *Cancer*, *118*, 2338–2366.

Hussein, M.R. & Hassan, H.I. (2006). Analysis of the mononuclear inflammatory cell infiltrate in the normal breast, benign proliferative breast disease, *in situ* and infiltrating ductal breast carcinomas: preliminary observations. *Journal of Clinical Pathology*, *59*, 972–977.

Kumar, V., Abbas, A.K., Fausto, N., Robbins, S.L. & Cotran, R.S. (2005). *Robbins and Cotran Pathologic Basis of Disease, 7th Ed.* (pp. 4–7 and 1120–1151). Philadelphia, PA: Elsevier.

National Cancer Institute. (2012). Cancer Trends Progress Report – 2011/2012 Update. U.S. National Institutes of Health, Division of Cancer Control and Population Sciences, Bethesda, MD. [Online.] Available at http://progressreport.cancer.gov.

Polyak, K. & Kalluri, R. (2010). The role of the microenvironment in mammary gland development and cancer. *Cold Spring Harbor Perspectives in Biology*, *2*(11), a003244.

Ufnar, J.A., Kuner, S. & Shepherd, V.L. (2012). Moving beyond GK–12. *CBE Life Sciences Education*, *11*, 239–247.

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